MedQA Answers and Explanations

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Question 2

Two weeks after undergoing an emergency cardiac catherization with stenting for unstable angina pectoris, a 61-year-old man has decreased urinary output and malaise. He has type 2 diabetes mellitus and osteoarthritis of the hips. Prior to admission, his medications were insulin and naproxen. He was also started on aspirin, clopidogrel, and metoprolol after the coronary intervention. His temperature is 38°C (100.4°F), pulse is 93/min, and blood pressure is 125/85 mm Hg. Examination shows mottled, reticulated purplish discoloration of the feet. Laboratory studies show:
Hemoglobin count 14 g/dL
Leukocyte count 16,400/mm3
Segmented neutrophils 56%
Eosinophils 11%
Lymphocytes 31%
Monocytes 2%
Platelet count 260,000/mm3
Erythrocyte sedimentation rate 68 mm/h
Serum
Urea nitrogen 25 mg/dL
Creatinine 4.2 mg/dL
Renal biopsy shows intravascular spindle-shaped vacuoles. Which of the following is the most likely cause of this patient's symptoms?

Answer Choices:

(A) Renal papillary necrosis
(B) Cholesterol embolization
(C) Eosinophilic granulomatosis with polyangiitis
(D) Polyarteritis nodosa

Correct Answer:

(B)

OpenEvidence Response:

> **(B)** ✓

OpenEvidence Link: https://openevidence.com/ask/5f4e9acf-c010-45b4-a5ab-31685791e1f1

OpenEvidence Explanation

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The answer is **B. Cholesterol embolization**.

This presentation is classic for **cholesterol crystal embolization syndrome** (atheroembolic renal disease), which occurs when atheromatous plaques in the aorta are disrupted during vascular procedures such as cardiac catheterization, releasing cholesterol crystals that embolize to small arteries in the kidneys, skin, and other organs.[1]

The key features pointing to this diagnosis include:

- **Precipitating event**: Cardiac catheterization 2 weeks prior — the typical latency for subacute cholesterol embolization is days to weeks[2][3]
- **Renal failure**: Elevated creatinine (4.2 mg/dL) with decreased urine output, reflecting small-vessel occlusion in the kidneys
- **Skin findings**: Mottled, reticulated purplish discoloration of the feet ("livedo reticularis" / "blue toe syndrome") — a hallmark of distal cholesterol embolization[4]
- **Eosinophilia** (11%): A characteristic laboratory finding that raises suspicion for this diagnosis[1][4]
- **Elevated ESR** (68 mm/h) and low-grade fever: Reflecting the systemic inflammatory response to cholesterol crystals
- **Renal biopsy showing intravascular spindle-shaped vacuoles**: These represent **cholesterol clefts** — biconvex, needle-shaped spaces left behind

after cholesterol crystals dissolve during tissue processing, which is the pathognomonic histologic finding[2]

The typical at-risk patient is a **man older than 60 with known atherosclerotic disease** presenting with the classic triad of a precipitating event, acute/subacute renal failure, and peripheral skin findings.[1][2]

Why not the other options:

- **Renal papillary necrosis** (A): Associated with NSAID use and diabetes but would not explain eosinophilia, livedo reticularis, or cholesterol clefts on biopsy.
- **Eosinophilic granulomatosis with polyangiitis (EGPA)** (C): Requires asthma, marked hypereosinophilia, and pauci-immune necrotizing glomerulonephritis on biopsy — none of which are present here.[5]
- **Polyarteritis nodosa** (D): Affects medium-sized arteries with fibrinoid necrosis and microaneurysms, not intravascular cholesterol clefts, and lacks the temporal relationship to catheterization.

Would you like to explore the management strategies and prognosis for cholesterol embolization syndrome, including the role of statins and supportive care?

References

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Question 4

A 35-year-old man comes to the physician because of itchy, watery eyes for the past week. He has also been sneezing multiple times a day during this period. He had a similar episode 1 year ago around springtime. He has iron deficiency anemia and ankylosing spondylitis. Current medications include ferrous sulfate, artificial tear drops, and indomethacin. He works as an elementary school teacher. His vital signs are within normal limits. Visual acuity is 20/20 without correction. Physical examination shows bilateral conjunctival injection with watery discharge. The pupils are 3 mm, equal, and reactive to light. Examination of the anterior chamber of the eye is unremarkable. Which of the following is the most appropriate treatment?

Answer Choices:

(A) Erythromycin ointment
(B) Ketotifen eye drops
(C) Warm compresses
(D) Fluorometholone eye drops

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

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OpenEvidence Explanation

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The answer is **B. Ketotifen eye drops**.

This patient presents with classic **seasonal allergic conjunctivitis**: bilateral itchy, watery eyes with sneezing, conjunctival injection with watery discharge, a recurrent springtime pattern, normal visual acuity, and an unremarkable anterior chamber exam. **Topical antihistamines with mast cell–stabilizing activity (dual-activity agents) are the standard of care** for allergic conjunctivitis.[1]

Ketotifen is a dual-activity agent that blocks histamine H1 receptors and stabilizes mast cells, making it an ideal first-line treatment.[2][3] It has been shown to significantly reduce ocular itching and tearing compared to placebo.[4][5]

Why the other options are incorrect:

- **A. Erythromycin ointment** – Used for bacterial conjunctivitis, which typically presents with purulent (not watery) discharge and is more common in children. This patient has no features of bacterial infection.[1][6]
- **C. Warm compresses** – Appropriate for blepharitis or hordeolum/chalazion, not allergic conjunctivitis. Cold compresses (not warm) may provide symptomatic relief in allergic conjunctivitis through vasoconstriction.[1]
- **D. Fluorometholone eye drops** – A topical corticosteroid, which is reserved as second-line therapy for cases refractory to antihistamines/mast cell stabilizers. Steroids carry risks of cataract formation and increased intraocular pressure and should be used only for short courses (7–10 days) with ophthalmology involvement.[1][7]

Would you like to explore the comparative efficacy of different dual-activity topical agents (e.g., olopatadine vs. ketotifen) for seasonal allergic conjunctivitis?

Relevant images

(CONTENT OMITTED)

References

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Question 7

A 65-year-old man is brought to the emergency department 30 minutes after the onset of acute chest pain. He has hypertension and asthma. Current medications include atorvastatin, lisinopril, and an albuterol inhaler. He appears pale and diaphoretic. His pulse is 114/min and blood pressure is 130/88 mm Hg. An ECG shows ST-segment depressions in leads II, III, and aVF. Laboratory studies show an increased serum troponin T concentration. The patient is treated for acute coronary syndrome and undergoes percutaneous transluminal coronary angioplasty. At the time of discharge, echocardiography shows a left ventricular ejection fraction of 58%. In addition to aspirin, which of the following drugs should be added to this patient's medication regimen?

Answer Choices:

(A) Nifedipine
(B) Enoxaparin
(C) Clopidogrel
(D) Spironolactone

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

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OpenEvidence Explanation

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The answer is **C. Clopidogrel**.

After ACS treated with PCI, **dual antiplatelet therapy (DAPT)** with aspirin plus a P2Y12 inhibitor is the standard of care at discharge. Among the answer choices, **clopidogrel** is the P2Y12 inhibitor that should be added to aspirin.[1][2][3]

The 2025 ACC/AHA ACS guidelines and prior iterations recommend DAPT for at least 12 months in patients with ACS who are not at high bleeding risk.[1][4] While ticagrelor and prasugrel are generally preferred over clopidogrel due to greater potency and more predictable platelet inhibition, clopidogrel remains a guideline-endorsed P2Y12 inhibitor option and is the correct answer among the choices listed.[2][3]

Why the other options are incorrect:

- **A. Nifedipine** — A dihydropyridine calcium channel blocker; short-acting dihydropyridines should be avoided post-ACS. Nifedipine can cause reflex tachycardia and is not part of standard post-ACS discharge therapy.[5]
- **B. Enoxaparin** — A low-molecular-weight heparin used during the acute phase of ACS management but is not continued at discharge after successful PCI.
- **D. Spironolactone** — An aldosterone antagonist indicated post-MI only in patients with LVEF ≤40% and heart failure or diabetes. This patient's LVEF is 58%, so spironolactone is not indicated.[5]

Notably, this patient has asthma, which is a relative contraindication to beta-blockers (another standard post-ACS medication) — but that was not among the answer choices. The key discharge medication to add from the options provided is clopidogrel for DAPT.

Would you like to explore the evidence comparing clopidogrel, ticagrelor, and prasugrel in terms of efficacy and bleeding risk after PCI for ACS?

Relevant images

(CONTENT OMITTED)

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Question 8

A 37-year-old-woman presents to her primary care physician requesting a new form of birth control. She has been utilizing oral contraceptive pills (OCPs) for the past 8 years, but asks to switch to an intrauterine device (IUD). Her vital signs are: blood pressure 118/78 mm Hg, pulse 73/min and respiratory rate 16/min. She is afebrile. Physical examination is within normal limits. Which of the following past medical history statements would make copper IUD placement contraindicated in this patient?

> **Answer Choices:**
>
> (A) A history of stroke or venous thromboembolism
> (B) Active or recurrent pelvic inflammatory disease (PID)
> (C) Past medical history of breast cancer
> (D) Known liver neoplasm

> **Correct Answer:**
>
> **(B)**
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> **OpenEvidence Response:**
>
> **(B)** ✓

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OpenEvidence Explanation

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The answer is **B. Active or recurrent pelvic inflammatory disease (PID)**.

Active PID is a contraindication to copper IUD placement. The FDA-approved labeling for ParaGard (copper IUD) explicitly lists acute PID as a contraindication.[1] The U.S. Medical Eligibility Criteria (US MEC) assigns a **Category 4** (unacceptable health risk) to IUD initiation in the setting of active PID.[2] The AAP guidelines, adapted from the US MEC, confirm that active pelvic infection — including PID, purulent cervicitis, and active gonorrhea/chlamydia — is an absolute contraindication to both copper and levonorgestrel IUD placement.[3]

The other options are not contraindications to the copper IUD specifically:

- **A. History of stroke or VTE** — The copper IUD is nonhormonal and carries no increased risk of thromboembolism. The US MEC assigns a **Category 1** (no restriction) for copper IUD use in women with a history of DVT/PE not on anticoagulants. The AHA also notes that copper IUDs are safe for all cardiac conditions with no increased thromboembolism risk.[4][5][6]
- **C. Breast cancer** — Current breast cancer is a contraindication to the **LNG-IUD** (hormonal) and the subdermal implant, but it is explicitly **not contraindicated** for the copper IUD, which has no hormonal component.[3][7]
- **D. Known liver neoplasm** — Liver neoplasms are a concern with estrogen-containing contraceptives (Category 4 for CHCs). The copper IUD, being nonhormonal, is not contraindicated in this setting.[8][9]

This question highlights a key clinical distinction: the copper IUD is a nonhormonal method, so contraindications related to hormonal effects (thromboembolism, breast cancer, liver tumors) do not apply. Its contraindications are primarily related to **uterine/pelvic factors** — active infection, uterine cavity distortion, Wilson disease, and copper hypersensitivity.[1][10]

Would you like to explore the specific clinical scenarios in which an IUD can be retained versus must be removed when PID develops after insertion?

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Question 10

A 24-year-old G2P1 woman at 39 weeks' gestation presents to the emergency department complaining of painful contractions occurring every 10 minutes for the past 2 hours, consistent with latent labor. She says she has not experienced vaginal discharge, bleeding, or fluid leakage, and is currently taking no medications. On physical examination, her blood pressure is 110/70 mm Hg, heart rate is 86/min, and temperature is 37.6°C (99.7°F). She has had little prenatal care and uses condoms inconsistently. Her sexually transmitted infections status is unknown. As part of the patient's workup, she undergoes a series of rapid screening tests that result in the administration of zidovudine during delivery. The infant is also given zidovudine to reduce the risk of transmission. A confirmatory test is then performed in the mother to confirm the diagnosis of HIV. Which of the following is most true about the confirmatory test?

Answer Choices:

(A) It is a Southwestern blot, identifying the presence of DNA-binding proteins
(B) It is a Northern blot, identifying the presence of RNA
(C) It is a Northern blot, identifying the presence of DNA
(D) It is an HIV-1/HIV2 antibody differentiation immunoassay

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/a84fb968-3bba-435f-847a-d8c286a8d619

OpenEvidence Explanation

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The correct answer is **D. It is an HIV-1/HIV-2 antibody differentiation immunoassay**.

In this scenario, a woman with unknown HIV status presents in labor and undergoes rapid point-of-care HIV screening, which is reactive, prompting intrapartum zidovudine prophylaxis. Per the current CDC-recommended HIV testing algorithm, the **confirmatory (supplemental) test** following a reactive initial screening is an **HIV-1/HIV-2 antibody differentiation immunoassay**, which distinguishes between HIV-1 and HIV-2 antibodies.[1][2] This has replaced the Western blot, which is no longer recommended due to its subjectivity, labor intensity, and limited accessibility.[2]

Why the other options are incorrect:

- **A (Southwestern blot):** This is a laboratory technique used to identify DNA-binding proteins (e.g., transcription factors) and has no role in HIV diagnosis.
- **B (Northern blot identifying RNA):** While a Northern blot does detect RNA, it is a research technique for gene expression analysis and is not used clinically for HIV confirmation.
- **C (Northern blot identifying DNA):** This is doubly incorrect — Northern blots detect RNA, not DNA (Southern blots detect DNA), and neither is used for HIV confirmation.

Notably, the Western blot — historically the gold standard confirmatory test — was itself an immunochromatographic assay that detected antibodies to individual HIV proteins (e.g., p24, gp41, gp120/160), not a Northern or Southwestern blot.[3][4] The current algorithm replaces it with the antibody differentiation immunoassay, which offers faster turnaround, less subjectivity, and the ability to distinguish HIV-1 from HIV-2, which is clinically important because monitoring and therapy differ between the two.[1][2]

Would you like to explore the specific management algorithm for a newborn exposed to HIV during delivery, including the recommended antiretroviral prophylaxis regimen?

Relevant images

(CONTENT OMITTED)

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Question 13

A 47-year-old executive schedules an appointment his physician for a routine medical check-up. He currently has no complaints and claims to be “as fit as a fiddle.” The physical examination findings are unremarkable, except for a mid-systolic murmur heard in the 2nd left intercostal space that radiates to the carotids on auscultation. The physician instructs the patient to stand from a supine position with the stethoscope still placed on his chest. Which of the following changes would occur with this maneuver?

Answer Choices:

(A) An increase in right atrial pressure
(B) An increase in pulmonary capillary wedge pressure
(C) A reduction in the slope of the pacemaker potential
(D) A reduction in diastolic filling time

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/d5c2972c-075c-4bd6-b119-de3242e4d4fd

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OpenEvidence Explanation

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The correct answer is **D. A reduction in diastolic filling time**.

The clinical scenario describes a mid-systolic murmur at the 2nd left intercostal space radiating to the carotids, consistent with **aortic stenosis** (or possibly pulmonic stenosis/aortic sclerosis).[1][2] The question asks what happens physiologically when the patient stands from a supine position.

Hemodynamic effects of standing: Upon standing, approximately 500 mL of blood shifts from the chest to the venous capacitance system below the diaphragm due to gravity, resulting in decreased venous return, reduced central blood volume, and decreased ventricular preload.[3] This triggers a **baroreceptor-mediated reflex increase in heart rate** (approximately 20%) and sympathetic activation to compensate for the drop in stroke volume.[4]

Why each answer is correct or incorrect:

- **A. Increase in right atrial pressure** — Incorrect. Standing causes venous pooling in the lower extremities, which *decreases* right atrial pressure.[5]
- **B. Increase in pulmonary capillary wedge pressure** — Incorrect. Reduced venous return leads to *decreased* PCWP upon standing.[5]
- **C. Reduction in the slope of the pacemaker potential** — Incorrect. The compensatory sympathetic response to standing *increases* the slope of phase 4 (pacemaker) depolarization in the SA node, which is how heart rate increases. A reduction in slope would slow the heart rate, which is the opposite of what occurs.
- **D. Reduction in diastolic filling time — Correct.** The reflex tachycardia triggered by standing shortens the cardiac cycle, and diastolic filling time is disproportionately reduced as heart rate increases. This is the expected physiologic consequence of the baroreceptor-mediated increase in heart rate upon assuming an upright posture.[4]

Would you like to explore how dynamic auscultation maneuvers can help differentiate aortic stenosis from hypertrophic obstructive cardiomyopathy at the bedside?

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Question 17

A 3-month-old boy is brought the emergency department by his parents after an episode of cyanosis and muscle hypotonia that resolved after 2 minutes. Diagnostic evaluation fails to discover an exact etiology of the boy's symptoms and the episode is classified as a brief resolved unexplained event (BRUE). The risk profile for BRUE in infants remains largely unknown. The pediatrician who saw the boy in the emergency department is trying to identify risk factors for BRUE. She is aware of several confounders, including age, socioeconomic background, and family history of medical illness. She recruits 75 infants under 1 year of age with BRUE and 75 infants without BRUE of the same age, socioeconomic background, and family history of medical illness. She then compares the two groups with regard to history of feeding problems and history of recent upper respiratory infection. Which of the following methods was conducted to control confounding bias in the study?

Answer Choices:

(A) Blinding
(B) Restriction
(C) Randomization
(D) Matching

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/81223368-d967-4e51-ac42-44fcd776d579

OpenEvidence Explanation

(CONTENT OMITTED)

The answer is **D. Matching**.

In this case-control study, the pediatrician controlled for confounding by selecting controls (infants without BRUE) who share the same **age, socioeconomic background, and family history of medical illness** as the cases (infants with BRUE). This technique is called **matching** — specifically, individual (or frequency) matching — and is one of the principal methods used to control confounding in observational studies, particularly case-control designs.

Why the other options are incorrect:

- **A. Blinding** — Blinding is used to reduce information bias (observer or participant bias), not confounding. It involves concealing group allocation from participants, investigators, or assessors.
- **B. Restriction** — Restriction limits enrollment to a narrow range of a confounding variable (e.g., enrolling only males). Here, the study did not restrict enrollment to a single category of age or socioeconomic status; rather, it ensured that controls had the **same distribution** of these variables as cases.
- **C. Randomization** — Randomization is used in experimental studies (e.g., RCTs) to evenly distribute both known and unknown confounders across groups. This is an observational case-control study, so randomization was not performed.

The key distinction between **matching** and **restriction** is that matching selects controls to mirror the cases on specific confounding variables, whereas restriction excludes all participants who do not meet a single fixed criterion for the confounder. In this scenario, the investigator paired controls to cases based on multiple variables, which is the hallmark of matching.

Would you like to explore the differences between methods of controlling confounding at the design stage versus the analysis stage (e.g., stratification, multivariable regression)?

Question 18

A 29-year-old man presents to the emergency department due to central chest pain over the past 3 days which is constant and unrelated to exertion. The pain is sharp, severe, increases when lying down, and improves with leaning forward. The pain also radiates to his shoulders and neck. The patient has no past medical history. He has smoked 10 cigarettes per day for the past 7 years and occasionally drinks alcohol. He presents with vital signs: blood pressure 110/70 mm Hg, regular radial pulse of 95/min, and temperature 37.3°C (99.1°F). On physical exam, a scratching sound of to-and-from character is audible over the left sternal border at end-expiration with the patient leaning forward. His chest X-ray is normal and ECG is shown in the picture. Which of the following is the optimal therapy for this patient?

Answer Choices:

(A) Indomethacin +/- omeprazole
(B) Ibuprofen + colchicine +/- omeprazole
(C) Pericardiocentesis
(D) Pericardiectomy

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/4585655c-fd69-4a95-8695-0218e7580aab

OpenEvidence Explanation

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The answer is **B. Ibuprofen + colchicine +/- omeprazole**.

Practice Guideline

The American College of Cardiology recommends **high-dose aspirin or NSAID in combination with colchicine as first-line therapy for acute pericarditis**.[1] This patient presents with a classic case of acute pericarditis — sharp positional chest pain worsening when supine and improving with leaning forward, a pericardial friction rub (scratching to-and-fro sound at the left sternal border), and likely diffuse ST-segment elevation on ECG — meeting definitive diagnostic criteria (pleuritic chest pain plus ≥2 additional findings).[1]

First-line pharmacological treatment includes **dual anti-inflammatory therapy** with:[1]

- **NSAIDs** (e.g., ibuprofen 600–800 mg every 8 hours) starting at high dose and tapering after symptoms resolve and inflammatory markers normalize
- **Colchicine** for 3 months following a first episode (0.5 mg twice daily for patients >70 kg, or 0.5 mg once daily for ≤70 kg)
- **Proton pump inhibitors** (e.g., omeprazole) are often concomitantly prescribed for gastric protection

Exercise restriction for ≥1 month (maximal heart rate <100 bpm) until clinical remission is also recommended.[1] Corticosteroids should be restricted to cases refractory or intolerant to first-line therapies, and their early use in a first episode is associated with increased risk of recurrence.[1]

This presentation is textbook acute pericarditis in a young man without high-risk features (no large effusion, no tamponade, hemodynamically stable, low-grade fever). The ICAP trial demonstrated that adding colchicine to standard NSAID therapy reduced the rate of incessant or recurrent pericarditis from **37.5% to 16.7%** compared with placebo.[2] A JAMA review similarly concluded:

> "Treatment with NSAIDs and colchicine leads to a favorable prognosis in most patients, although 15% to 30% of patients develop recurrence."

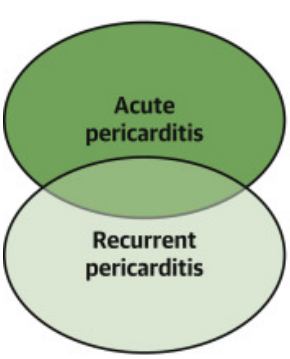
—Paul C. Cremer, MD, MS1 et al., Division of Cardiology, Bluhm Cardiovascular Institute, Departments of Medicine and Radiology, Northwestern University Feinberg School of Medicine, Chicago, Illinois and other institutions. Diagnosis, Risk Stratification, and Treatment of Pericarditis: A Review. JAMA. October 01, 2024.

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Why the other options are incorrect:

- **A (Indomethacin +/- omeprazole):** While indomethacin is an acceptable NSAID, this option omits colchicine, which is a critical component of first-line dual anti-inflammatory therapy and significantly reduces recurrence risk.[2][3]
- **C (Pericardiocentesis):** Reserved for cardiac tamponade or large effusions causing hemodynamic compromise. This patient has a normal chest X-ray and stable hemodynamics with no evidence of significant effusion.[4]
- **D (Pericardiectomy):** A surgical option reserved for refractory constrictive pericarditis or cases unresponsive to maximal medical therapy, not for an uncomplicated first episode of acute pericarditis.[1][4]

The following figure illustrates the treatment algorithm for acute and recurrent pericarditis, including dosing and duration of first-line therapies.



DRUG	DOSE	DURATION
Aspirin	750-1,000 mg every 8 h	1-2 weeks
Ibuprofen	600-800 mg every 8 h	1-2 weeks
Colchicine	0.5-1.2 mg in one or divided doses	3 months
Aspirin	750-1,000 mg every 8 h	Weeks-months
Ibuprofen	600-800 mg every 8 h	Weeks-months
Indomethacin	25-50 mg every 8 h	Weeks-months
Colchicine	0.5-1.2 mg in one or divided doses	At least 6 months
Prednisone	0.2-0.5 mg/kg/daily	Months
Anakinra	1-2 mg/kg/daily up to 100 mg/daily	Months
Rilonacept	320 mg once, then 160 mg weekly	Months
Azathioprine	1 mg/kg/daily up to 2-3 mg/kg/daily	Months
Methotrexate	10-15 mg weekly	Months
MMF	2,000 mg daily	Months
IVIGs	400-500 mg/kg/day	5 days

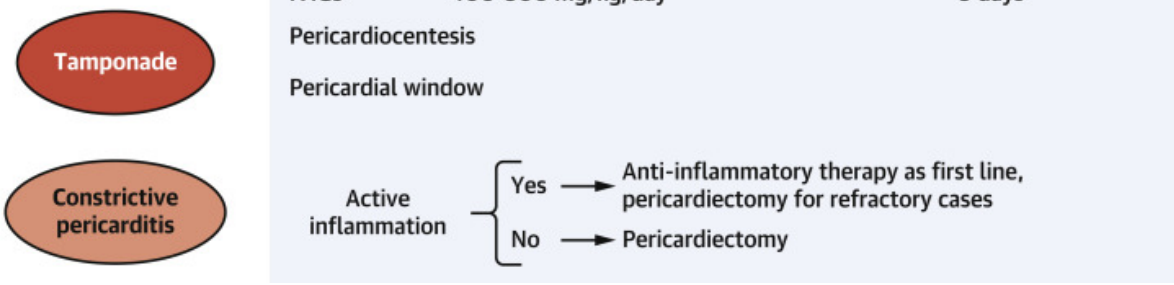


Figure 3. Treatment for Acute and Recurrent Pericarditis and Their Complications

Would you like to explore the risk stratification criteria that determine which patients with acute pericarditis require hospital admission versus outpatient management?

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Question 20

A 77-year-old woman presents to the emergency room with the complaints of fever, malaise, and night sweats. She recently observed an enlargement of her axillary lymph nodes, which she examines on a weekly basis. She has a remote history of breast cancer in her 60s that was treated with radiation and chemotherapy. She also reports a history of extensive travel to Africa and a 30-pack-year history of smoking. On physical exam, several axillary lymph nodes are palpable with a large non-tender palpable mass in her right axilla measuring 10 x 8 cm. Fine-needle aspiration demonstrates what the pathologist describes as a centroblastic and immunoblastic cell presence, suspicious for non-Hodgkin's lymphoma (NHL)–diffuse large B cell variant. Which of the following risk factors is responsible for this patient's condition?

Answer Choices:

(A) Travel to Africa
(B) Axillary lymph node involvement
(C) Previous radiation therapy
(D) Previous breast cancer

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/5c204cba-0b3d-4f73-a33e-eea71ad959cd

OpenEvidence Explanation

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The correct answer is **C. Previous radiation therapy**.

Previous radiation therapy is the risk factor most directly responsible for this patient's development of diffuse large B-cell lymphoma (DLBCL). This patient has a remote history of breast cancer treated with radiation and chemotherapy in her 60s, and she now presents approximately 15+ years later with NHL in the axillary region — a site within or adjacent to the prior radiation field.

Why radiation therapy is the key risk factor:

- A large SEER-based study of over 1.4 million cancer survivors found that NHL risk was significantly increased after initial radiotherapy for solid cancers (RR 1.13, 95% CI 1.06–1.20). Radiation exposure has been specifically associated with increased risk of mature B-cell lymphoma (RR 3.90 for 30 mGy vs. 0 mGy).[1][2]
- A systematic review and meta-analysis of over 522,000 breast cancer patients demonstrated that irradiated patients had an overall increased risk of second non-breast cancers (SIR 1.23), with risk progressively increasing over time and peaking at 10–15 years after treatment.[3]
- Secondary NHL risk increases after the first 5 years following completion of chemoradiotherapy and persists for more than three decades, reinforcing the need for long-term follow-up.[4]

Why the other options are less likely:

- **A. Travel to Africa** — While certain infections (e.g., EBV associated with Burkitt lymphoma, HIV) are linked to specific NHL subtypes, travel alone is not a recognized independent risk factor for DLBCL.[5][6]
- **B. Axillary lymph node involvement** — This describes the anatomic location of the disease, not a causative risk factor.
- **D. Previous breast cancer** — While breast cancer survivors do have a modestly elevated risk of second malignancies, this is largely attributable to the treatments received (radiation, chemotherapy) rather than the breast cancer diagnosis itself. The distinction is important: it is the radiation

therapy, not the cancer per se, that drives the secondary malignancy risk. [7][8]

Would you like to explore the recommended surveillance strategies for secondary malignancies in long-term breast cancer survivors who received radiation therapy?

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Question 22

A 30-year-old African American woman comes to the physician for the evaluation of a dry cough and chest discomfort for the past 3 days. During this period, the patient has had headaches, muscle aches, joint pain, fever, and chills. Ten days ago, she was hiking with her family in Mississippi. The patient has asthma that is treated with an albuterol inhaler. Her mother has a lung disease treated with methotrexate. The patient has smoked one pack of cigarettes daily for the past 10 years. Her temperature is 38°C (100.4°F). Physical examination shows slight wheezes throughout both lung fields. Laboratory studies and urinalysis are positive for polysaccharide antigen. Bronchoalveolar lavage using silver/PAS-staining shows macrophages filled with a dimorphic fungus with septate hyphae. Which of the following is the most likely cause of this patient's symptoms?

Answer Choices:

(A) Legionella pneumophila infection
(B) Pneumocystis pneumonia
(C) Histoplasma capsulatum infection
(D) Blastomyces dermatitidis infection

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/37307ee8-8d75-4542-9150-ecfb0abee0ac

OpenEvidence Explanation

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The correct answer is **C. Histoplasma capsulatum infection**.

This clinical presentation is classic for **acute pulmonary histoplasmosis**. Several key features point to this diagnosis:

- **Epidemiologic exposure**: The patient was hiking in **Mississippi**, which lies within the Mississippi River Valley — the region of highest endemicity for *Histoplasma capsulatum* in North America.[1]
- **Timeline**: Symptoms developed approximately **10 days after exposure**, consistent with the typical 2–3 week incubation period for histoplasmosis.[2]
- **Clinical presentation**: Dry cough, chest discomfort, fever, chills, headaches, myalgias, and arthralgias are characteristic of acute pulmonary histoplasmosis. Arthralgias in particular are a recognized feature.[2][3]
- **Positive polysaccharide antigen**: Histoplasma antigen (a polysaccharide) can be detected in urine and serum, with sensitivity up to 75–81% in immunocompetent patients with acute pulmonary infection.[4][5]
- **BAL findings**: On GMS (silver) and PAS staining, *Histoplasma capsulatum* appears as small (2–4 μm) oval yeast forms with single budding found inside macrophages. While the question describes "septate hyphae," *Histoplasma* is a **dimorphic fungus** that exists as a mold with septate hyphae in the environment (mycelial phase) and converts to yeast in tissue — the description of a "dimorphic fungus" within macrophages is the hallmark finding.[2]
- **Mother's lung disease treated with methotrexate**: This is a clue suggesting the mother likely has pulmonary sarcoidosis, which is important because sarcoidosis and histoplasmosis can mimic each other clinically and radiographically.[1]

Why not the other options?

- **A. Legionella pneumophila** — A bacterial infection, not a dimorphic fungus; would not show fungal elements on silver stain.

- **B. Pneumocystis pneumonia** — *Pneumocystis jirovecii* is not dimorphic and typically occurs in immunocompromised patients; it does not produce a positive polysaccharide antigen in urine.
- **D. Blastomyces dermatitidis** — Also a dimorphic fungus endemic to similar regions, but characteristically shows **broad-based budding yeast** (8–15 μm), not small intracellular yeast within macrophages. Blastomycosis more commonly presents with skin lesions and tends to have a longer, more indolent course.

Would you like to explore the treatment approach for acute pulmonary histoplasmosis in immunocompetent patients, including when antifungal therapy is indicated versus observation?

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Question 24

A 6-year-old boy is brought to the emergency department by his mother for worsening wheezing and shortness of breath over the past day. He has not had a fever, cough, vomiting, or diarrhea. He has asthma and eczema. He uses a glucocorticoid inhaler and an albuterol inhaler but has missed his medications for the past week while on vacation. He appears uncomfortable. His temperature is 36°C (96.8°F), pulse is 120/min, respirations are 40/min, and blood pressure is 100/80. Expiratory and inspiratory wheezing is heard throughout both lung fields. There are moderate intercostal and subcostal retractions and a decreased inspiratory to expiratory ratio. Nebulized albuterol and ipratropium treatments and intravenous methylprednisolone are given in the emergency department for a presumed asthma exacerbation. One hour later, the child is limp and lethargic. Magnesium sulfate is administered. His temperature is 36°C (96.8°F), pulse is 150/min, respirations are 22/min, and blood pressure is 100/70. No wheezing is heard on repeat pulmonary examination. Which of the following is the most appropriate next step in management?

Answer Choices:

(A) Intubate with mechanical ventilation
(B) Perform needle thoracostomy at the 2nd intercostal space
(C) Perform bronchoscopy
(D) Provide additional dose of methylprednisolone

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/8d992da7-39a2-47c0-85d3-b4e38cb064ec

OpenEvidence Explanation

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The most appropriate next step is **A. Intubate with mechanical ventilation**.

This child is presenting with signs of **impending respiratory failure** despite maximal medical therapy. The key clinical findings that indicate this are:

- **Absent wheezing** ("silent chest") — this is an ominous sign in the context of a severe asthma exacerbation. Rather than indicating improvement, the disappearance of wheezing in a child who is now **limp and lethargic** reflects such severe airflow limitation that there is insufficient air movement to generate wheezing.[1]
- **Altered mental status** (limp, lethargic) — drowsiness, confusion, or lethargy in the setting of an asthma exacerbation is a sign of life-threatening severity and impending respiratory arrest.[1][2]
- **Decreased respiratory rate** (from 40 to 22/min) — in this context, the drop in respiratory rate is not a sign of improvement but rather of **respiratory muscle fatigue and impending respiratory failure**.
- **Persistent tachycardia** (150/min) despite treatment further supports ongoing physiologic distress.

The child has already received appropriate escalation therapy — nebulized albuterol, ipratropium, IV methylprednisolone, and magnesium sulfate — without clinical improvement.[3][4] Patients with altered mental status, exhaustion, or a silent chest should be considered for immediate intubation and ventilatory support.[5] Endotracheal intubation should not be delayed when clinical improvement is not achieved with conservative therapies.[4][6]

Why not the other options:

- **B. Needle thoracostomy** — There is no clinical evidence of tension pneumothorax (e.g., unilateral absent breath sounds, tracheal deviation, hypotension). The bilateral absence of wheezing is more consistent with severe bronchospasm and minimal air movement.

- **C. Bronchoscopy** — Not indicated in acute status asthmaticus; this would delay definitive airway management.
- **D. Additional methylprednisolone** — Steroids have already been administered and take hours to exert their anti-inflammatory effect. Additional dosing will not address the immediate respiratory failure.

Would you like to explore the ventilator management strategy and permissive hypercapnia approach recommended after intubation for pediatric status asthmaticus?

Relevant images

(CONTENT OMITTED)

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Question 26

A 3-year-old boy presents to the emergency department with a 'cough-like-a-seal bark' and a high-pitched inspiratory noise that is audible without a stethoscope. His mother reports that his cough has worsened over the last few hours. The patient's blood pressure is 118/78 mm Hg, pulse is 90/min, respiratory rate is 35/min, and temperature is 38.3°C (101.1°F). On physical examination, the boy is sitting and leaning forward in apparent respiratory distress with suprasternal and intercostal retractions. Auscultation reveals inspiratory stridor without wheezing. He has a frequent barking cough and a hoarse voice when he speaks. What is a chest X-ray likely to show?

Answer Choices:

(A) Increased interstitial markings
(B) Lobar consolidation in the lingual
(C) Thumbprint sign on the lateral image
(D) Steeple sign

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/8de4abc3-b2f6-4388-a3e6-147bdcd5e9c9

OpenEvidence Explanation

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The correct answer is **D. Steeple sign**.

This presentation — a 3-year-old with "seal-bark" cough, inspiratory stridor, hoarseness, low-grade fever, and suprasternal/intercostal retractions — is classic for **croup** (acute viral laryngotracheobronchitis). On an anteroposterior (AP) neck/chest radiograph, croup characteristically produces the **steeple sign**, which represents symmetric subglottic narrowing of the tracheal air column below the vocal cords, creating a tapered, church-steeple appearance.[1][2]

The following figure demonstrates this classic finding:

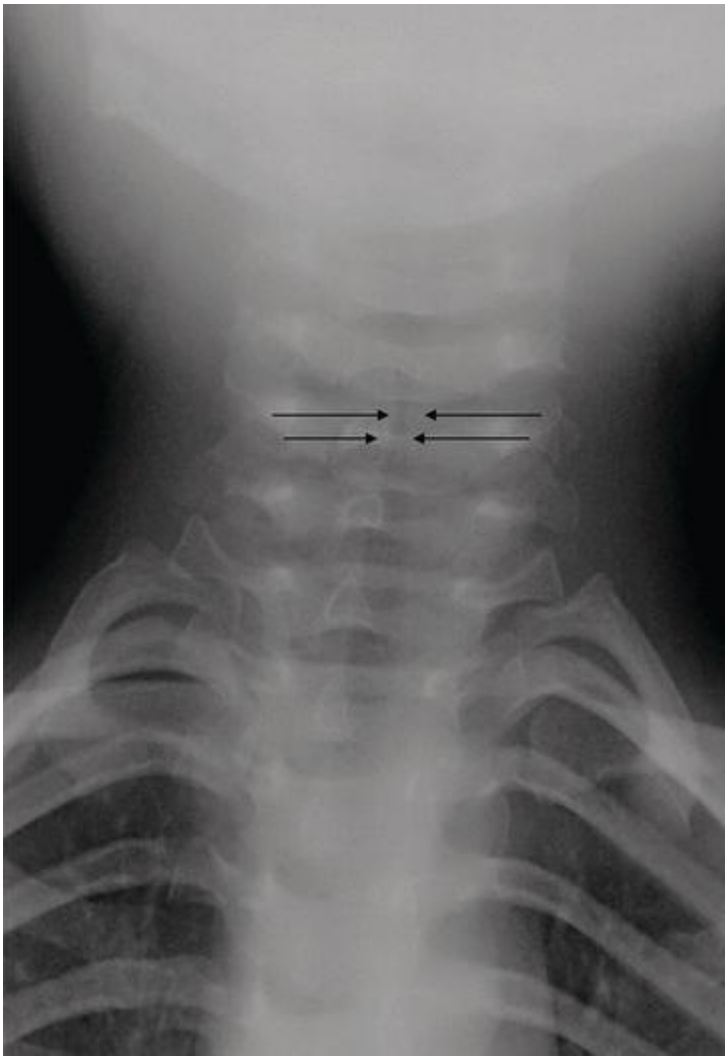


Figure 3. Anteroposterior radiograph of the neck show narrowing of the upper trachea that is most evident on the anteroposterior view (black arrows). This type of narrowing is typically present in croup and is known as the steeple sign on the anteroposterior radiograph given its similarity to a church steeple.

Why the other options are incorrect:

- **A. Increased interstitial markings** — This would suggest a lower respiratory process such as bronchiolitis or viral pneumonia, not an upper airway obstructive process like croup.
- **B. Lobar consolidation in the lingula** — This indicates bacterial pneumonia, which does not present with barking cough, stridor, and hoarseness.
- **C. Thumbprint sign on the lateral image** — The thumbprint sign on a lateral neck radiograph is the hallmark of **epiglottitis**, caused by a swollen epiglottis. Epiglottitis classically presents with drooling, dysphagia, and a toxic appearance — features absent here. Notably, the barking cough characteristic of croup is typically absent in epiglottitis.[4][5][6]

It is worth noting that while the steeple sign is the expected radiographic finding, it is present in only about 50% of croup cases, and radiography is generally not necessary when the clinical presentation is classic.[3][7]

Would you like to explore the evidence-based management of moderate-to-severe croup, including dexamethasone dosing and indications for nebulized epinephrine?

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Question 35

A 67-year-old man who was diagnosed with arthritis 16 years ago presents with right knee swelling and pain. His left knee was swollen a few weeks ago, but now with both joints affected, he has difficulty walking and feels frustrated. He also has back pain which makes it extremely difficult to move around and be active during the day. He says his pain significantly improves with rest. He also suffers from dandruff for which he uses special shampoos. Physical examination is notable for pitting of his nails. Which of the following is the most likely diagnosis?

Answer Choices:

(A) Psoriatic arthritis
(B) Arthritis mutilans
(C) Rheumatoid arthritis
(D) Mixed connective tissue disease

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/5b0f8511-9fab-45f6-98b8-a92bcc624854

OpenEvidence Explanation

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The correct answer is **A. Psoriatic arthritis**.

This patient presents with a classic constellation of findings pointing to psoriatic arthritis (PsA): asymmetric oligoarticular joint involvement (right knee, then left knee), **axial disease** (back pain), **nail pitting**, and **scalp psoriasis** (described as "dandruff" requiring special shampoos). These features align with the CASPAR classification criteria for PsA.[1][2]

Several key features support this diagnosis:

- **Nail pitting** is present in **80–90% of patients with PsA** and is a hallmark finding that distinguishes it from other arthritides. Nail dystrophy is one of the CASPAR criteria for classification.[1][3]
- **Scalp involvement** is a common site for psoriasis, and the patient's "dandruff" treated with special shampoos likely represents scalp psoriasis — a subtle presentation that can be overlooked. In approximately 85% of PsA patients, skin psoriasis precedes or occurs concurrently with arthritis.[3][4]
- **Asymmetric large joint involvement** with migratory pattern (left knee → bilateral knees) is characteristic of the oligoarticular subtype of PsA.[4]
- **Axial disease** (back pain) occurs in over 40% of PsA patients and usually accompanies peripheral arthritis.[4]

Why not the other options?

- **Arthritis mutilans (B)** is actually a severe, destructive *subtype* of PsA characterized by telescoping digits and marked osteolysis — not a separate diagnosis, and there is no description of such deformities here.[4]
- **Rheumatoid arthritis (C)** typically presents with symmetric small joint involvement (MCPs, PIPs) with sparing of DIPs, and is not associated with nail pitting or scalp psoriasis.[4]
- **Mixed connective tissue disease (D)** presents with overlapping features of SLE, scleroderma, and polymyositis (e.g., Raynaud phenomenon, sclerodactyly, anti-U1 RNP antibodies), none of which are described here.

The following figure illustrates the diverse clinical manifestations of psoriatic arthritis, including nail changes, joint involvement patterns, and enthesitis.



Figure 1. Clinical Features of Psoriatic Arthritis.

Used under license from The New England Journal of Medicine.

Would you like to explore the current treatment approach for psoriatic arthritis with axial and peripheral involvement based on the ACR/NPF guidelines?

References

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Question 38

A 53-year-old man with recurrent pancreatic adenocarcinoma is enrolled in a clinical trial for a novel chemotherapeutic agent that his physician believes may be beneficial to his condition. The novel drug was previously tested in a small population and is now undergoing a larger phase 3 trial in preparation for FDA approval. A dose-response trial had the following results:

10 mg dose - 6/59 patients demonstrated improvement
20 mg dose - 19/49 patients demonstrated improvement
30 mg dose - 26/53 patients demonstrated improvement
40 mg dose - 46/51 patients demonstrated improvement

The same trial also had the following safety profile:

20 mg dose - 5/49 patients had a treatment related adverse event
40 mg dose - 11/51 patients had a treatment related adverse event
60 mg dose - 15/42 patients had a treatment related adverse event
80 mg dose - 23/47 patients had a treatment related adverse event
100 mg dose - 47/52 patients had a treatment related adverse event

Based on this study, which of the following represents the most likely therapeutic index for this novel chemotherapeutic agent?

Answer Choices:

(A) 0.375
(B) 0.5
(C) 2.5
(D) 2.67

Correct Answer:

(D)

OpenEvidence Response:

> **(D)** ✓

OpenEvidence Link: https://openevidence.com/ask/a9189c72-fc34-4044-812f-52a329fbe9f0

OpenEvidence Explanation

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The answer is **D. 2.67**.

The **therapeutic index (TI)** is calculated as the ratio of the **TD50** (the dose at which 50% of patients experience a toxic/adverse effect) to the **ED50** (the dose at which 50% of patients demonstrate a therapeutic effect):[1][2]

$$TI = \frac{TD_{50}}{ED_{50}}$$

Determining ED50 from the efficacy data:

- 10 mg: 6/59 = ~10% improvement
- 20 mg: 19/49 = ~39% improvement
- 30 mg: 26/53 = ~49% improvement
- 40 mg: 46/51 = ~90% improvement

The 50% response rate falls between 30 mg and 40 mg. By linear interpolation, the ED50 is approximately **30 mg** (since 30 mg yields ~49%, which is essentially 50%).

Determining TD50 from the safety data:

- 20 mg: 5/49 = ~10% adverse events
- 40 mg: 11/51 = ~22% adverse events
- 60 mg: 15/42 = ~36% adverse events

- 80 mg: 23/47 = ~49% adverse events
- 100 mg: 47/52 = ~90% adverse events

The 50% adverse event rate falls between 80 mg and 100 mg. By linear interpolation, the TD50 is approximately **80 mg** (since 80 mg yields ~49%, which is essentially 50%).

Calculating the therapeutic index:

$$TI = \frac{TD_{50}}{ED_{50}} = \frac{80}{30} \approx 2.67$$

A therapeutic index of 2.67 indicates a relatively **narrow therapeutic window**, meaning the toxic dose is only about 2.67 times the effective dose. In pharmacology, drugs with a TI < 5 are generally considered to have a narrow therapeutic index, requiring careful dose monitoring.[2] This is consistent with many chemotherapeutic agents, which typically have narrow therapeutic windows due to their inherent cytotoxicity.

Would you like to explore how the therapeutic index influences dosing strategies and monitoring requirements for chemotherapeutic agents in clinical practice?

References

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Question 39

A 67-year-old male is seen by neurology after he was noticed to be speaking strangely by his family. After acute treatment with tissue plasminogen activator (tPA), the patient is able to recover most of his speech. Subsequent neurologic exam finds that the patient is fluent while speaking and is able to comprehend both one and two step instructions. Noticeably the patient remains unable to complete tasks involving verbal repetition. Residual damage to which of the following structures is most likely responsible for this patient's syndrome?

Answer Choices:

(A) Arcuate fasciculus
(B) Superior temporal gyrus
(C) Inferior frontal gyrus + superior temporal gyrus
(D) Arcuate fasciculus + inferior frontal gyrus + superior temporal gyrus

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/fd6a19b2-d292-4a86-9e41-5b011f74ecf3

OpenEvidence Explanation

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The answer is **A. Arcuate fasciculus**.

This patient presents with **conduction aphasia**, characterized by the classic triad of **fluent speech, intact comprehension, and impaired verbal repetition**. In the traditional Wernicke-Geschwind model, this syndrome results from damage to the **arcuate fasciculus**, the white matter tract that connects Wernicke's area (superior temporal gyrus, responsible for comprehension) to Broca's area (inferior frontal gyrus, responsible for speech production).[1]

The key reasoning for each answer choice:

- **A. Arcuate fasciculus** — Correct. Because both fluency (Broca's area intact) and comprehension (Wernicke's area intact) are preserved, the cortical language centers themselves are functioning. The isolated repetition deficit localizes to the connection between them — the arcuate fasciculus. DTI studies have confirmed that damage to the arcuate fasciculus correlates with impaired speech repetition, particularly sentence repetition.[2][3][4]
- **B. Superior temporal gyrus** — This would produce Wernicke's aphasia (fluent but with impaired comprehension), which does not match this presentation.
- **C. Inferior frontal gyrus + superior temporal gyrus** — Damage to both cortical areas would produce a global aphasia with impaired fluency and comprehension, inconsistent with this case.
- **D. Arcuate fasciculus + inferior frontal gyrus + superior temporal gyrus** — This would also produce global aphasia, not an isolated repetition deficit.

It is worth noting that more recent neuroimaging research has complicated the classical model, with some studies implicating cortical damage in the left temporoparietal junction (supramarginal gyrus, area Spt) rather than pure white matter disconnection as the primary substrate of conduction aphasia.[4][5] However, for standard examination purposes, the arcuate fasciculus remains the classic and expected answer.

Would you like to explore the differences between the classical disconnection model and modern cortical models of conduction aphasia?

References

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Question 40

A 27-year-old woman presents to the office with concerns about her long struggle with her physical appearance since adolescence. She says she has always been large and was constantly targeted by her classmates and coworkers for being so. Her main concern at the moment is her acne and unwanted facial hair on her upper lip, for which she often visits a local spa. She has tried numerous diet plans, exercise regimens, and cosmetic products with little to no effect. Recently, she underwent a glucose tolerance test that showed a plasma glucose level of 160 mg/dL (8.9 mmol/L) after 2 hours of a 75 g dose of oral glucose. She has a family history of type 2 diabetes mellitus and a menstrual cycle that occurs every 45 days. Her pulse is 72/min and the blood pressure is 138/80 mm Hg. On physical examination, her height is 160 cm (5 ft 3 in) and her weight is 85 kg (187 lb), and she has severe inflammatory acne over the cheeks and forehead and dark coarse hairs on the back. What is the most likely diagnosis of this patient?

Answer Choices:

(A) Hypothyroidism
(B) Idiopathic hirsutism
(C) Polycystic ovarian syndrome (PCOS)
(D) Ovarian hyperthecosis

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/ed4ad822-1c2f-477e-bb65-c87600b32313

OpenEvidence Explanation

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The most likely diagnosis is **C. Polycystic ovarian syndrome (PCOS)**.

This patient presents with a classic constellation of PCOS features that satisfy the **Rotterdam diagnostic criteria** (requiring ≥2 of 3: hyperandrogenism, ovulatory dysfunction, polycystic ovaries on ultrasound):[1][2]

1. **Clinical hyperandrogenism** — severe inflammatory acne and hirsutism (dark coarse hairs on the back, unwanted facial hair on the upper lip)[2]
2. **Ovulatory dysfunction** — oligomenorrhea with a 45-day menstrual cycle[2]

When both irregular menstrual cycles and hyperandrogenism are present, the 2023 International Evidence-based Guideline confirms that **ultrasound or AMH is not required** for diagnosis.[1][3]

The additional findings strongly support PCOS over the other options:

- **Obesity** (BMI ~33 kg/m²) and **impaired glucose tolerance** (2-hour OGTT of 160 mg/dL) are hallmark metabolic features of PCOS. Women with PCOS have an increased risk of IGT and type 2 diabetes regardless of age and BMI.[1][3]
- **Family history of type 2 diabetes** is a recognized risk factor commonly associated with PCOS.[4]
- **Onset since adolescence** with a chronic, gradual course is typical of PCOS.

Why not the other options:

- **A. Hypothyroidism** — Can cause menstrual irregularity and weight gain but does not cause hirsutism or severe acne. Should be excluded as part of the workup, but the clinical picture is not consistent.[5]
- **B. Idiopathic hirsutism** — Defined as hirsutism in **eumenorrheic** women without hyperandrogenemia or other evidence of an endocrine disorder. This patient has oligomenorrhea, acne, obesity, and impaired glucose tolerance — far beyond isolated hirsutism.[4]

- **D. Ovarian hyperthecosis** — Typically presents in **postmenopausal** women with more severe hyperandrogenism (virilization, markedly elevated testosterone). The 2023 guidelines specifically note ovarian hyperthecosis as a consideration "after menopause". This young woman's gradual-onset presentation is much more consistent with PCOS.[1][3]

Would you like to discuss the recommended metabolic workup or management approach for this patient?

References

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Question 41

A 43-year-old man presents with tingling and numbness of the lower limbs for 2 weeks. He also complains of persistent pain in his legs which is not relieved by over-the-counter analgesics. Past medical history is significant for type 2 diabetes mellitus for 2 years, inconsistently managed with metformin and glimepiride. On physical examination, there is decreased sensation to pain in both lower limbs, but deep tendon reflexes are intact. His vital signs include: blood pressure 122/84 mm Hg, temperature 36.7°C (98.1°F), and respiratory rate 10/min. His ankle-brachial pressure index (ABPI) on the right side is 1.1. His blood sugar analyses are as follows:
Fasting 141 mg/ dL
2 hours Post-Prandial 235 mg/ dL
HbA1c 8.1%
Which of the following is the best measure to prevent the progression of the symptoms present in this patient?

Answer Choices:

(A) Use of atorvastatin
(B) Femoro-Ileal artery bypass
(C) Strict blood glucose control
(D) Lower limb amputation

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/37f5cbc7-6d6a-46f6-8dab-6cb4c3317f7f

OpenEvidence Explanation

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The correct answer is **C. Strict blood glucose control**.

This patient presents with classic **diabetic peripheral neuropathy (DPN)** — symmetric tingling, numbness, and pain in the lower limbs with decreased pain sensation but intact deep tendon reflexes, in the setting of poorly controlled type 2 diabetes (HbA1c 8.1%). The normal ABPI of 1.1 effectively rules out peripheral arterial disease, making vascular interventions (femoro-ileal bypass, amputation) inappropriate. Atorvastatin addresses dyslipidemia but is not the primary intervention for preventing neuropathy progression.

Why the other options are incorrect:

- **A. Atorvastatin** — While lipid management may play a supportive role in multifactorial risk reduction, it is not the primary measure to prevent DPN progression.
- **B. Femoro-ileal artery bypass** — This is indicated for peripheral arterial disease with limb-threatening ischemia. The normal ABPI (1.1) excludes significant arterial disease.[1]
- **D. Lower limb amputation** — Amputation is reserved for non-salvageable limbs with gangrene, severe infection, or critical ischemia — none of which are present here.

Evidence supporting strict glycemic control:

The ADA 2026 Standards of Care recommend optimizing glucose management to **slow the progression of neuropathy** in type 2 diabetes.[1] The DCCT demonstrated 50–76% reductions in microvascular complications (including neuropathy) with intensive glycemic control in type 1 diabetes, and the UKPDS showed lower rates of microvascular complications with intensive control in type 2 diabetes.[2] The ACCORD trial also demonstrated a modest but significant DPN risk reduction with intensive glycemia intervention in type 2 diabetes.[3] This patient's inconsistent medication adherence and HbA1c of 8.1% represent a clear opportunity for improvement, as the greatest absolute risk reduction in

microvascular complications comes from lowering HbA1c from high to moderate levels.[2]

No disease-modifying pharmacotherapy currently exists for DPN; therefore, glycemic optimization remains the cornerstone of prevention and slowing progression.[1][4]

Would you like to explore the specific pharmacologic options for managing this patient's neuropathic pain alongside glycemic optimization?

Relevant images

(CONTENT OMITTED)

References

1. 12. Retinopathy, Neuropathy, and Foot Care: Standards of Care in Diabetes-2026. American Diabetes Association Professional Practice Committee for Diabetes*.. Diabetes Care. 2026;49(Supplement_1):S261-S276. doi:10.2337/dc26-S012.

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Question 42

A one-day-old male is evaluated in the hospital nursery for bilious vomiting. The patient has urinated multiple times since birth but has not yet passed meconium. He was born at 38 weeks gestation to a 36-year-old gravida 3 via vaginal delivery. The pregnancy was complicated by gestational diabetes. The patient's mother received routine prenatal care and declined first trimester screening. She subsequently underwent a quadruple screen at 15 weeks gestation that demonstrated decreased maternal serum alpha-fetoprotein (AFP), increased beta-hCG, decreased unconjugated estriol, and increased inhibin A. Her last ultrasound prior to onset of labor demonstrated an amniotic fluid index (AFI) of 28 cm. The patient's two older siblings are both healthy. The patient's temperature is 97.8°F (36.6°C), blood pressure is 58/37 mmHg, pulse is 166/min, and respirations are 38/min. On physical exam, the patient is in moderate distress. His abdomen is firm and distended with hypoactive bowel sounds.

Which of the following is the most likely etiology of this fetus's presentation?

Answer Choices:

(A) Duodenal atresia
(B) Meconium ileus
(C) Necrotizing enterocolitis
(D) Pyloric stenosis

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/e8b97e21-a9cf-431a-8d6f-9563abb7705b

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OpenEvidence Explanation

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The most likely etiology is **A. Duodenal atresia**.

This case presents a neonate with bilious vomiting, failure to pass meconium, abdominal distension, and polyhydramnios (AFI 28 cm) — all consistent with congenital intestinal obstruction. The critical unifying feature is the **quadruple screen pattern**: decreased AFP, increased beta-hCG, decreased unconjugated estriol, and increased inhibin A. This is the classic pattern for **trisomy 21 (Down syndrome)**.[1][2] The mother declined first-trimester screening, and this abnormal quad screen was not followed up with diagnostic testing.

Duodenal atresia is strongly associated with trisomy 21, occurring in approximately **30–40%** of affected neonates.[3][4][5] Polyhydramnios is a well-recognized prenatal finding in duodenal atresia due to impaired fetal swallowing of amniotic fluid, reported in 32–81% of cases.[5] The combination of bilious vomiting (indicating a post-ampullary obstruction, which accounts for ~85% of duodenal atresias), failure to pass meconium, and abdominal distension in a neonate with prenatal markers strongly suggestive of trisomy 21 makes duodenal atresia the most likely diagnosis.[3][5]

Why the other options are less likely:

- **Meconium ileus (B)** — Associated with cystic fibrosis, not trisomy 21. While it can present with bilious vomiting and failure to pass meconium, the quad screen findings pointing to trisomy 21 make this far less likely.[6]
- **Necrotizing enterocolitis (C)** — Primarily affects premature, low-birth-weight neonates and typically presents later (after initiation of enteral feeds). This is a near-term infant presenting on day one of life, making NEC unlikely.

- **Pyloric stenosis (D)** — Presents with nonbilious, projectile vomiting, typically at 2–6 weeks of age, not on day one of life.[7]

While the gestational diabetes raises consideration for **neonatal small left colon syndrome** (a functional obstruction associated with infants of diabetic mothers), this is not among the answer choices, and the quad screen findings strongly implicate trisomy 21 with duodenal atresia as the unifying diagnosis.[8][9]

Would you like to discuss the diagnostic workup (e.g., abdominal radiograph for the classic "double bubble" sign) or the surgical management of duodenal atresia in this clinical context?

References

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Question 46

A medical research study is evaluating an investigational novel drug (medication 1) compared with standard therapy (medication 2) in patients presenting to the emergency department with myocardial infarction (MI). The study enrolled a total of 3,000 subjects, 1,500 in each study arm. Follow-up was conducted at 45 days post-MI. The following are the results of the trial:

Endpoints Medication 1 Medication 2 P-Value

Primary: death from cardiac causes 134 210 0.03

Secondary: hyperkalemia 57 70 0.4

What is the number needed to treat (NNT) for the primary endpoint of death from cardiac causes? (Round to the nearest whole number.)

Answer Choices:

(A) 5
(B) 16
(C) 20
(D) 50

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/82ee03e5-7752-47ee-a162-4faaf5b40c7c

OpenEvidence Explanation

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The answer is **C. 20**.

Number Needed to Treat (NNT) is calculated as **1 / Absolute Risk Reduction (ARR)**.

Step-by-step:

1. **Event rate in the control group (Medication 2):** 210 / 1,500 = **14.0%**
2. **Event rate in the treatment group (Medication 1):** 134 / 1,500 = **8.9%**
3. **Absolute Risk Reduction (ARR):** 14.0% − 8.9% = **5.1%**
4. **NNT = 1 / ARR** = 1 / 0.0507 ≈ **19.7**, which rounds to **20**

This means approximately **20 patients** need to be treated with Medication 1 instead of Medication 2 to prevent one additional death from cardiac causes at 45 days. The result is statistically significant (p = 0.03).

Would you like to explore how NNT changes across different baseline risk populations, or how to interpret NNT alongside the number needed to harm (NNH) for the hyperkalemia endpoint?

Question 47

A 55-year-old man comes to the physician because of a 6-week history of tingling pain in the sole of his right foot when he raises it above chest level during exercises. He reports that he started exercising regularly 2 months ago and that his right calf cramps when he uses the incline feature on the treadmill, forcing him to take frequent breaks. The pain completely disappears after resting for a few minutes. He has an 8-year history of type 2 diabetes mellitus. He has smoked two packs of cigarettes daily for 34 years. His only medication is metformin. His pulse is 82/min, and blood pressure is 170/92 mm Hg. Straight leg raise test elicits pallor and tingling pain in the right foot. There is no pain in the back. His muscle strength is normal. Femoral pulses are palpable; right pedal pulses are absent. Which of the following is the most likely diagnosis?

Answer Choices:

(A) Femoropopliteal artery stenosis
(B) Acute thrombosis of right popliteal vein
(C) Lumbar spinal stenosis
(D) Aortoiliac artery stenosis

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/cb09be32-3f8a-4ddb-abf5-95a3f3c18110

OpenEvidence Explanation

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The most likely diagnosis is **A. Femoropopliteal artery stenosis**.

The key clinical features localizing the disease to the **femoropopliteal segment** (superficial femoral artery) are:

1. **Calf claudication** — exertional calf cramping on the treadmill that resolves within minutes of rest is the hallmark of superficial femoral artery disease. Calf claudication specifically results from disease in the superficial femoral artery, whereas hip, thigh, and buttock claudication occurs with aortoiliac disease.[1][2]

2. **Palpable femoral pulses with absent pedal pulses** — this pulse pattern localizes the obstruction to the femoropopliteal segment, distal to the femoral artery but proximal to the pedal vessels. In aortoiliac disease, the femoral pulses themselves would be diminished or absent.[1][3]

3. **Elevation pallor on straight leg raise** — pallor of the foot with leg elevation (Buerger's test) is a classic sign of peripheral artery disease indicating inadequate arterial perfusion, consistent with significant arterial stenosis.[4]

4. **No back pain** — this effectively rules out lumbar spinal stenosis, which typically presents with pain radiating from the low back and is relieved by lumbar flexion (e.g., sitting or leaning forward), not simply by rest. Neurogenic claudication from spinal stenosis is also worsened by standing and posture changes, unlike vascular claudication.[2][5][6][7]

Why the other options are less likely:

- **B. Acute popliteal vein thrombosis** — DVT presents with leg swelling, warmth, and pain at rest, not exertional claudication that resolves with rest. It would not cause elevation pallor or absent pedal pulses.

- **C. Lumbar spinal stenosis** — Absent pedal pulses and elevation pallor are vascular findings not explained by spinal stenosis. Additionally, there is no back pain, and symptoms are exercise-induced and quickly relieved by rest (vascular pattern) rather than posture-dependent.[5][6]

- **D. Aortoiliac stenosis** — Would present with buttock/thigh claudication and diminished or absent femoral pulses, neither of which is present here. [1][2][3]

The patient's strong risk factors — 68 pack-year smoking history, longstanding type 2 diabetes, and hypertension — are all major contributors to peripheral artery disease.[8]

Would you like to explore the recommended diagnostic workup with ankle-brachial index testing and the management approach for femoropopliteal PAD?

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Question 50

A 65-year-old male is treated for anal carcinoma with therapy including external beam radiation. How does radiation affect cancer cells?

Answer Choices:

(A) Induces the formation of thymidine dimers
(B) Induces the formation of disulfide bonds
(C) Induces deamination of cytosine
(D) Induces breaks in double-stranded DNA

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/88b123b7-f4b5-4495-b988-75e626cf7b8e

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OpenEvidence Explanation

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The correct answer is **D. Induces breaks in double-stranded DNA**.

Ionizing radiation used in external beam radiation therapy kills cancer cells primarily by inducing **DNA double-strand breaks (DSBs)**, which are the most

lethal form of radiation-induced DNA damage.[1][2] This occurs through two mechanisms:

- **Direct damage:** Radiation particles directly collide with DNA molecules, causing chemical alterations and structural breaks in both strands.[1][3]
- **Indirect damage:** Radiation ionizes water molecules surrounding DNA, generating reactive oxygen species (ROS) and hydroxyl radicals that subsequently damage DNA. This indirect mechanism accounts for approximately 60–70% of radiation-induced DNA damage.[1][4][5]

DSBs are particularly consequential because they are difficult to repair accurately. Even a single unrepaired DSB can trigger cell death.[2] Cells attempt repair via homologous recombination or nonhomologous end-joining, but erroneous repair leads to chromosomal aberrations, loss of genetic material, and mitotic catastrophe.[1][6][7]

The following figure illustrates the direct and indirect mechanisms of radiation-induced DNA damage and the resulting cellular fate decisions:

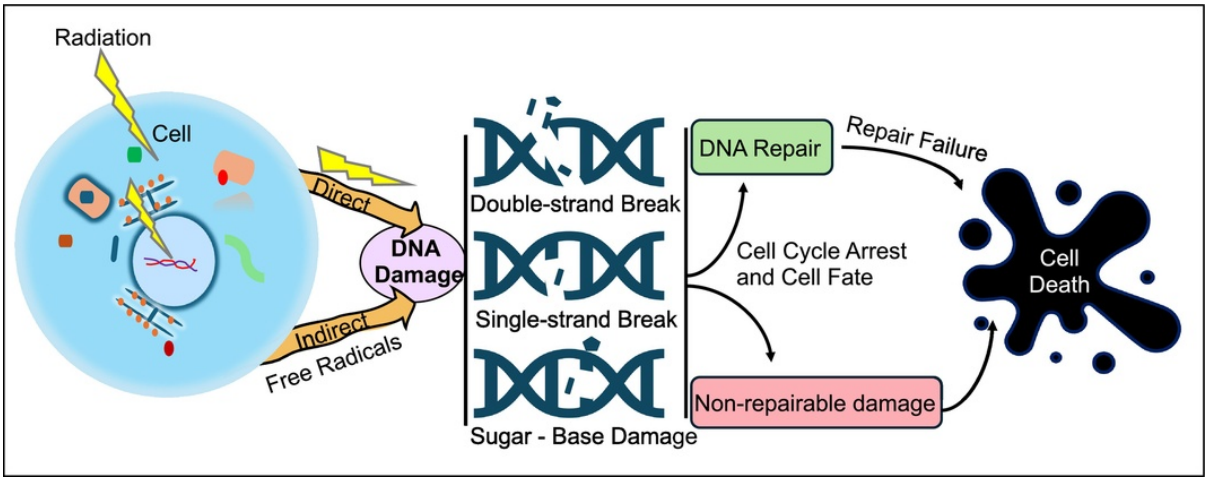


Figure 1. Ionizing radiation-induced DNA damage and cell fate. Ionizing radiation can promote DNA damage directly by radiation-induced DNA break, or indirectly via the generation of free radicals. Ionizing radiation promotes single-strand break, double-strand break, and base and sugar damage in DNA strands. This DNA damage triggers the cell to arrest its cycle, leading to a decision point: The cell may either initiate repair pathways or undergo cell death.

Why the other options are incorrect:

- **A (Thymidine dimers):** Thymidine (pyrimidine) dimers are characteristically caused by ultraviolet (UV) radiation, not ionizing radiation used in radiotherapy.

- **B (Disulfide bonds):** Disulfide bond formation is a protein chemistry phenomenon unrelated to the mechanism of radiation-induced cell killing.
- **C (Deamination of cytosine):** Spontaneous deamination of cytosine to uracil is an endogenous DNA lesion, not a primary effect of ionizing radiation.

Would you like to explore the specific chemoradiation regimens used for anal carcinoma and how concurrent chemotherapy enhances radiosensitivity?

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Question 51

A 56-year-old man with a history of hypertension presents to his physician with progressive fatigue and new onset muscle cramps. He has had no recent changes to his medication regimen, which includes hydrochlorothiazide, lisinopril, and amlodipine. His temperature is 98.0°F (36.7°C), blood pressure is 174/111 mmHg, pulse is 70/min, respirations are 12/min, and oxygen saturation is 98% on room air. The patient's cardiopulmonary and abdominal exams are unremarkable. Laboratory values are ordered as seen below.

Serum:
Na+: 138 mEq/L
Cl-: 100 mEq/L
K+: 3.3 mEq/L
HCO3-: 33 mEq/L
BUN: 20 mg/dL
Glucose: 129 mg/dL

What is the most likely underlying etiology of this patient's hypertension?

Answer Choices:

(A) Aldosterone excess
(B) Catecholamine-secreting mass
(C) Cortisol excess
(D) Impaired kidney perfusion

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/85503a98-cc55-4577-8b3a-bc67e88cf893

OpenEvidence Explanation

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The answer is **A. Aldosterone excess**.

This patient presents with the classic triad of **primary aldosteronism**: resistant hypertension (uncontrolled BP of 174/111 despite three antihypertensive agents), **hypokalemia** (K^+ 3.3 mEq/L), and **metabolic alkalosis** (HCO_3^- 33 mEq/L), along with fatigue and muscle cramps — all hallmark features of this condition.[1][2]

Why aldosterone excess fits best:

Aldosterone acts on the mineralocorticoid receptor in the distal nephron, stimulating sodium reabsorption via the epithelial sodium channel (ENaC) while driving potassium and hydrogen ion secretion into the tubular lumen.[3] This mechanism directly explains the hypokalemia, metabolic alkalosis, sodium retention, volume expansion, and hypertension seen in this patient. The 2025 ACC/AHA guidelines identify primary aldosteronism as a common cause of secondary hypertension (5–25% prevalence), with clinical indications for screening including resistant hypertension, hypokalemia (spontaneous or diuretic-induced), and muscle cramps or weakness.[4]

Why the other options are less likely:

- **B. Catecholamine-secreting mass (pheochromocytoma)** — Typically presents with paroxysmal hypertension, headache, sweating, palpitations, and tachycardia. This patient has a normal heart rate (70/min) and lacks episodic symptoms.[1][4]
- **C. Cortisol excess (Cushing syndrome)** — Can cause hypokalemia and hypertension, but is typically accompanied by central obesity, moon facies, striae, proximal muscle weakness, and more prominent hyperglycemia. The

prevalence is <0.1%, and the clinical presentation here lacks Cushingoid features.[1][5]

- **D. Impaired kidney perfusion (renovascular disease)** — Can cause resistant hypertension but does not characteristically produce hypokalemia with metabolic alkalosis unless secondary hyperaldosteronism develops. The BUN is normal, and there is no mention of abdominal bruits or flash pulmonary edema.[1][4]

Would you like to explore the recommended screening approach and confirmatory testing for primary aldosteronism, including the plasma aldosterone-to-renin ratio and its interpretation?

Relevant images

(CONTENT OMITTED)

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Question 52

A 65-year-old man comes to the physician because of a 1-week history of yellowish discoloration of his skin and generalized pruritus. Examination shows jaundice of the skin and scleral icterus. Urinalysis shows an elevated concentration of bilirubin and a low concentration of urobilinogen. Which of the following is the most likely underlying cause of these findings?

Answer Choices:

(A) Absent UDP-glucuronosyltransferase activity
(B) Increased hemoglobin breakdown
(C) Increased intestinal bilirubin reabsorption
(D) Defective hepatic bile excretion

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/136a0749-fdcb-4a9d-82b1-84957849e3b2

OpenEvidence Explanation

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The correct answer is **D. Defective hepatic bile excretion**.

The urinalysis findings are the key to this question: **elevated urine bilirubin** combined with **low urobilinogen** points to an obstructive or cholestatic process — that is, defective excretion of bile from the liver into the intestines.

Here is the reasoning:

- **Bilirubin in urine** indicates conjugated (direct) hyperbilirubinemia, since only conjugated bilirubin is water-soluble enough to be filtered by the kidneys.[1]
- **Low urobilinogen** indicates that conjugated bilirubin is not reaching the intestines, where bacteria normally convert it to urobilinogen. The absence of urobilinogen is characteristic of impaired bile flow (cholestasis/obstruction).[1][2]
- Together, these findings indicate that the liver is conjugating bilirubin normally, but bile excretion into the intestinal tract is impaired — consistent with **defective hepatic bile excretion** (either intrahepatic cholestasis or extrahepatic biliary obstruction).[1][3]

Why the other options are incorrect:

- **A. Absent UDP-glucuronosyltransferase activity** — This would cause unconjugated hyperbilirubinemia (as in Crigler-Najjar syndrome). Unconjugated bilirubin is not water-soluble and would not appear in the urine.[1][3]
- **B. Increased hemoglobin breakdown** — Hemolysis causes predominantly unconjugated hyperbilirubinemia with increased (not decreased) urobilinogen, since more bilirubin reaches the gut and is converted to urobilinogen.[2][3]
- **C. Increased intestinal bilirubin reabsorption** — This would increase enterohepatic circulation of bilirubin but would not produce the pattern of elevated urine bilirubin with low urobilinogen seen here.

The following figure illustrates the diagnostic approach to elevated bilirubin, showing how fractionation into conjugated versus unconjugated forms guides the differential diagnosis.

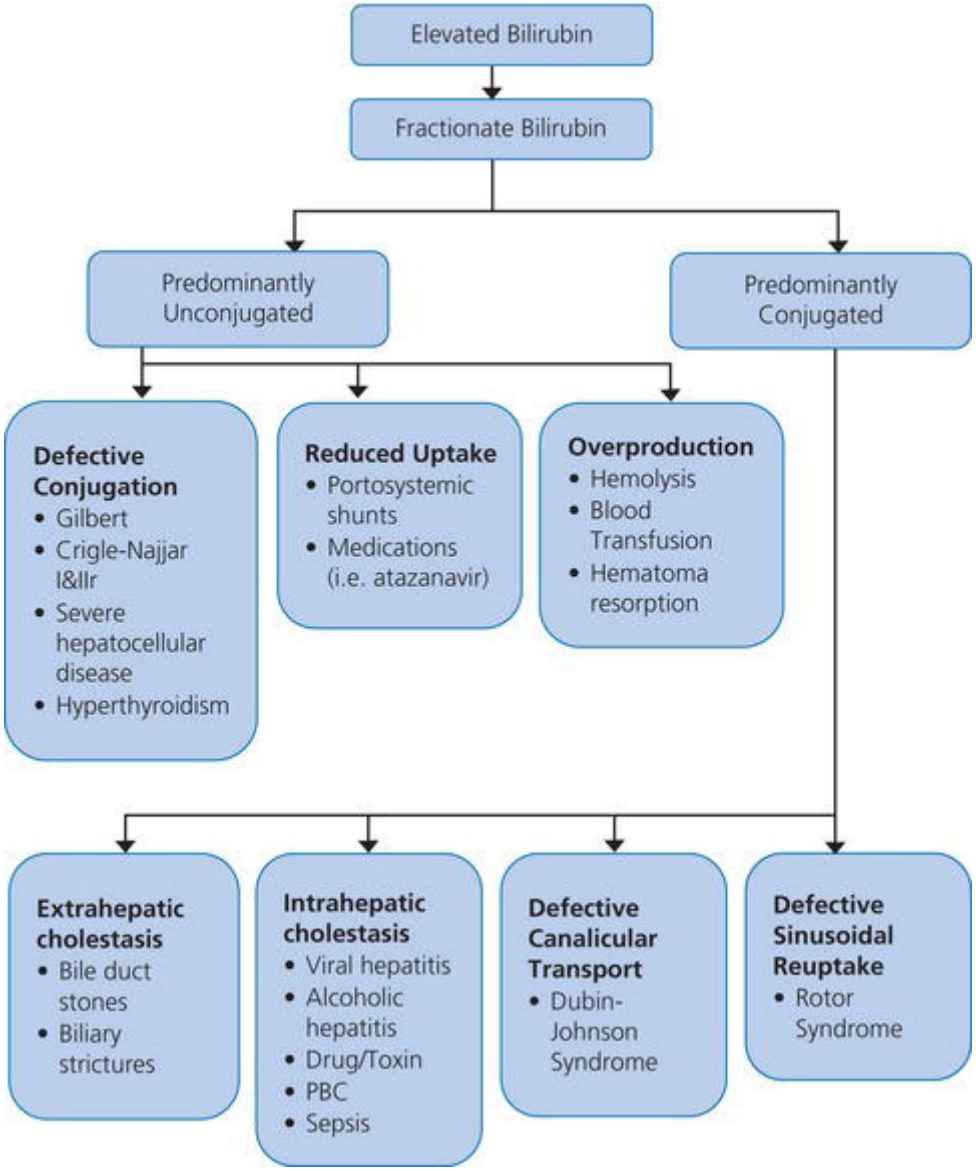


Figure 5. Diagnostic approach to elevated bilirubin. PBC, primary biliary cholangitis.

Would you like to explore the specific etiologies of obstructive jaundice in a 65-year-old man and the recommended diagnostic workup?

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Question 53

A 72-year-old woman is brought to the physician by her daughter because of a 6-month history of worsening short-term memory deficits and social withdrawal. Treatment with galantamine is initiated. Two weeks later, the patient develops vomiting, mild crampy abdominal pain, and watery, nonbloody diarrhea. Which of the following is the most appropriate pharmacotherapy?

Answer Choices:

(A) Bethanechol
(B) Metoclopramide
(C) Atropine
(D) Oxybutynin

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/6f0e6601-d41e-4dd7-b940-9175e06cd7a3

OpenEvidence Explanation

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The answer is **C. Atropine**.

Galantamine is an **acetylcholinesterase inhibitor** used for mild to moderate Alzheimer's dementia. By inhibiting acetylcholinesterase, it increases

acetylcholine levels at synapses, which produces therapeutic cognitive effects but also causes excessive cholinergic (muscarinic) stimulation as a side effect. The most common adverse reactions include **nausea, vomiting, diarrhea, and abdominal cramping** — all manifestations of parasympathetic overstimulation of the GI tract.[1][2]

Atropine, a muscarinic receptor antagonist (anticholinergic), directly counteracts these excessive cholinergic effects. The galantamine FDA label specifically identifies tertiary anticholinergics such as atropine as the antidote for cholinergic toxicity from galantamine.[1][2][3]

Why the other options are incorrect:

- **A. Bethanechol** — A muscarinic agonist (cholinomimetic) that would worsen the symptoms by further stimulating the parasympathetic nervous system.
- **B. Metoclopramide** — A prokinetic/antiemetic that acts on dopamine receptors; it does not address the underlying cholinergic mechanism and would further increase GI motility.
- **D. Oxybutynin** — While technically an antimuscarinic agent, it is selective for the bladder (M3 receptors) and is used for urinary incontinence, not for treating systemic cholinergic side effects like GI symptoms.

Would you like to explore the comparative side effect profiles and management strategies for the different cholinesterase inhibitors used in Alzheimer's disease (donepezil, rivastigmine, galantamine)?

References

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Question 54

A 61-year-old man with schizophrenia in a locked inpatient psychiatry unit was observed making an unusual smacking motion with his lips, pursing his mouth, and blinking excessively. These symptoms started slowly about 2 weeks ago and have become more pronounced, but they do not seem to bother the patient. He resides in an inpatient psychiatric facility where he has been successfully treated with haloperidol for the past several months. His physical exam and vitals are within normal limits. Which of the following accurately describes his symptoms?

Answer Choices:

(A) Tardive dyskinesia
(B) Acute dystonia
(C) Pseudoparkinsonism
(D) Palsy

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/fe6307b5-339f-42fe-8903-775c137b07d8

OpenEvidence Explanation

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The answer is **A. Tardive dyskinesia**.

This patient's presentation — **lip smacking, mouth pursing, and excessive blinking** with insidious onset during chronic haloperidol therapy — is classic for **tardive dyskinesia (TD)**. Several features of this case point specifically to TD:

- **Movement phenomenology**: Lip smacking, puckering/pursing of the lips, and rapid eye blinking are hallmark orofacial movements of TD. These repetitive, involuntary, purposeless movements are the most frequently described manifestation of classic TD.[1][2][3][4]
- **Insidious onset**: TD characteristically has a slow, insidious onset, with signs that are initially minimal and may escape notice except by a keen observer — consistent with the gradual worsening over 2 weeks described here.[1]
- **Temporal relationship to antipsychotic use**: The patient has been on haloperidol (a first-generation antipsychotic and potent D2 blocker) for several months. The DSM-5-TR requires at least 3 months of exposure (or 1 month in patients ≥60 years old, as in this case).[1]
- **Lack of patient distress**: TD is often not bothersome to the patient despite being noticeable to observers.[1]

Why the other options are incorrect:

- **B. Acute dystonia** presents with sustained muscle contractions (e.g., torticollis, oculogyric crisis, tongue protrusion) occurring acutely within **hours to days** of starting or increasing an antipsychotic — not after months of stable therapy.[1][4][5]
- **C. Pseudoparkinsonism (drug-induced parkinsonism)** manifests as bradykinesia, rigidity, and a rhythmic resting tremor (3–6 Hz), which are distinctly different from the choreiform/athetoid orofacial movements seen here. It also develops within weeks of initiating therapy, not after months.[1][6]
- **D. Palsy** refers to paralysis or weakness (e.g., Bell's palsy, cerebral palsy) and does not describe involuntary hyperkinetic movements.

Haloperidol, as a high-potency first-generation antipsychotic, carries a notably higher risk of TD compared to second-generation agents, with a prevalence of approximately **32%** among adults treated with first-generation drugs versus 13% with second-generation agents.[7]

Would you like to explore the current evidence on VMAT2 inhibitors (valbenazine, deutetrabenazine) for the treatment of tardive dyskinesia?

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Question 55

A 17-year-old football player with no significant past medical history, social history, or family history presents to his pediatrician with itching in his groin. He says this started during summer workouts leading up to this season. He denies having any rash anywhere else on his body. The blood pressure is 123/78 mm Hg, pulse is 67/min, respiratory rate is 15/min, and temperature is 38.1°C (98.7°F). Physical examination reveals an erythematous, well-demarcated patch with peripheral scale on the left thigh, pubic region, and perineum. There is no apparent scrotal involvement with the rash. How can you confirm the suspected diagnosis?

Answer Choices:

(A) KOH examination of lesion scrapings
(B) Nikolsky's sign on physical exam
(C) Gram stain of skin scrapings
(D) AFB stain of skin scrapings

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/9e1784fb-6eba-4083-bbe2-85b418ea1bc0

OpenEvidence Explanation

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The answer is **A. KOH examination of lesion scrapings**.

The clinical presentation — an erythematous, well-demarcated patch with peripheral scale in the groin, thigh, and perineum with **scrotal sparing** in a young athlete during summer — is classic for **tinea cruris** (jock itch), a dermatophyte infection. The diagnosis is confirmed by scraping the **leading edge** of the lesion and performing a **potassium hydroxide (KOH) preparation**, which dissolves keratin and allows visualization of fungal hyphae under microscopy.[1][2][3]

The following figure illustrates a typical presentation of tinea cruris with the characteristic scrotal sparing:



Figure 2. Tinea cruris. Reprinted with permission from Ely JW, Rosenfeld S, Seabury Stone M. Diagnosis and management of tinea infections. Am Fam Physician. 2014;90(10):705.

Why the other options are incorrect:

- **B. Nikolsky's sign** — This is elicited in blistering disorders (e.g., pemphigus vulgaris, Stevens-Johnson syndrome/TEN) where lateral pressure causes epidermal separation. It is not relevant to dermatophyte infections.
- **C. Gram stain** — This identifies bacteria, not fungi. Tinea cruris is caused by dermatophytes (most commonly Trichophyton rubrum), which are not visualized on Gram stain.

- **D. AFB stain** — This is used to detect acid-fast bacilli such as Mycobacterium species and has no role in diagnosing dermatophyte infections.

KOH preparation has a sensitivity of approximately **91–94%** for detecting dermatophytes in tinea cruris.[5] The IDSA and American College of Sports Medicine guidelines both support KOH preparation with microscopy as the standard confirmatory test for suspected dermatophyte infections.[1][3]

Would you like to explore the recommended topical and oral antifungal treatment regimens for tinea cruris in adolescent athletes, including return-to-sport clearance criteria?

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Question 56

An otherwise healthy 26-year-old man comes to the physician for medication counseling after recently being diagnosed with schizophrenia. Risperidone therapy is initiated. This patient is at increased risk for which of the following adverse effects?

Answer Choices:

(A) Agranulocytosis
(B) Shortened QT interval
(C) Gynecomastia
(D) Weight loss

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/cf6dbf3a-bfe3-4288-b6c2-877ac929c437

OpenEvidence Explanation

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The correct answer is **C. Gynecomastia**.

Risperidone is well known for causing **hyperprolactinemia** — more so than any other antipsychotic — due to its potent dopamine D2 receptor antagonism. The FDA label explicitly states that risperidone is "associated with higher levels of prolactin elevation than other antipsychotic agents," and that **galactorrhea,**

amenorrhea, gynecomastia, and impotence have been reported.[1] In men, hyperprolactinemia manifests as gynecomastia, erectile dysfunction, and impaired spermatogenesis.[2]

A case-control study of males aged 15–25 found that current risperidone users had approximately **four times the risk** of developing gynecomastia compared to non-users (RR = 3.91, 95% CI 2.01–7.62), with the risk rising to five-fold in those ≤18 years.[3] An analysis of the FAERS database found that risperidone accounted for **80.81% of all gynecomastia reports** among nervous system drugs, with a reporting odds ratio of 602.38.[4] The adjusted ROR for hyperprolactinemia with risperidone was 212, compared to 3.9–8.2 for other antipsychotics.[2]

The following figure illustrates the comparative adverse event profiles of commonly prescribed antipsychotics, highlighting risperidone's exceptionally high association with hyperprolactinemia.

	SGA					FGA
SMQ	Clozapine	Aripiprazole	Olanzapine	Quetiapine	Risperidone	Haloperidol
Accidents / injuries						
Agranulocytosis	2.0					
TdP / QT prolongation	2.7		5.7	6.3	3.2	6.8
Anticholinergic syndrome	4.1	2.4	16.2	14.9	13.0	15.2
Weight gain		5.9	10.1	5.5	12.1	9.8
Dyslipidaemia		2.0	9.3	6.8		
Hyperglycaemia			7.9	8.7		
Akathisia		45.2	18.3	7.9	14.4	28.7
Dyskinesia	2.6	23.5	8.5	10.0	12.9	20.7
Dystonia	3.6	19.0	11.9	7.1	17.8	45.7
Parkinson-like events	2.8	12.3	10.1	6.7	10.9	27.5
NMS	3.6	8.5	16.1	11.4	11.6	32.5
Suicide		2.7	4.0	6.5	3.7	6.2
Sedation	2.3	3.8	7.2	6.1	4.6	5.3
Cognitive impairment		5.9	3.6	2.7	2.0	3.3
SIADH / Hyponatriaemia			4.7		3.1	3.1
Hyperprolactinaemia		7.5	8.2	3.9	211.9	6.0
Sexual dysfunction		3.2	2.6	2.3	2.2	

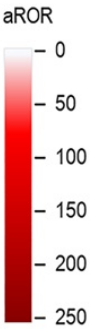


Figure 1. Heat map displaying reporting odds ratios (RORs) adjusted for age group and sex. Cells are left blank if the adjusted ROR is < 2 and/or the Bonferroni-Holm corrected p -value is ≥ 0.05. FGA, first-generation antipsychotic; NMS, neuroleptic malignant syndrome; SGA, second-generation antipsychotic; SIADH, syndrome of inappropriate antidiuretic hormone secretion; TdP, torsade de pointes.

Why the other options are incorrect:

- **A. Agranulocytosis** — This is classically associated with **clozapine**, which requires mandatory blood monitoring (REMS program). While agranulocytosis is listed as a rare warning for risperidone, it is not a characteristic or high-risk adverse effect.[2][5]
- **B. Shortened QT interval** — Antipsychotics are associated with QT **prolongation**, not shortening. Risperidone can cause modest QTc prolongation.[6]
- **D. Weight loss** — Risperidone causes **weight gain**, not weight loss. It is listed among antipsychotics with more weight gain than several comparators.[6]

Would you like to explore the management strategies for risperidone-induced hyperprolactinemia, including when to switch agents versus add adjunctive therapy?

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Question 60

A 14-year-old girl is brought to the physician by her father because of fever, chills, abdominal pain, and profuse non-bloody diarrhea. Her symptoms began one week ago, when she had several days of low-grade fever and constipation. She returned from Indonesia 2 weeks ago, where she spent the summer with her grandparents. Her temperature is 39.3°C (102.8°F). Examination shows diffuse abdominal tenderness and mild hepatosplenomegaly. There is a faint salmon-colored maculopapular rash on her trunk and abdomen. Which of the following is the most likely causal organism?

Answer Choices:

(A) Giardia lamblia
(B) Schistosoma mansoni
(C) Salmonella typhi
(D) Clostridium perfringens

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/df771f81-ab37-42f8-b035-aa13065d16b6

OpenEvidence Explanation

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The answer is **C. Salmonella typhi**.

This presentation is classic for **typhoid fever (enteric fever)**, caused by *Salmonella typhi*. The key features pointing to this diagnosis include:

- **Travel to a typhoid-endemic region** (Indonesia)
- **Stepwise clinical course**: initial low-grade fever with constipation (first week), followed by high fever, abdominal pain, and diarrhea (second week) — this biphasic pattern is characteristic
- **Hepatosplenomegaly**
- **Salmon-colored, blanching maculopapular rash** on the trunk — known as "**rose spots,**" which are pathognomonic for typhoid fever
- **Diffuse abdominal tenderness** consistent with involvement of Peyer's patches in the ileum

Why not the other options?

- **A. Giardia lamblia** — Causes watery, foul-smelling diarrhea and bloating but does not produce high fever, hepatosplenomegaly, or rose spots.
- **B. Schistosoma mansoni** — Can cause hepatosplenomegaly in chronic infection, but acute schistosomiasis (Katayama fever) presents with urticaria and eosinophilia, not rose spots or this stepwise fever pattern.
- **D. Clostridium perfringens** — Causes a brief, self-limited food poisoning (6–24 hours of watery diarrhea and cramping) that would not produce a week-long illness with hepatosplenomegaly and rash.

Would you like to explore the recommended diagnostic workup and antibiotic treatment for typhoid fever, including considerations for multidrug-resistant strains common in Southeast Asia?

Question 61

A 22-year-old female college student is treated with metronidazole after presenting to student health services with itching, discharge, and pain in her vagina. At a party shortly afterward she experiences facial flushing, nausea, tachycardia, dyspnea, headache, and abdominal cramps after consuming alcohol. Serum levels of which of the following are likely elevated in this patient following alcohol consumption:

Answer Choices:

(A) Acetaldehyde
(B) Uric acid
(C) Cytochrome P-450 enzymes
(D) Amylase

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/f3e5cf7e-48fc-40c8-a79b-e6b216ee9233

OpenEvidence Explanation

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The answer is **A. Acetaldehyde**.

This clinical scenario describes a classic **disulfiram-like reaction** caused by the interaction between metronidazole and alcohol. The traditionally accepted

mechanism involves metronidazole inhibiting **aldehyde dehydrogenase (ALDH)**, the enzyme responsible for converting acetaldehyde to acetic acid in the ethanol metabolism pathway.[1][2] When ALDH is inhibited, **acetaldehyde accumulates**, producing the characteristic symptoms this patient experienced: facial flushing, nausea, tachycardia, dyspnea, headache, and abdominal cramps.[3][4]

The clinical presentation — a young woman treated with metronidazole for vaginitis (likely trichomoniasis) who then develops these symptoms after alcohol consumption — is the textbook presentation of this drug-alcohol interaction. The FDA label for metronidazole specifically warns that abdominal cramps, nausea, vomiting, headaches, and flushing may occur with concurrent alcohol use.[3][5]

Why not the other options:

- **B. Uric acid** — Elevated uric acid is associated with gout, tumor lysis syndrome, or chronic alcohol use, but does not explain this acute reaction.
- **C. Cytochrome P-450 enzymes** — While metronidazole does interact with the CYP system, CYP enzyme levels are not acutely elevated in this scenario and would not explain the symptom complex.
- **D. Amylase** — Elevated amylase suggests pancreatitis, which is not the mechanism here despite the abdominal cramps.

It is worth noting that more recent evidence has questioned whether metronidazole truly causes a clinically significant disulfiram-like reaction. A controlled study in human volunteers found that metronidazole did not raise blood acetaldehyde levels when co-administered with ethanol, and a 2026 systematic review concluded that the available evidence does not strongly support this interaction.[6][7] Animal data suggest the mechanism may involve intracolonic rather than systemic acetaldehyde accumulation.[8] Nonetheless, the traditional teaching — and the expected exam answer — remains acetaldehyde accumulation.

Would you like to explore the evolving evidence on whether the metronidazole-alcohol interaction is truly clinically significant, and how this affects counseling practices?

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Question 63

An 80-year-old man is transferred from a step-down unit to a med-surg floor in the hospital. He had undergone a successful hernia surgery 14 hours ago. Before the surgery, he was pre-treated with atropine, scopolamine, and morphine and recovered well in the PACU after the surgery. There were no complications in the step-down unit and the patient continued to recover. On the med-surg floor, his temperature is 36.8°C (98.2°F), the heart rate is 98/min, the respiratory rate is 15/min, the blood pressure is 100/75 mm Hg, the oxygen saturation is 90%. On physical exam, he is a well-developed, obese man. His heart has a regular rate and rhythm and his lungs are clear to auscultation bilaterally. His incision site is clean, dry, and intact with an appropriate level of swelling and erythema. During the physical, the patient mentions some discomfort in his abdomen and pelvis and during a records review it is noted that he has not passed urine in the PACU, step-down unit, or since arriving on the med-surg floor. A bladder scan is inconclusive due to body habitus. What is the next best step in the treatment of this patient?

Answer Choices:

(A) Insert a 'straight cath' into the patient's bladder
(B) Aggressive IV fluids
(C) Digital rectal exam
(D) Renal ultrasound

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/5b91779c-7657-40fd-b307-a56cbec94ee7

OpenEvidence Explanation

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The answer is **A. Insert a 'straight cath' (intermittent straight catheterization) into the patient's bladder**.

This patient presents with classic **postoperative urinary retention (POUR)**, which is the most likely diagnosis given the clinical picture:

- **80-year-old male** (advanced age and male sex are major risk factors)[1]
- **Hernia surgery** (POUR occurs in ~5.8% of males after inguinal hernia repair, rising to ~9.5% in men >65 years)[1]
- **Pre-treated with atropine, scopolamine (anticholinergics), and morphine (opioid)** — all of which impair detrusor contractility and are well-established risk factors for POUR[1]
- **No urine output for ~14 hours** with abdominal/pelvic discomfort — consistent with a distended bladder
- **Bladder scan inconclusive** due to obesity, which is a recognized limitation of portable bladder scanners (reliability drops to "fair" in patients with BMI ≥30)[2]

Why straight catheterization is correct: When a bladder scanner is unavailable or inconclusive, expert consensus supports proceeding with **intermittent straight catheterization (ISC)** in symptomatic patients, particularly when there has been prolonged absence of urine output.[3] ISC is preferred over indwelling catheterization because it reduces catheter exposure time and lowers complication rates.[4][5] It serves both a diagnostic purpose (confirming retention by measuring volume) and a therapeutic purpose (decompressing the bladder to prevent overdistension injury).[6]

Why the other options are less appropriate:

- **B. Aggressive IV fluids** — This patient's vital signs (mild tachycardia, borderline BP) could suggest hypovolemia, but the primary concern is urinary retention, not inadequate urine production. Aggressive fluids

without addressing bladder outlet obstruction would worsen bladder overdistension.

- **C. Digital rectal exam** — While it could assess for prostatic enlargement, it would not change the immediate management (the bladder still needs to be decompressed).

- **D. Renal ultrasound** — This would evaluate for hydronephrosis or renal pathology but does not address the acute need for bladder decompression and is not the immediate next step.

Would you like to explore the risk stratification and prophylactic strategies (such as alpha-blockers) for preventing POUR in high-risk surgical patients?

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Question 66

A 4-year-old boy is brought to the emergency department because of severe abdominal pain and bilious vomiting for 6 hours. He has not had bowel movements in the past 24 hours. He appears ill. His temperature is 37.8°C (100°F) and pulse is 122/min. Examination shows a distended abdomen. There is tenderness to palpation in the lower abdomen; guarding and rebound tenderness are present. Bowel sounds are decreased. An x-ray of the abdomen shows dilated loops of bowel. He has been accompanied by his 14-year-old brother. The surgeon recommends an emergency laparotomy. The parents are away visiting friends and cannot be reached. Which of the following is the most appropriate next best step in management?

Answer Choices:

(A) Get consent from the patient's brother
(B) Get consent from the patient
(C) Perform emergency laparotomy
(D) Delay surgery until parental consent

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/3346caf2-1e6e-4143-8839-d3e839630cd6

OpenEvidence Explanation

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The correct answer is **C. Perform emergency laparotomy**.

This case presents a 4-year-old with signs of an acute surgical abdomen (severe abdominal pain, bilious vomiting, absent bowel movements, distension, guarding, rebound tenderness, and dilated bowel loops on x-ray), constituting a life-threatening **emergency medical condition (EMC)**. The key medicolegal principles are:

Why the other options are incorrect:

- **A (Brother's consent):** A 14-year-old sibling is a minor and has no legal authority to provide consent for another minor's medical treatment. Only parents, legal guardians, or formally designated surrogate decision makers can provide consent by proxy.[1]
- **B (Patient's consent):** A 4-year-old child lacks the cognitive capacity to provide informed consent or even meaningful assent for a surgical procedure.[1][2]
- **D (Delay surgery):** Delaying life-saving treatment to obtain parental consent is inappropriate and potentially dangerous. Both the American College of Emergency Physicians (ACEP) and the American Academy of Pediatrics (AAP) explicitly state that emergency treatment should **never be withheld or delayed** because of problems obtaining consent.[1][3]

Why proceeding with surgery is correct:

Under the "**emergency exception rule**" (also called the "**doctrine of implied consent**"), when an EMC is identified and consent cannot be obtained, the hospital must provide treatment. This doctrine presumes that a reasonable parent, if present, would consent to life-saving treatment in the best interest of the child.[1] EMTALA mandates treatment of emergency medical conditions regardless of age or consent status.[1] The facts and circumstances should be documented in the medical record, including why immediate treatment was felt to be in the patient's best interest.[1]

Would you like to explore how documentation requirements differ when treating minors under implied consent versus standard informed consent?

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Question 68

A 57-year-old female with a past medical history of alcoholism presents to the emergency room vomiting bright red blood. She is accompanied by her partner, who reports that she had been complaining of black and tarry stools for the past several days. Vital signs are temperature 37 degrees celsius, heart rate 141 beats per minute, blood pressure 90/60, respiratory rate 20, and oxygen saturation 99% on room air. On physical examination, she has splenomegaly and a positive fluid wave. The remainder of her examination is within normal limits. The patient is stabilized with intravenous fluids, and her blood pressure improves. Subsequent emergent upper endoscopy reveals bleeding from the submucosal veins in the lower 1/3 of the esophagus, but no gastric bleed. In the endoscopy suite she also receives IV octreotide. After intervention and resolution of her acute bleed, which of the following pharmacologic agents is indicated?

Answer Choices:

(A) Phentolamine
(B) Prazosin
(C) Nifedipine
(D) Nadalol

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/830874b6-013a-4e39-953e-645b70b0b804

OpenEvidence Explanation

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The correct answer is **D. Nadolol**.

This patient presents with classic features of **decompensated alcoholic cirrhosis** — splenomegaly, ascites (positive fluid wave), and esophageal variceal hemorrhage (hematemesis and melena with bleeding from submucosal veins in the lower esophagus). After acute stabilization with IV fluids, endoscopic intervention, and octreotide, the next step is **secondary prophylaxis** to prevent variceal rebleeding.

Nadolol is a **nonselective beta-blocker (NSBB)** and is one of the standard agents — along with propranolol and carvedilol — recommended for secondary prophylaxis of variceal bleeding.[1] NSBBs reduce portal pressure by decreasing cardiac output (beta-1 blockade) and causing splanchnic vasoconstriction via unopposed alpha-1 activity (beta-2 blockade).[2] The AASLD Practice Guidance specifically lists propranolol, nadolol, and carvedilol as appropriate agents for secondary prophylaxis, ideally combined with endoscopic band ligation.[1] Without prophylaxis, the risk of rebleeding is up to **60% at 1 year**.[1]

Why the other options are incorrect:

- **A. Phentolamine** — A non-selective alpha-blocker used for hypertensive crises (e.g., pheochromocytoma). It would cause vasodilation and worsen hypotension without reducing portal pressure effectively.
- **B. Prazosin** — A selective alpha-1 blocker used for hypertension and BPH. Not indicated for variceal prophylaxis.
- **C. Nifedipine** — A dihydropyridine calcium channel blocker. It does not reduce portal pressure and is not part of variceal bleeding prophylaxis.

The following figure illustrates the management algorithm for secondary prophylaxis after esophageal variceal bleeding:

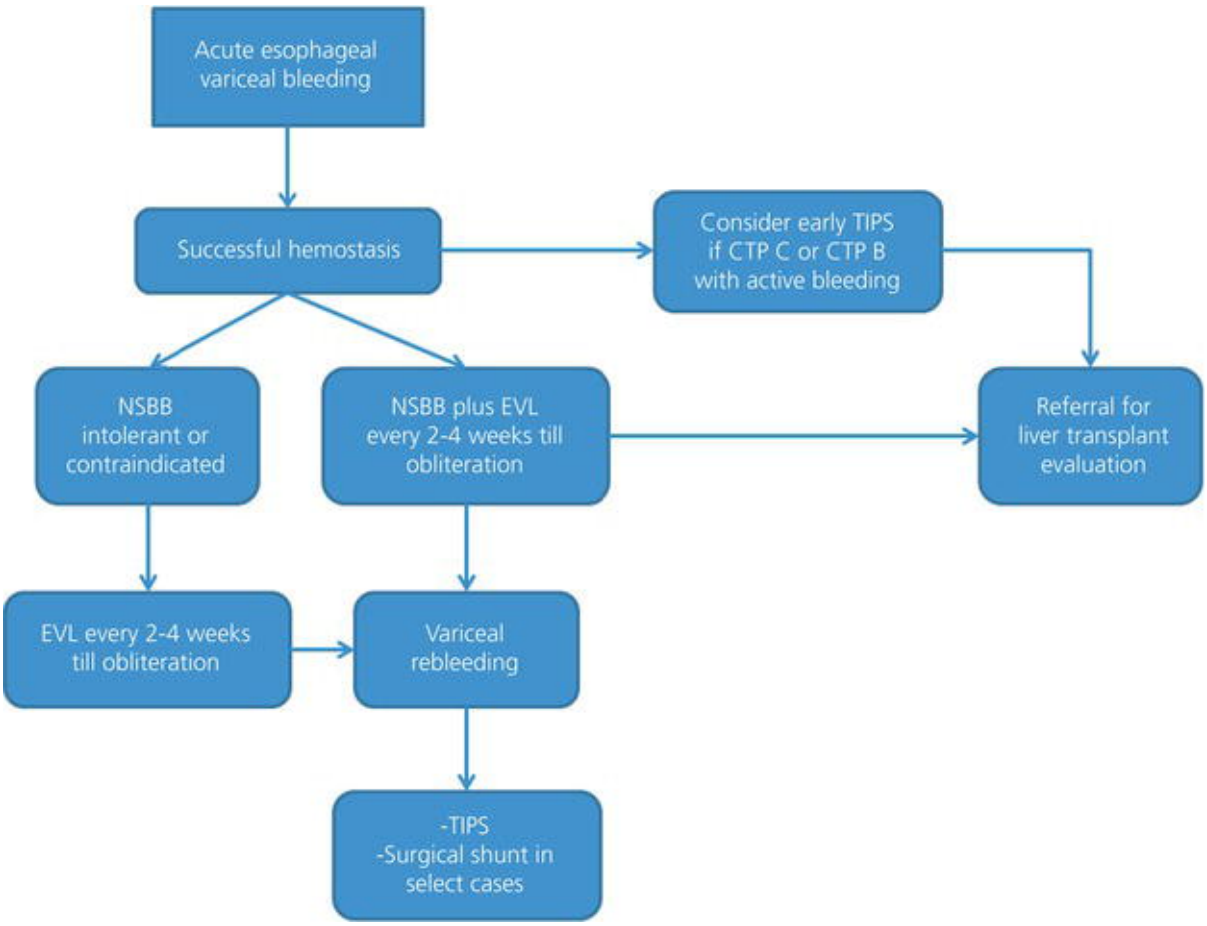


Figure 23. Management algorithm for secondary prophylaxis of esophageal variceal bleeding. CTP, Child-Turcotte-Pugh; EVL, endoscopic variceal ligation; NSBB, nonselective β-blocker; TIPS, transjugular intrahepatic portosystemic shunt.

Would you like to explore the comparative efficacy and dosing strategies of carvedilol versus traditional NSBBs (propranolol/nadolol) for portal hypertension management?

References

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Question 70

A 66-year-old man is brought to the emergency room by his wife due to abdominal distension and persistent somnolence for the past 2 weeks. The patient's wife says that he has been sleeping much more than usual for the past 5 days. His bowel and bladder habit have not changed. His past medical history is significant for alcoholic liver cirrhosis. His vital signs include: pulse 76/min, respiratory rate 15/min, temperature 38.0°C (100.4°F) and blood pressure 122/75 mm Hg. On physical examination, the patient is altered and not responsive to commands. Oriented x 0. The abdomen is significantly distended. Shifting dullness is present and a positive fluid wave can be elicited. Hyperreflexia and asterixis are noted. Laboratory findings are significant for the following:
Laboratory test
Sodium 140 mEq/L
Potassium 3.5 mEq/L
Chloride 97 mEq/L
Glucose 90 mg/dL
Ammonia 100 µg/dL (ref: 19-60 µg/dL)
Arterial blood gas
pH 7.4
pCO2 40 mm Hg
pO2 90 mm Hg
HCO3 26 mEq/L
An abdominal ultrasound shows surface nodularity compatible with cirrhosis but no other changes aside from ascites. An upper GI endoscopy is performed which shows gastric varices with no signs of active bleeding. An MRI of the brain is insignificant. What is the most likely precipitating factor that led to this patient's condition?

Answer Choices:

(A) Spontaneous bacterial peritonitis
(B) Metabolic alkalosis
(C) Portal vein thrombosis

(D) Hypoglycemia

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/e777ce98-41dc-4ecd-aa29-bca7f2d48741

OpenEvidence Explanation

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The answer is **A. Spontaneous bacterial peritonitis (SBP)**.

This patient presents with **overt hepatic encephalopathy** (altered mental status, oriented x 0, hyperreflexia, asterixis, elevated ammonia) in the setting of alcoholic liver cirrhosis with significant ascites. The key to identifying the precipitating factor lies in systematically eliminating the other options and recognizing the clinical picture:

- **Metabolic alkalosis (B)** — The ABG shows a pH of 7.4, pCO2 of 40 mmHg, and HCO3 of 26 mEq/L, which is entirely normal. Alkalosis is not present.
- **Hypoglycemia (D)** — Glucose is 90 mg/dL, which is normal.
- **Portal vein thrombosis (C)** — The abdominal ultrasound showed no changes aside from cirrhosis and ascites, making this unlikely.

SBP is the most likely precipitant in this clinical scenario. The patient has a low-grade fever (38.0°C), significant ascites, and encephalopathy — a classic presentation. Notably, up to one-third of patients with SBP may be asymptomatic or present with **only encephalopathy and/or acute kidney injury**

as the sole manifestation, without typical abdominal pain or tenderness.[1][2] Infections, particularly SBP, are among the most potent precipitants of hepatic encephalopathy in cirrhosis. SBP was found to be the strongest independent predictor of HE among infections, with an adjusted odds ratio of **5.13** (95% CI 3.03–8.69).[3] The AASLD guidelines recommend that a **diagnostic paracentesis should be performed in any cirrhotic patient with ascites who is hospitalized emergently**, regardless of symptoms, to rule out SBP.[1]

Would you like to explore the recommended empiric antibiotic regimens and diagnostic workup for spontaneous bacterial peritonitis in cirrhotic patients?

Relevant images

(CONTENT OMITTED)

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5. Ascites, Hyponatremia, Spontaneous Bacterial Peritonitis, and Hepatorenal Syndrome. Salvatore Piano, Marta Tonon, Paolo Angeli. Chapter 43

Question 71

A 27-year-old man presents to the emergency department after a motor vehicle collision. The patient was the front seat unrestrained driver in a head on collision. The patient's echocardiogram (ECG) is notable only for sinus tachycardia. His temperature is 99.5°F (37.5°C), blood pressure is 107/58 mmHg, pulse is 120/min, respirations are 17/min, and oxygen saturation is 98% on room air. The patient is given 2 liters of Ringer lactate solution and morphine. Initial workup demonstrates that the patient's pulmonary capillary wedge pressure and troponins are elevated. The patient is currently complaining of chest pain. Physical exam is notable for an uncomfortable young man with bruising over his chest wall. Which of the following is the most likely diagnosis?

Answer Choices:

(A) Cardiac contusion
(B) Hemorrhage
(C) Pulmonary contusion
(D) Takotsubo cardiomyopathy

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/0c646b56-8940-476e-b03c-4c2651b03e1d

OpenEvidence Explanation

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The most likely diagnosis is **A. Cardiac contusion**.

This presentation is classic for **blunt cardiac injury (myocardial contusion)** following high-energy blunt chest trauma. The key findings supporting this diagnosis include:

- **Mechanism**: Unrestrained driver in a head-on MVC — the steering wheel impact to the anterior chest is the most common cause of cardiac contusion[1][2]
- **Chest wall bruising**: Direct evidence of significant anterior thoracic impact
- **Elevated troponins**: Reflect myocardial cell injury/necrosis from direct cardiac trauma[1][3]
- **Elevated pulmonary capillary wedge pressure (PCWP)**: Indicates impaired ventricular function (diastolic dysfunction or reduced systolic output) from the contused myocardium, leading to elevated left-sided filling pressures[2][4]
- **Sinus tachycardia**: A common ECG finding in cardiac contusion and consistent with pain, sympathetic activation, and impaired cardiac function[5]

Why not the other options?

- **Hemorrhage (B)**: While tachycardia and borderline hypotension could suggest hemorrhage, the PCWP would be **low** (not elevated) in hypovolemic shock. The elevated PCWP points to a cardiac etiology.
- **Pulmonary contusion (C)**: Would present with hypoxemia, pulmonary infiltrates, and respiratory distress — not elevated troponins or elevated PCWP. This patient's oxygen saturation is 98% on room air.
- **Takotsubo cardiomyopathy (D)**: Occurs predominantly in **postmenopausal women** (>90% of cases) and is triggered by emotional or physical stress with wall motion abnormalities extending beyond a single coronary territory. A 27-year-old male with direct chest trauma and troponin elevation is far more consistent with direct myocardial contusion.[6][7]

The Eastern Association for the Surgery of Trauma (EAST) guidelines recommend screening for blunt cardiac injury with ECG and troponin measurement; abnormalities in either warrant telemonitoring for arrhythmias and echocardiographic evaluation.[3][5]

Is there additional imaging (e.g., echocardiogram findings or CT chest results) available for this patient that might help further characterize the injury?

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Question 72

A 56-year-old man presents to the emergency department for progressively worsening fatigue, malaise, fever, and abdominal pain. He reports that his symptoms began approximately 1 week ago and he has noticed episodes of diarrhea. He recently started melatonin and magnesium supplementation in hopes of improving his sleep. Medical history is significant for alcohol use disorder that required multiple hospital admissions for management of acute pancreatitis and cirrhosis. He states that he occasionally injects heroin intravenously. Temperature is 100°F (37.8°C), blood pressure is 105/70 mmHg, pulse is 92/min, and respirations are 17/min. Physical examination is significant for scleral icterus, hepatomegaly, ascites, and diffuse abdominal tenderness. Laboratory testing is significant for leukocytosis and metabolic acidosis. A paracentesis is performed and he is admitted into the hospital to receive intravenous cefotaxime and albumin. Ascitic fluid analysis demonstrates a polymorphonuclear cell count of 280 cells/mm^3, serum-ascites albumin gradient of 1.3 g/dL, and a culture positive for Escherichia coli sensitive to cefotaxime and ceftriaxone. On hospital day 2, the nurse reports that the patient is oliguric in the setting of constant fluid intake. Physical examination is unchanged. Laboratory testing is significant for a serum sodium of 131 mEq/L and creatinine of 1.8 mg/dL (it was 0.9 mg/dL on admission). Urine studies are significant for a low urine sodium level, without evidence of blood or protein. Since the hospital admission, he has not been started on any new medications. Which of the following will be the best treatment option for this patient?

> **Answer Choices:**
>
> (A) Adding dopamine to his treatment regimen
> (B) Adding lisinopril to his treatment regimen
> (C) Liver transplantation
> (D) Transjugular intrahepatic portosystemic shunting

> **Correct Answer:**
>
> (C)

> **OpenEvidence Response:**
>
> (C) ✓

OpenEvidence Link: https://openevidence.com/ask/63b2c609-bca3-4c1e-ad4d-d8af3c69b1b5

OpenEvidence Explanation

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The best treatment option is **C. Liver transplantation**.

This patient has cirrhosis complicated by spontaneous bacterial peritonitis (SBP) — confirmed by ascitic fluid PMN count of 280 cells/mm³ and E. coli culture — who is now developing **hepatorenal syndrome (HRS-AKI)**. The clinical picture is classic: oliguria, doubling of serum creatinine (0.9 → 1.8 mg/dL), low urine sodium, and absence of proteinuria or hematuria, all in the setting of decompensated cirrhosis with SBP as the precipitant.[1]

Why liver transplantation is the definitive treatment:

HRS-AKI is a functional renal failure driven by the underlying liver disease — specifically, splanchnic vasodilation and reduced effective arterial blood volume. Vasoconstrictors (terlipressin, norepinephrine) combined with albumin are the pharmacologic mainstay and serve as a **bridge to transplantation**, but they do not improve survival independently because they do not address the underlying hepatic pathology.[1] The AASLD 2021 and 2024 guidelines state that **liver transplantation is the definitive treatment for HRS-AKI** and that all patients with cirrhosis and AKI should be considered for urgent transplant evaluation given the high short-term mortality, even in vasoconstrictor responders.[2][3]

Why the other options are incorrect:

- **A. Dopamine** — Low-dose ("renal dose") dopamine has not been shown to be effective in HRS and is not recommended by any guideline.[2][3]

- **B. Lisinopril** — ACE inhibitors cause vasodilation and would worsen the already compromised renal perfusion in HRS. They are contraindicated in this setting.[1]

- **D. TIPS** — Transjugular intrahepatic portosystemic shunting may have a role in refractory ascites but is not a standard treatment for HRS-AKI and carries significant risks in patients with advanced liver disease.[4]

This patient is already receiving appropriate initial management with cefotaxime for SBP and albumin for volume expansion. The next critical step is vasoconstrictor therapy as a bridge, with **liver transplantation as the ultimate definitive treatment**.[1][2][3]

Would you like to explore the specific criteria and timing for simultaneous liver-kidney transplantation versus liver transplant alone in patients with HRS-AKI?

Relevant images

(CONTENT OMITTED)

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Question 73

A 29-year-old woman presents to the clinic after several months of weight loss. She noticed a 6.8 kg (15 lb) unintentional weight loss over the preceding several months. She has not changed her diet or exercise habits. She also reports feuding with her boyfriend over the temperature of their shared apartment, as she always feels warmer than he does. The vital signs include: heart rate 110/min and blood pressure 146/78 mm Hg. The physical exam is notable for warm and slightly moist skin. She also exhibits a fine tremor in her hands when her arms are outstretched. The urine pregnancy test is negative. Which of the following is the best single treatment option for this patient?

Answer Choices:

(A) Glucocorticoids
(B) Methimazole
(C) Propranolol
(D) Radioiodine therapy

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/8e7f4d93-629d-4240-a7ce-046f0049785e

OpenEvidence Explanation

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The best single treatment option is **B. Methimazole**.

This patient presents with classic features of hyperthyroidism — unintentional weight loss, heat intolerance, tachycardia (HR 110), widened pulse pressure (146/78), warm moist skin, and fine tremor — most consistent with Graves disease in a young woman. The question asks for the **best single treatment**, which is the key distinction among the answer choices.

Why methimazole over propranolol? While beta-blockers like propranolol provide symptomatic relief (controlling tachycardia, tremor, and heat intolerance), they do not address the underlying excess thyroid hormone production.[1][2] Beta-blockers are adjunctive therapy used "until thyroid hormone levels can be normalized".[2] Methimazole is the **preferred first-line antithyroid drug** that directly inhibits thyroid hormone synthesis and can restore euthyroidism, with the potential for disease remission after 12–18 months of therapy.[1] If only one treatment can be chosen, methimazole addresses the disease itself.

Why not the other options?

- **Glucocorticoids** are not standard first-line therapy for uncomplicated hyperthyroidism; they are reserved for thyroid storm or severe Graves ophthalmopathy.
- **Radioiodine therapy** is a definitive treatment option but is not the best single initial choice in a 29-year-old woman of childbearing potential, as it is contraindicated in pregnancy and requires avoidance of conception for at least 6 months after administration. Current practice patterns have shifted strongly toward antithyroid drugs over radioiodine as initial therapy, with 91.5% of endocrinologists worldwide now selecting ATDs first-line.[3][4][5]

Would you like to explore the monitoring parameters and side effect profile of methimazole, including the risk of agranulocytosis?

Relevant images

(CONTENT OMITTED)

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Question 75

A 5-year-old female is brought to a speech therapist for continuing work on improving her communication skills. She is only able to verbalize two word sentences and has generalized developmental delay. When she was born it was noticed that she had a high pitched mewing cry and subsequent physical exam revealed microcephaly, prominent epicanthal folds, and a holosystolic murmur best heard in the left 5th intercostal space near the sternum. An abnormality of which of the following chromosomes is most likely responsible for this patient's disorder?

Answer Choices:

(A) 5
(B) 7
(C) 18
(D) 21

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/b2c31621-ca68-4244-9913-4a1310c5189f

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OpenEvidence Explanation

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The answer is **A. Chromosome 5**.

This presentation is classic for **Cri-du-chat syndrome** (5p deletion syndrome), caused by a partial deletion of the short arm of **chromosome 5**. The key diagnostic clues in this vignette are:

- **High-pitched mewing cry** — the hallmark feature, described as a "cat-like cry" (French: cri du chat), caused by laryngeal and nervous system abnormalities
- **Microcephaly** and **prominent epicanthal folds** — characteristic craniofacial features
- **Severe intellectual disability** with significant speech delay (only two-word sentences at age 5)
- **Holosystolic murmur at the left 5th intercostal space near the sternum** — consistent with a **ventricular septal defect (VSD)**, which is the most common cardiac anomaly in this syndrome

Per the AHA Scientific Statement on the genetic basis for congenital heart disease, deletion 5p (cri-du-chat) is associated with a catlike cry, prenatal and postnatal growth retardation, round face, widely spaced eyes, epicanthal folds, single palmar transverse crease, and severe intellectual disability, with congenital heart defects (VSD, ASD, PDA) occurring in **30–60%** of affected individuals.[1]

Why not the other options?

- **Chromosome 7** (B) — Deletion 7q11.23 causes Williams syndrome, characterized by elfin facies, hypercalcemia, supravalvar aortic stenosis, and an overly social personality — not a mewing cry.[1]
- **Chromosome 18** (C) — Trisomy 18 (Edwards syndrome) presents with clenched fists, rocker-bottom feet, and severe cardiac defects, but not a cat-like cry.
- **Chromosome 21** (D) — Trisomy 21 (Down syndrome) features hypotonia, upslanting palpebral fissures, flat nasal bridge, and atrioventricular septal defects — but no mewing cry, and microcephaly is not a prominent feature.[2][3]

Would you like to explore the long-term neurodevelopmental outcomes and speech therapy interventions specific to children with cri-du-chat syndrome?

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Question 78

A newborn is found to be extremely cyanotic immediately after birth. He then develops progressive respiratory failure and is admitted to the neonatal ICU. A single loud S2 heart sound is appreciated as well as a machine-like murmur at the left upper sternal border. Radiography shows an enlarged egg-shaped heart. The newborn is then taken for a atrial septostomy to alleviate the condition pending definitive surgical correction. Which of the following is the most likely cause of this newborn's condition?

> **Answer Choices:**
>
> (A) Coarctation of the aorta
> (B) Persistent truncus arteriosus
> (C) Transposition of great vessels
> (D) Tricuspid atresia

> **Correct Answer:**
>
> (C)
>
> **OpenEvidence Response:**
>
> (C) ✓

OpenEvidence Link: https://openevidence.com/ask/1f249f3a-2fb1-4956-be10-41ba7444d010

OpenEvidence Explanation

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The correct answer is **C. Transposition of great vessels**.

This presentation is classic for **d-transposition of the great arteries (d-TGA)**, in which the aorta arises anteriorly from the right ventricle and the pulmonary artery arises from the left ventricle, creating two parallel circulations with complete separation of systemic and pulmonary blood flow.[1] Each key clinical feature points to this diagnosis:

- **Severe cyanosis immediately after birth** — results from the parallel circulations with inadequate mixing between the two circuits.[1]
- **Single, loud S2** — due to the anterior position of the aorta, which brings the aortic valve closure sound closer to the chest wall.[1]
- **Machine-like murmur at the left upper sternal border** — consistent with a patent ductus arteriosus (PDA), which serves as one of the communications allowing mixing between the two circuits.[1]
- **Egg-shaped (or "egg on a string") heart on chest radiograph** — a classic radiographic sign of TGA, caused by the narrow superior mediastinum from the anteroposterior relationship of the great arteries.[2]
- **Balloon atrial septostomy (Rashkind procedure)** — this is the hallmark palliative intervention for d-TGA, first described in 1966, performed to enlarge the atrial communication and enhance bidirectional mixing of blood between the pulmonary and systemic circuits. Up to 30% of neonates with TGA require this procedure.[3][4]

Why the other options are incorrect:

- **A. Coarctation of the aorta** — typically presents with differential cyanosis (lower extremity), diminished femoral pulses, and hypertension in the upper extremities rather than severe generalized cyanosis; the chest radiograph classically shows a "figure of three" sign.[2]
- **B. Persistent truncus arteriosus** — presents with a single S2 (since there is only one semilunar valve), but the radiograph does not show an egg-shaped heart, and atrial septostomy is not the standard palliative intervention.
- **D. Tricuspid atresia** — presents with cyanosis but typically shows left axis deviation on ECG and decreased pulmonary blood flow; while BAS can occasionally be needed if the atrial communication is restrictive, the egg-shaped heart and single loud S2 are not characteristic findings.[3]

Would you like to explore the definitive surgical management of d-TGA, including the arterial switch operation and its long-term outcomes?

Relevant images

(CONTENT OMITTED)

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Question 80

A post-mortem lung examination of a 68-year-old male overweight male with evidence of chronic lower extremity edema, a 60 pack-year smoking history and daily productive cough would be most likely to reveal:

Answer Choices:

(A) Hypereosinophilia
(B) Reid Index > 50%
(C) Non-caseating granulomas
(D) Evidence of a necrotizing infection

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/14dd75cf-01fe-4a23-b911-5e5cd1fce6a3

OpenEvidence Explanation

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The answer is **B. Reid Index > 50%**.

This clinical vignette describes a 68-year-old overweight male with a **60 pack-year smoking history**, **daily productive cough**, and **chronic lower extremity edema** — a classic presentation of **chronic bronchitis** (the "blue bloater" phenotype of COPD). The post-mortem finding most consistent with this diagnosis is an elevated Reid Index exceeding 50%.

The Reid Index is the ratio of bronchial mucous gland thickness to total bronchial wall thickness. In normal individuals, this ratio is less than 0.4 (40%), whereas in chronic bronchitis it characteristically exceeds **0.5 (50%)**.[1][2] Reid originally described that bronchial mucous glands are enlarged in chronic bronchitis and used this gland-to-wall ratio as a pathological diagnostic yardstick.[1] The characteristic pathological changes in the central airways of chronic bronchitis include inflammatory cellular infiltration and **mucous gland enlargement**, with increased mucus production, defective mucociliary clearance, and disruption of the epithelial barrier.[1][3]

Why the other options are incorrect:

- **A. Hypereosinophilia** — Eosinophilic infiltration is characteristic of asthma, not chronic bronchitis/COPD. In COPD, the predominant inflammatory cells are neutrophils, macrophages, and CD8+ T lymphocytes; eosinophils are not prominent except during exacerbations or in patients with concomitant asthma.[4]
- **C. Non-caseating granulomas** — This is the hallmark of sarcoidosis, not COPD or chronic bronchitis.
- **D. Evidence of necrotizing infection** — While chronic bronchitis patients are susceptible to respiratory infections, the clinical presentation described (chronic productive cough, edema, heavy smoking) points to chronic bronchitis pathology rather than a necrotizing infectious process.

The combination of chronic lower extremity edema (suggesting cor pulmonale from chronic hypoxemia) with productive cough and heavy smoking history firmly places this patient in the chronic bronchitis/"blue bloater" category, making mucous gland hypertrophy with an elevated Reid Index the expected post-mortem finding.[1][5]

Would you like to explore the pathophysiological differences between the "blue bloater" and "pink puffer" phenotypes of COPD and their distinct histopathological features?

Relevant images

(CONTENT OMITTED)

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Question 82

A 44-year-old African-American woman comes to the physician for a routine examination. She is concerned about cancer because her uncle died of metastatic melanoma 1 year ago. She has no history of serious illness and does not take any medication. She has been working in a law firm for the past 20 years and travels to the Carribean regularly with her husband. Examination of her skin shows no abnormal moles or warts. This woman is at greatest risk of which of the following types of melanoma?

> **Answer Choices:**
>
> (A) Desmoplastic
> (B) Nodular
> (C) Acral lentiginous
> (D) Superficial spreading

> **Correct Answer:**
>
> (C)
>
> **OpenEvidence Response:**
>
> (C) ✓

OpenEvidence Link: https://openevidence.com/ask/48c98de6-60c5-4196-9522-23372271fab4

OpenEvidence Explanation

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The correct answer is **C. Acral lentiginous melanoma**.

Acral lentiginous melanoma (ALM) is the most common specific histologic subtype of melanoma diagnosed in African-American patients. In a National Cancer Database analysis of 2,464 Black patients with cutaneous melanoma, ALM was the most common defined histologic subtype at **20.3%**, followed by superficial spreading melanoma at only 9.4%.[1] CDC data similarly show that ALM accounted for **16.7%** of melanomas with defined histology in non-Hispanic Black individuals.[2] A single-institution case series found that **75% of cutaneous melanomas** in Black patients were located on acral skin (palms, soles, nail beds), even though not all were histologically classified as ALM.[3]

ALM arises on non-sun-exposed glabrous skin of the palms, soles, and nail beds. Unlike other melanoma subtypes, it is **not driven by ultraviolet radiation** and has a distinct molecular profile with fewer BRAF V600 mutations and lower tumor mutational burden.[4][5] The absolute incidence of ALM is actually similar across racial groups, but because other UV-associated melanoma subtypes (superficial spreading, lentigo maligna) occur at much lower rates in darker-skinned populations, ALM constitutes a disproportionately high proportion of melanomas in Black, Hispanic, and Asian patients.[6][7]

The following figure illustrates the distribution of melanoma subtypes by race, demonstrating the predominance of ALM among Black patients compared to other racial groups.

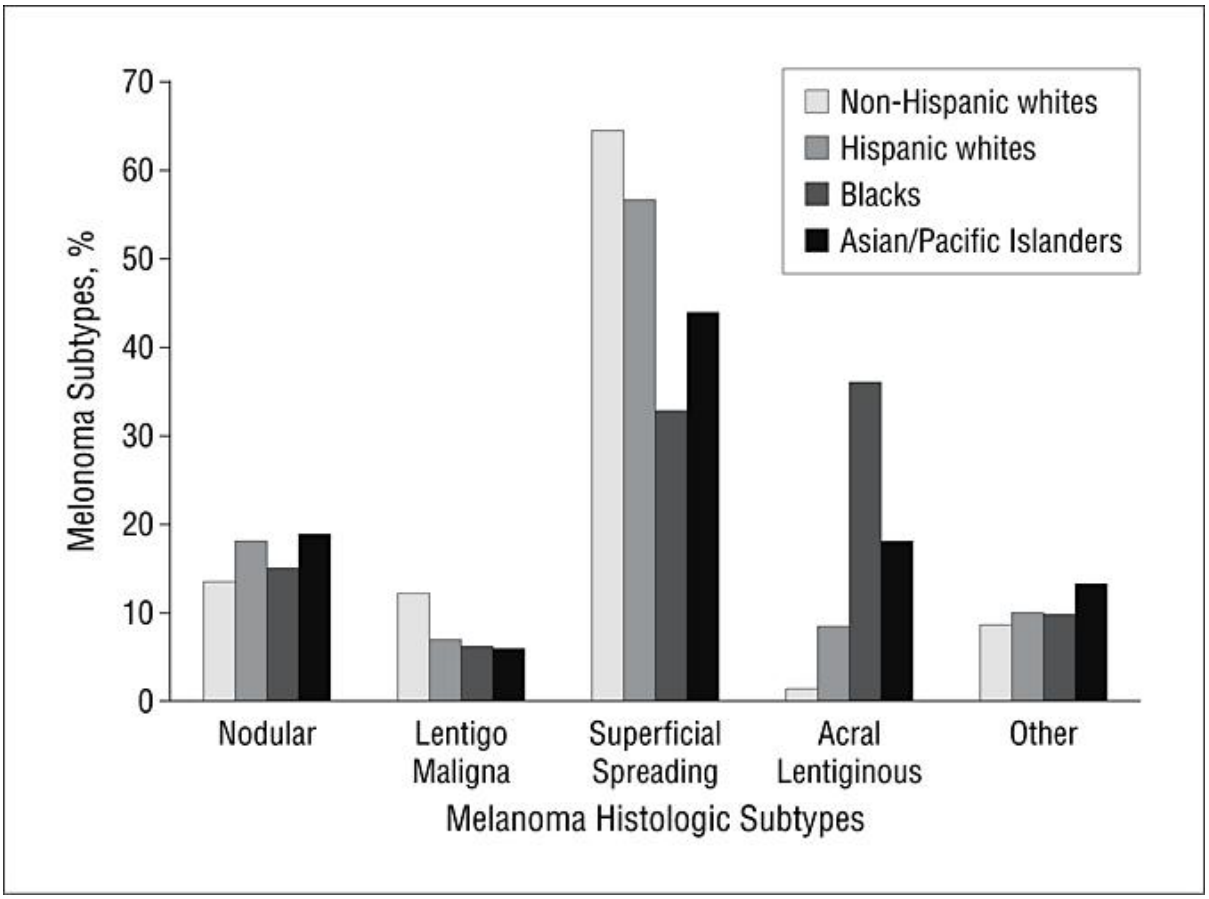


Figure 1.

Used under license from JAMA Network.

Key distinguishing features of the other answer choices:

- **Superficial spreading melanoma** (D) is the most common subtype overall and in non-Hispanic White individuals but not in African Americans.[9]
- **Nodular melanoma** (B) is the second most common subtype overall and is not disproportionately represented in any racial group.
- **Desmoplastic melanoma** (A) is a rare subtype typically occurring on chronically sun-damaged skin of the head and neck in older White individuals.

Would you like to explore the recommended screening strategies and clinical features that aid in early detection of acral lentiginous melanoma in patients with skin of color?

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Question 83

A 60-year-old woman is brought to the clinic by her daughter for evaluation. The daughter reports that her mother has recently been having difficulty combing her hair in the mornings. The patient's family history is significant for an ischemic stroke in her father. The patient's past medical history is positive for diverticulosis. She takes no medication. Her blood pressure is 120/70 mm Hg, heart rate is 75/min, respiratory rate is 14/min, and temperature is 37.6°C (99.7°F). On physical examination, the patient's neck is stiff and she also has bilateral shoulder tenderness; muscle strength is intact. Laboratory work is performed and presented below:
Hemoglobin 12.9 g/dL
Hematocrit 37.7%
Leukocyte count 5,500/mm3
Neutrophils 65%
Lymphocytes 30%
Monocytes 5%
Mean corpuscular volume 82.2 µm3
Platelet count 190,000/mm3
Erythrocyte sedimentation rate 65 mm/h
C-reactive protein 44 mg/dL
For which of the symptoms below should the patient be screened?

Answer Choices:

(A) Jaw claudication
(B) Heliotrope rash
(C) Gastroesophageal reflux
(D) Pink plaques with silvery scales

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/e9da0cc8-8ec4-441e-b5d6-229dbb041795

OpenEvidence Explanation

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The answer is **A. Jaw claudication**. This patient's presentation — a 60-year-old woman with difficulty raising her arms (combing hair), neck stiffness, bilateral shoulder tenderness, intact muscle strength, and markedly elevated inflammatory markers (ESR 65 mm/h, CRP 44 mg/dL) — is classic for **polymyalgia rheumatica** (PMR).[1][2] All patients with PMR should be screened for symptoms of **giant cell arteritis** (GCA), including jaw claudication, because the two conditions frequently coexist and may represent a disease spectrum.[3][4]

Why jaw claudication? Approximately 40–60% of patients with biopsy-proven GCA also have PMR, and 10–30% of patients presenting with isolated PMR are subsequently diagnosed with GCA.[4] Jaw claudication carries the highest positive likelihood ratio (4.90) among symptoms for diagnosing GCA and is an independent predictor of severe cranial ischemic complications including vision loss and stroke.[5][6] Screening for GCA symptoms — headache, scalp tenderness, visual disturbances, and jaw claudication — is essential because ischemic complications (particularly irreversible vision loss in up to 20% of GCA patients) typically occur before treatment is initiated.[7]

Why not the other options?

- **B. Heliotrope rash** — associated with dermatomyositis, which presents with proximal muscle weakness (not just pain/stiffness with intact strength).
- **C. Gastroesophageal reflux** — not a screening concern in this clinical context.

- **D. Pink plaques with silvery scales** — characteristic of psoriasis, unrelated to this presentation.

Would you like to explore the recommended diagnostic workup and initial treatment approach for polymyalgia rheumatica with suspected concurrent giant cell arteritis?

Relevant images

(CONTENT OMITTED)

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Question 84

A 30-year-old woman comes to the physician because she has been unable to conceive for 3 years. Analysis of her husband's semen has shown normal sperm counts during this time. The patient also reports episodic pelvic and back pain accompanied by painful diarrhea for 5 years. She has about one such episode on average per month for 4–6 days. She has taken ibuprofen for the pain, which has provided some relief. Menses have occurred at regular 29-day intervals since menarche at the age of 14 years and last for 7 days. She is sexually active with her husband and does not use contraception. Vital signs are within normal limits. Pelvic and bimanual examinations are normal; rectal examination is unremarkable. A hysterosalpingogram 6 months prior showed normal results. Which of the following is the most likely underlying mechanism of this patient's symptoms?

Answer Choices:

(A) Loss of fallopian tube function following infection
(B) Smooth muscle tumor arising from the myometrium
(C) Endometrial tissue outside the uterine cavity
(D) Increased secretion of androgens and luteinizing hormone

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/fd63383b-1035-4c2a-93a1-c38e367b3901

OpenEvidence Explanation

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The answer is **C. Endometrial tissue outside the uterine cavity** (endometriosis).

This presentation is classic for **endometriosis**: a young woman with **infertility** and **cyclical pelvic/back pain with painful diarrhea** occurring monthly for 4–6 days, temporally correlating with menses. The cyclic nature of symptoms reflects hormonally responsive endometrial tissue implanted outside the uterine cavity — commonly on the ovaries, uterosacral ligaments, cul-de-sac, and bowel serosa — which undergoes proliferation, breakdown, and bleeding with each menstrual cycle.

Key features supporting this diagnosis:

- **Cyclic pelvic pain and diarrhea** — GI symptoms (diarrhea, dyschezia) occur when endometrial implants involve the rectosigmoid or cul-de-sac, and they characteristically worsen during menstruation.
- **Infertility with normal HSG and normal semen analysis** — Endometriosis can cause infertility even without tubal obstruction, through mechanisms including chronic inflammation, altered peritoneal environment, impaired oocyte quality, and disrupted implantation.
- **Normal pelvic and rectal exams** — A normal exam does not exclude endometriosis; many patients with mild-to-moderate disease have unremarkable findings on examination.
- **Partial response to ibuprofen** — NSAIDs provide symptomatic relief by inhibiting prostaglandin synthesis but do not treat the underlying ectopic tissue.

Why not the other options?

- **A (PID/salpingitis)** — Would typically present with tubal abnormalities on HSG and lacks the cyclical pattern.
- **B (Uterine leiomyoma)** — Would more likely cause heavy menstrual bleeding and an enlarged/irregular uterus on exam, not cyclical diarrhea.

- **D (PCOS)** — Would present with oligomenorrhea/amenorrhea, hirsutism, and acne — inconsistent with this patient's regular 29-day cycles.

Would you like to explore the current evidence on empiric medical management versus laparoscopic diagnosis in suspected endometriosis-related infertility?

Question 85

A 55-year-old truck driver is brought to a physician by his wife. She states that her husband developed a fever and began feeling weak 3 days ago, but has refused medical help. He has been unable to go to work because of his symptoms. The patient has been previously hospitalized for a tricuspid valve replacement surgery 1 year ago and takes aspirin daily. The medical history is also relevant for myocardial infarction 3 years ago and hypertension for the past 10 years, for which he takes lisinopril. His blood pressure is 140/80 mm Hg, the pulse is 82/min, the respirations are 18/minute, and the temperature is 37.2°C (98.9°F). On examination, several hemorrhages are noted on the nail beds of several fingers. Which of the following findings would be most helpful in establishing a diagnosis?

Answer Choices:

(A) Bicuspid valve
(B) Friable irregular masses attached to the valve
(C) Papillary muscle rupture
(D) Annular calcification

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/e99f5361-3d50-4b7f-ae7f-37dfde5dc109

OpenEvidence Explanation

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The answer is **B. Friable irregular masses attached to the valve** (vegetations).

This clinical scenario describes a patient with a **prosthetic tricuspid valve**, fever, weakness, and **splinter hemorrhages** (nail bed hemorrhages) — a classic presentation of **infective endocarditis (IE)**. The finding most helpful in establishing the diagnosis would be the identification of vegetations, which appear as friable, irregular masses attached to the valve on echocardiography or at pathologic examination.[1][2]

Why vegetations are diagnostic:

- An oscillating intracardiac mass (vegetation) on a valve or supporting structures is a **major criterion** in the Modified Duke Criteria for diagnosing IE.[1][3]
- Vegetations are composed of fibrin, platelets, inflammatory cells, and microorganisms, and characteristically appear as friable, irregular masses adherent to valve leaflets.[2][4]
- This patient has multiple risk factors: a **prosthetic valve** (a core cardiac risk factor) and clinical features consistent with IE including fever, malaise, and splinter hemorrhages — the latter classified as a vascular phenomenon and minor criterion in the Duke criteria.[1][5][6]

Why the other options are incorrect:

- **A. Bicuspid valve** — A congenital abnormality that predisposes to IE but is not a diagnostic finding for it. It would not be relevant to a patient with a prosthetic tricuspid valve.
- **C. Papillary muscle rupture** — A complication of acute myocardial infarction, not endocarditis.
- **D. Annular calcification** — A degenerative finding that may predispose to IE but does not establish the diagnosis.

Splinter hemorrhages, while only present in approximately 5–10% of IE cases, have a specificity of about **83%** for IE and are a supportive clinical finding.[2][5][6]

Would you like to explore the recommended empiric antibiotic regimens and surgical indications for prosthetic valve endocarditis?

Relevant images

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Question 86

A previously healthy 30-year-old woman comes to the physician for the evaluation of pain during sexual intercourse for 6 months. She also reports frequent episodes of crampy pelvic pain that starts one day before menses and lasts for 7 days. Her symptoms are not relieved with pain medication. Menses occur at regular 28-day intervals and last 5 days. Her last menstrual period was 2 weeks ago. She is sexually active with her husband. She uses a combined oral contraceptive pill. Her vital signs are within normal limits. Physical examination shows rectovaginal tenderness. Cervical and urethral swabs are negative. Transvaginal ultrasonography shows no abnormalities. Which of the following is the most appropriate next step in management?

Answer Choices:

(A) Measurement of CA-125 levels
(B) Hysterectomy
(C) Laparoscopy
(D) Hysteroscopy

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/c74257df-9ead-4ebc-8aed-8e1d2433e694

OpenEvidence Explanation

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The correct answer is **C. Laparoscopy**.

This patient presents with classic features of **endometriosis**: dyspareunia, cyclic pelvic pain (dysmenorrhea), rectovaginal tenderness on exam, and negative infectious workup with a normal transvaginal ultrasound. Critically, she is already on a combined oral contraceptive pill — the **first-line empiric treatment** for endometriosis — yet her symptoms persist and are not relieved with pain medication. This makes her a candidate for surgical evaluation rather than continued empiric medical therapy.

Why laparoscopy? Diagnostic laparoscopy is the appropriate next step when first-line hormonal therapy has failed in a patient with clinically suspected endometriosis.[1][2] It serves a dual purpose: confirming the diagnosis through direct visualization and biopsy of lesions, and providing the opportunity for concurrent surgical treatment (excision/ablation of endometriotic implants).[2] ACOG guidelines note that laparoscopy is appropriate "as part of a stepwise approach if empiric medical therapy fails".[2] Superficial peritoneal endometriosis — the most common form — is frequently missed on transvaginal ultrasound, so a normal ultrasound does not exclude the diagnosis.[1][3]

Why not the other options?

- **A. CA-125 levels** — ACOG explicitly recommends against the use of blood biomarkers to diagnose endometriosis (strong recommendation). CA-125 lacks adequate sensitivity and specificity.[2]
- **B. Hysterectomy** — This is a fourth-line/definitive therapy reserved for patients who have failed both medical and surgical treatment of lesions. It is premature without a confirmed diagnosis.[4]
- **D. Hysteroscopy** — This evaluates the uterine cavity and is useful for intrauterine pathology (polyps, fibroids, synechiae), not for endometriosis, which involves extra-uterine implants.

Would you like to explore the stepwise approach to second-line medical therapies (GnRH agonists/antagonists) versus surgical management when first-line hormonal treatment fails in endometriosis?

Relevant images

(CONTENT OMITTED)

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Question 88

A 26-year-old woman is brought to the emergency department 20 minutes after being involved in a high-speed motor vehicle collision in which she was a restrained passenger. On arrival, she is lethargic and incoherent. She has severe facial lacerations and is in respiratory distress. Her pulse is 130/min, respirations are 29/min, and blood pressure is 90/58 mm Hg. Pulse oximetry on room air shows an oxygen saturation of 70%. Examination shows multiple facial lacerations. There is dullness to percussion and decreased breath sounds over the left lung base. Abdominal examination shows diffuse tenderness with no guarding or rebound. Bowel sounds are normal. The remainder of the examination shows no abnormalities. Her hemoglobin concentration is 12.1 g/dL. An x-ray of the chest shows a fractured left second rib, depression of the left mainstem bronchus, deviation of the nasogastric tube to the right, and a widened mediastinum. Which of the following is the most likely diagnosis?

Answer Choices:

(A) Diaphragmatic rupture
(B) Traumatic bronchial rupture
(C) Thoracic aortic rupture
(D) Tension pneumothorax

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/7e467875-86db-4f21-a979-7e485a93fdd9

OpenEvidence Explanation

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The most likely diagnosis is **C. Thoracic aortic rupture**.

The constellation of chest X-ray findings in this case — **widened mediastinum, depression of the left mainstem bronchus, and deviation of the nasogastric tube to the right** — represents the classic radiographic triad of traumatic thoracic aortic injury following a high-speed deceleration mechanism.[1][2]

Why thoracic aortic rupture fits best:

- **Nasogastric tube deviation to the right** results from mediastinal hematoma displacing the esophagus and has been identified as one of the most reliable plain-film signs of acute traumatic rupture of the thoracic aorta. A study by Tisnado et al. found this to be the most reliable radiographic sign for this diagnosis.[2][3]
- **Depression of the left mainstem bronchus** (below 40° from horizontal) occurs due to periaortic hematoma compressing the bronchus from above, and along with NG tube deviation, was one of only two statistically significant signs associated with aortic rupture in a study of 86 consecutive blunt chest trauma patients.[4]
- **Widened mediastinum** reflects mediastinal hemorrhage from the aortic injury.[1]
- The mechanism (high-speed MVC with deceleration) is the classic cause of aortic rupture at the isthmus, near the ligamentum arteriosum.[5][6]

Why the other options are less likely:

- **Diaphragmatic rupture (A):** Would typically show bowel herniation into the thorax or an elevated hemidiaphragm, not the mediastinal signs described here.[7]
- **Traumatic bronchial rupture (B):** Classically presents with persistent pneumothorax (especially after chest tube), subcutaneous emphysema,

pneumomediastinum, and the "fallen lung" sign — none of which are described in this case.[5][8]

- **Tension pneumothorax (D):** Would show hyperresonance (not dullness) to percussion, tracheal deviation away from the affected side, and absent breath sounds — the dullness to percussion here suggests hemothorax from mediastinal hemorrhage rather than pneumothorax.

The dullness to percussion and decreased breath sounds at the left base are consistent with a **left hemothorax** secondary to mediastinal hemorrhage tracking into the pleural space, which is a recognized association with aortic injury.[1]

Would you like to explore the current guidelines on CT angiography versus conventional aortography for confirming traumatic aortic injury and the role of endovascular repair (TEVAR) in management?

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Question 89

A 26-year-old G1P0 woman presents to her primary care physician's office with feelings of anxiety and trouble with sleep. She finds it difficult initiating sleep, occasionally has palpitations, and feels fatigued. She denies having similar symptoms in the past or starting any new medications or illicit drugs. She is currently 10 weeks pregnant and is closely followed by her obstetrician. Her temperature is 98.6°F (37°C), blood pressure is 125/70 mmHg, pulse is 105/min, and respirations are 18/min. On physical exam, the patient is mildly diaphoretic. The skin is warm and the thyroid gland is diffusely enlarged with thyroid bruits. Laboratory studies are significant for a thyroid-stimulating hormone level of 0.01 μU/mL (normal is 0.5-5.0 μU/mL) and an elevated free thyroxine (FT4) that is inappropriate for her pregnancy. Which of the following is the best treatment option for this patient?

Answer Choices:

(A) Methimazole
(B) Propylthiouracil
(C) Radioiodine therapy
(D) Thyroidectomy

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/a0d5402f-f9a7-45d1-ad54-e306947db344

OpenEvidence Explanation

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The best treatment option is **B. Propylthiouracil (PTU)**.

This patient presents with classic features of **Graves' disease** — diffuse goiter with thyroid bruits, suppressed TSH, elevated FT4, tachycardia, diaphoresis, and anxiety — at **10 weeks gestation** (first trimester). The key considerations for each option:

- **Propylthiouracil** is the preferred antithyroid drug in the first trimester because methimazole is associated with a rare but significant embryopathy including aplasia cutis, esophageal atresia, choanal atresia, and abdominal wall defects. A meta-analysis of over 5 million pregnancies confirmed a lower adjusted relative risk of congenital anomalies with PTU (aRR 1.16) compared to methimazole (aRR 1.28). ACOG guidelines recommend PTU for first-trimester hyperthyroidism, with consideration of switching to methimazole after the first trimester due to PTU's risk of hepatotoxicity.[1] [2]
- **Methimazole (A)** is avoided in the first trimester due to its teratogenic risk. A review of nearly 6,000 live births to women with Graves' disease showed a twofold increase in major fetal malformations with methimazole versus PTU.[1]
- **Radioiodine therapy (C)** is **absolutely contraindicated** in pregnancy — it crosses the placenta and destroys the fetal thyroid gland, causing permanent neonatal hypothyroidism.[2][3]
- **Thyroidectomy (D)** is reserved for cases where antithyroid drugs are contraindicated or fail to control hyperthyroidism, and if needed, should be performed in the second trimester to minimize anesthetic teratogenicity. [3]

Would you like to explore the monitoring strategy and dose adjustment approach for PTU during pregnancy, including when and whether to transition to methimazole after the first trimester?

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Question 90

A 32-year-old woman comes to the physician because of a 3-week history of intermittent loose stools and a 1.2-kg (2.6-lb) weight loss. She immigrated to the US from Uganda 6 weeks ago. Abdominal examination shows diffuse tenderness with no guarding or rebound. The liver is firm and palpable 3 cm below the right costal margin, and the spleen is palpable just below the left costal margin. Her leukocyte count is 12,800/mm3 (12% eosinophils). Stool culture shows several oval-shaped eggs with lateral spines. Microscopic examination of a liver biopsy specimen shows granulomatous inflammation with periportal fibrosis. Exposure to which of the following is most likely to have played a role in the development of this patient's symptoms?

Answer Choices:

(A) Undercooked pork meat
(B) Undercooked fish meat
(C) Dog feces
(D) Freshwater snails

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/3ae1cd53-77af-4c37-b538-70ef05a50542

OpenEvidence Explanation

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The answer is **D. Freshwater snails**.

This clinical presentation is classic for **Schistosoma mansoni** infection (intestinal schistosomiasis):

- **Epidemiology**: The patient recently immigrated from **Uganda**, which is endemic for *S. mansoni* (particularly around Lake Victoria).
- **Clinical features**: Intermittent loose stools, weight loss, **hepatosplenomegaly**, and **peripheral eosinophilia** (12%) are hallmark findings.
- **Stool findings**: **Oval-shaped eggs with lateral spines** are pathognomonic for *S. mansoni* (as opposed to *S. haematobium*, which has a terminal spine).
- **Liver biopsy**: **Granulomatous inflammation with periportal fibrosis** (Symmer's pipestem fibrosis) results from the host immune response to eggs deposited in the portal venous system.

Life cycle and exposure: *Schistosoma* species require **freshwater snails** (genus *Biomphalaria* for *S. mansoni*) as intermediate hosts. Cercariae are released from snails into freshwater and penetrate human skin during activities such as swimming, bathing, or wading. There is no ingestion required — the route of infection is percutaneous contact with contaminated freshwater.

The other options correspond to different parasites:

- **A. Undercooked pork** → *Taenia solium* (tapeworm/cysticercosis) or *Trichinella spiralis*
- **B. Undercooked fish** → *Clonorchis sinensis* or *Diphyllobothrium latum*
- **C. Dog feces** → *Echinococcus granulosus* (hydatid disease) or *Toxocara canis*

Would you like to explore the treatment approach for schistosomiasis, including praziquantel dosing and monitoring for hepatosplenic disease?

Question 91

A 3-month-old girl is brought to a pediatrician by her parents. She has central cyanosis without signs of respiratory distress or signs of heart failure. An echocardiogram reveals severe pulmonary outflow obstruction, right ventricular hypertrophy, a ventricular septal defect, and an overriding of the aorta. An elective primary surgical repair is planned at 4 months of age. Which of the following statements is true about this girl's condition?

Answer Choices:

(A) The tricuspid valve is the most common valve affected by bacterial endocarditis in uncorrected tetralogy of Fallot.
(B) Normal hemoglobin in patients with tetralogy of Fallot does not rule out iron deficiency anemia.
(C) Cerebral arterial thrombosis is more common than cerebral venous thrombosis.
(D) Refractory heart failure is a common complication of tetralogy of Fallot.

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/85ebe1e3-8aa8-4207-b8fd-7da8d21521ef

OpenEvidence Explanation

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The correct answer is **B. Normal hemoglobin in patients with tetralogy of Fallot does not rule out iron deficiency anemia.**

This is a key hematologic principle in cyanotic congenital heart disease. In TOF, chronic hypoxemia drives secondary erythrocytosis, which elevates hemoglobin and hematocrit as a compensatory mechanism. Because of this baseline elevation, a patient can have significant iron deficiency yet still maintain a "normal" hemoglobin level — the iron deficiency is effectively masked by the erythrocytotic response.[1][2] The 2018 AHA/ACC guidelines emphasize that iron deficiency requires assessment of **serum iron, ferritin, and transferrin saturation levels**, because mean corpuscular volume is not a reliable screening test in this population, and hemoglobin alone is insufficient.[1][3] Iron deficiency in cyanotic CHD reduces hemoglobin content per red cell without proportionally lowering hematocrit, thereby compromising oxygen transport while paradoxically increasing viscosity risk.[4]

Why the other options are incorrect:

- **A (Tricuspid valve most common in endocarditis):** In uncorrected TOF, the **aortic valve** is the most commonly affected valve by endocarditis, not the tricuspid valve. The overriding aorta and the high-velocity jet across the VSD create turbulent flow that damages the aortic valve endothelium, predisposing it to vegetation formation.[5][6]
- **C (Cerebral arterial thrombosis more common than venous):** In children with cyanotic CHD, **cerebral venous thrombosis** is actually more common than arterial thrombosis. The polycythemia, hyperviscosity, and iron deficiency associated with cyanotic CHD particularly predispose to venous sinus thrombosis. Iron deficiency anemia is a well-established risk factor for cerebral venous sinus thrombosis in children.[7][8][9]
- **D (Refractory heart failure is a common complication):** Heart failure is **not** a common complication of uncorrected TOF. The large VSD equalizes ventricular pressures, and the right ventricular outflow tract obstruction limits pulmonary blood flow, so volume overload of the pulmonary circulation does not occur. Heart failure is more characteristic of the late sequelae of *repaired* TOF (from chronic pulmonary regurgitation and RV dilation) rather than the uncorrected lesion.[1][10]

Would you like to explore the management of iron deficiency in cyanotic congenital heart disease, including monitoring strategies and safe iron supplementation protocols?

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Question 92

Six days after undergoing surgical repair of a hip fracture, a previously healthy 79-year-old woman is agitated and confused. She is unarousable during the day, but then is awake and impulsive during the night, requiring frequent reorientation. Her husband says that she usually drinks one to two glasses of wine weekly. Her only current medication is oxycodone for pain. Her vital signs are within normal limits. She is distressed and oriented to person but not to place or time. Neurologic examination shows inattentiveness but no focal deficits. Urine dipstick is normal. Which of the following is the most likely cause of her current condition?

Answer Choices:

(A) Dementia
(B) Opioid intoxication
(C) Delirium
(D) Urinary tract infection

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/18c104bb-fca2-4c9e-aabf-f90318c5bae1

OpenEvidence Explanation

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The answer is **C. Delirium**.

This presentation is classic for **postoperative delirium**, which is the most common complication in elderly patients after hip fracture surgery, with incidence rates ranging from **35–65%**. Several features strongly support this diagnosis:

- **Acute onset** with fluctuating course (unarousable during the day, awake and agitated at night — a hallmark "sundowning" pattern)
- **Inattentiveness** on neurologic exam — inattention is the cardinal feature of delirium
- **Disorientation** to place and time with preserved orientation to person
- **Altered level of consciousness** that fluctuates

Why not the other options?

- **A. Dementia** — Dementia is chronic and progressive, not acute in onset. It does not typically present with the fluctuating arousal and sleep-wake cycle disruption seen here. While dementia is a risk factor for delirium, the acute postoperative timeline points to delirium.
- **B. Opioid intoxication** — While opioids (oxycodone) can contribute to delirium and cause sedation, pure opioid intoxication would present with persistent somnolence, miosis, and respiratory depression rather than the characteristic fluctuating pattern with nocturnal agitation and impulsivity.
- **D. Urinary tract infection** — The urine dipstick is normal, making UTI unlikely as the primary cause.

Key risk factors present in this patient include **advanced age (≥65)**, **hip fracture surgery**, and **opioid use** — all well-established precipitants of postoperative delirium. Management priorities include addressing modifiable contributors (minimizing opioids, optimizing sleep hygiene, reorientation strategies, and ensuring adequate hydration/nutrition).

Would you like to explore evidence-based non-pharmacologic and pharmacologic strategies for preventing and managing postoperative delirium in elderly hip fracture patients?

Question 93

A 54-year-old woman with a past medical history of mental retardation, hypertension, and diabetes presents to the emergency department with a change in her behavior. Her caretakers state that the patient's gait suddenly became ataxic, and she became less responsive than her normal non-verbal baseline. Her temperature is 98.5°F (36.9°C), blood pressure is 125/68 mmHg, pulse is 90/min, respirations are 15/min, and oxygen saturation is 99% on room air. Physical exam is notable for an unremarkable HEENT exam with normal facial features and no signs of airway compromise. Neurological exam is remarkable for new onset spasticity. The patient has 3+ reflexes and a positive Babinski sign. Musculoskeletal exam is only notable for symmetric swelling and deformities of the patient's hands bilaterally. Additionally, there is a clunk when posterior force is applied to the head while anterior force is applied to the cervical spine. Which of the following is the most likely risk factor that predisposed this patient to this condition?

Answer Choices:

(A) Cerebral palsy
(B) Diabetes mellitus
(C) Down syndrome
(D) Rheumatoid arthritis

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/7ff87bfa-afef-45e3-9701-3e4dc16ecccd

OpenEvidence Explanation

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The answer is **D. Rheumatoid arthritis**.

This patient is presenting with **atlantoaxial subluxation** (AAS), evidenced by the positive "clunk test" (posterior force on the head with anterior force on the cervical spine), combined with upper motor neuron signs of cervical myelopathy — new-onset spasticity, hyperreflexia (3+ reflexes), positive Babinski sign, and ataxic gait. The key distinguishing feature pointing to the predisposing risk factor is the **symmetric swelling and deformities of the hands bilaterally**, which is characteristic of rheumatoid arthritis (RA).

Why rheumatoid arthritis and not Down syndrome?

While both RA and Down syndrome are well-established risk factors for atlantoaxial instability, the clinical presentation here favors RA as the predisposing condition:[1][2]

- The patient has **symmetric hand joint deformities** — a hallmark of RA, not Down syndrome.[3]
- The HEENT exam describes **normal facial features**, which argues against Down syndrome (which typically presents with characteristic facial dysmorphism such as epicanthal folds, flat nasal bridge, and upslanting palpebral fissures).[4]
- Although the patient has intellectual disability, this alone is not specific to Down syndrome and can occur in many conditions.

Mechanism in RA: Rheumatoid arthritis causes pannus formation (synovial tissue proliferation) around the odontoid process and erosion of the transverse ligament, leading to C1-C2 instability and potential spinal cord compression.[3][5] A 59-year-old woman with RA presenting with progressive gait difficulties, hyperreflexia, and MRI-confirmed anterior subluxation of the atlas with retrodental pannus has been described as a classic presentation.[3]

Mechanism in Down syndrome: Atlantoaxial instability in Down syndrome results from ligamentous laxity at C1-C2, with prevalence of approximately 10–30%, though symptomatic myelopathy occurs in only 1–2%.[6][7][8]

The other answer choices — **cerebral palsy** and **diabetes mellitus** — are not recognized risk factors for atlantoaxial subluxation.

Would you like to explore the diagnostic workup and management approach for atlantoaxial subluxation in the setting of rheumatoid arthritis, including imaging modalities and surgical indications?

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Question 95

A 40-year-old man presents to his primary-care doctor for a follow-up of his hypertension. He is asymptomatic at his office visit and denies any new complaints. He has a 10-year history of hypertension that remains poorly controlled on maximum doses of lisinopril, hydrochlorothiazide, and amlodipine. His past medical history is otherwise unremarkable. He has no smoking history, drinks alcohol occasionally, and denies any illicit drug use. His father required a kidney transplant in his forties. The physical exam is notable for palpable flank masses bilaterally. Laboratory studies show a creatinine of 2.5. The physician orders a renal ultrasound, and the results are shown. Which of the following is the most appropriate test to screen for additional complications of this patient's condition?

Answer Choices:

(A) Colonoscopy
(B) Esophagogastroduodenoscopy
(C) Liver function tests
(D) MR angiography of the brain

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/6f8822b6-f55f-4351-9e74-da1369c58bc0

OpenEvidence Explanation

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The correct answer is **D. MR angiography of the brain**.

This patient's presentation — young-onset resistant hypertension, bilateral palpable flank masses, elevated creatinine, and a father who required kidney transplant in his forties — is classic for **autosomal dominant polycystic kidney disease (ADPKD)**. The most important additional complication to screen for is **intracranial aneurysm (ICA)**, which is detected by MR angiography of the brain.

Why MR angiography? Patients with ADPKD have a 4–5-fold increased risk of intracranial aneurysms compared to the general population, with an overall prevalence of approximately **12.6%**.[1][2] Although most are small and asymptomatic, rupture can cause subarachnoid hemorrhage with significant morbidity and mortality. The KDIGO 2025 guidelines recommend screening with **time-of-flight MRA without gadolinium** as the preferred modality.[3] Screening is particularly recommended in patients with a family history of ICA, SAH, or unexplained sudden death, and should also be discussed in patients with poorly controlled hypertension — a modifiable risk factor for both ICA development and rupture.[3] This patient's father required a kidney transplant in his forties (suggesting severe ADPKD), and the patient himself has poorly controlled hypertension and stage 3–4 CKD, both of which are independent risk factors for ICA detection.[1]

Why not the other options?

- **A. Colonoscopy** — While colonic diverticulosis can occur in ADPKD, routine surveillance colonoscopy is not recommended in asymptomatic patients.[4]
- **B. EGD** — Not a recognized screening recommendation in ADPKD.
- **C. Liver function tests** — Hepatic cysts are extremely common in ADPKD (>90% of patients over age 35), but they rarely cause hepatic dysfunction, and LFTs are not the appropriate screening test for this complication.[5]

Would you like to explore the specific management approach when an intracranial aneurysm is detected on screening in ADPKD, including size thresholds for intervention versus observation?

Relevant images

(CONTENT OMITTED)

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Question 97

A 26-year-old male presents to his primary care physician with complaints of burning with urination, penile discharge, and intermittent fevers. A urethral smear shows gram negative diplococci within white blood cells. The organism grows well when cultured on Thayer-Martin agar. The patient is prescribed a course of ceftriaxone and the infection resolves without further complication. One year later, the patient returns with the same infection. Which of the following best explains this lack of lasting immunity?

Answer Choices:

(A) Exotoxin release
(B) Antigenic variation
(C) Polysaccharide capsule
(D) Bruton's agammaglobulinemia

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/87e35c49-86b0-44dc-ae94-90fcff887fca

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OpenEvidence Explanation

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The correct answer is **B. Antigenic variation**.

The clinical vignette describes a classic case of **gonococcal urethritis** caused by *Neisseria gonorrhoeae* — identified by gram-negative intracellular diplococci on urethral smear and growth on Thayer-Martin (selective chocolate agar) media. The key question is why the patient can be reinfected one year later despite a prior immune response.

Antigenic variation is the primary mechanism by which N. *gonorrhoeae* evades lasting immunity. The organism undergoes rapid variation of multiple surface antigens, including:

- **Pilin (type IV pili):** Antigenic variation occurs through recombination between the expressed *pilE* gene and multiple silent *pilS* gene copies, at a rate exceeding 4×10^{-3} events per cell per generation — the highest reported for any pathogenic organism.[1]
- **Opacity-associated (Opa) proteins:** Phase and antigenic variation of these outer membrane proteins occurs through changes in repetitive DNA sequences, with each genome containing 9–12 *opa* loci encoding on average 7 distinct alleles.[2][3]
- **Lipooligosaccharide (LOS):** Additional surface variation further diversifies the antigenic profile.[3]

This continuous reshuffling of surface antigens means that antibodies generated against one set of surface structures during the initial infection are ineffective against the antigenically distinct variants encountered upon reinfection.[4][5] Additionally, N. *gonorrhoeae* actively suppresses adaptive immunity by inducing Th17 responses while suppressing Th1/Th2 responses and specific antibody production via TGF-β and regulatory T cells.[5][6]

Why the other options are incorrect:

- **A. Exotoxin release** — N. *gonorrhoeae* does not produce classical exotoxins; this is not a mechanism of immune evasion for this organism.
- **C. Polysaccharide capsule** — N. *gonorrhoeae* does not have a polysaccharide capsule (unlike N. *meningitidis*).
- **D. Bruton's agammaglobulinemia** — This X-linked immunodeficiency would present with recurrent infections from early childhood across many

pathogens, not isolated reinfection with a single STI in an otherwise healthy 26-year-old.

Would you like to explore the current evidence on cross-protective immunity from meningococcal B vaccines against gonococcal infection?

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Question 98

A 37-year-old man with no significant past medical history is rear-ended in a motor vehicle accident. He reported significant neck pain to emergency responders, but otherwise denies weakness, numbness or tingling in his extremities. His vitals on presentation to the ED are HR 90, BP 140/80, RR 20, SpO2 98%. What is the most appropriate next step upon presentation to the emergency room?

> **Answer Choices:**
>
> (A) Lateral cervical film
> (B) Cervical immobilization
> (C) IV methylprednisolone
> (D) Observation overnight

> **Correct Answer:**
>
> **(B)**
>
> **OpenEvidence Response:**
>
> **(B)** ✓

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OpenEvidence Explanation

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The most appropriate next step is **B. Cervical immobilization**. In a trauma patient presenting with significant neck pain after a motor vehicle accident, the standard of care is to maintain **cervical spine motion restriction** until the spine can be properly evaluated and cleared.[1]

Why cervical immobilization first:

The recommended standard of care for patients transported by EMS after blunt trauma is maintenance of cervical spine motion restriction until further assessment by an appropriate provider.[1] This patient reports significant neck pain, which is a key symptom that prevents immediate clinical clearance. Both the **NEXUS** and **Canadian C-Spine Rule (CCR)** criteria require the absence of midline cervical tenderness and the ability to actively rotate the head 45° in each direction before the cervical spine can be cleared without imaging.[1][2] Until these assessments are performed, immobilization must be maintained.

Why not the other options:

- **A. Lateral cervical film** — Plain radiography alone is insufficient. If imaging is indicated, **CT without contrast** is the recommended initial imaging modality for adults ≥16 years with suspected cervical spine blunt trauma, as it has near 100% sensitivity for clinically significant injuries. Imaging is a subsequent step after immobilization and clinical assessment, not the immediate first action.[3]
- **C. IV methylprednisolone** — High-dose methylprednisolone for acute spinal cord injury is no longer recommended as standard of care and is not indicated here, particularly given the absence of neurological deficits.
- **D. Observation overnight** — Observation alone without immobilization or proper cervical spine evaluation would be inappropriate and potentially dangerous.

The clinical sequence is: immobilize → assess using NEXUS/CCR criteria → obtain CT cervical spine if criteria are met → clear or continue immobilization based on results.[1][4]

Would you like to explore the specific steps for applying the NEXUS and Canadian C-Spine Rule criteria to determine whether this patient requires cervical spine imaging?

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Question 101

A 65-year old man presents with gradually worsening rigidity of his arms and legs and slowness in performing tasks. He says he has also noticed hand tremors, which increase at rest and decrease with focused movements. On examination, the patient does not swing his arms while walking and has a shortened, shuffling gait. An antiviral drug is prescribed which alleviates the patient's symptoms. Which of the following drugs was most likely prescribed to this patient?

> **Answer Choices:**
>
> (A) Amantadine
> (B) Ribavirin
> (C) Levodopa
> (D) Zidovudine

> **Correct Answer:**
>
> **(A)**
>
> **OpenEvidence Response:**
>
> **(A)** ✓

OpenEvidence Link: https://openevidence.com/ask/4d308afb-5962-418d-8f3c-863b41bc9241

OpenEvidence Explanation

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The correct answer is **A. Amantadine**.

The clinical presentation — resting tremor, rigidity, bradykinesia, shuffling gait, and decreased arm swing — is classic for **Parkinson disease**.[1][2][3] The question's key distinguishing detail is that the prescribed drug is described as an **antiviral** agent.

Amantadine was originally developed as an antiviral drug for influenza A prophylaxis and treatment, but was serendipitously discovered to have antiparkinsonian activity.[4][5] It improves akinesia, rigidity, and tremor through multiple mechanisms including augmentation of dopamine release, blockade of dopamine reuptake, and NMDA receptor antagonism.[6] It is FDA-approved for both influenza A and Parkinson disease.[4]

Why not the other options:

- **Levodopa (C)** is the most effective treatment for Parkinson disease motor symptoms and is the first-line agent, but it is **not an antiviral drug** — it is a dopamine precursor.[1][7]
- **Ribavirin (B)** is an antiviral used for hepatitis C and RSV; it has no role in Parkinson disease.
- **Zidovudine (D)** is an antiretroviral (nucleoside reverse transcriptase inhibitor) used for HIV; it has no antiparkinsonian activity.

The question specifically asks for an antiviral drug that alleviates parkinsonian symptoms, which uniquely identifies amantadine — the only medication that bridges both antiviral and antiparkinsonian indications.[4][8]

Would you like to explore the specific mechanisms by which amantadine exerts its antiparkinsonian effects, including its NMDA receptor antagonism and dopaminergic properties?

Relevant images

(CONTENT OMITTED)

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Question 105

A 28-year-old woman presents following a suicide attempt 2 days ago. She says that her attempt was a result of a fight with her boyfriend and that she slit her wrists in an attempt to keep him from breaking up with her. In the past, she has had many turbulent relationships, both romantic and in her family life. Her family members describe her as being very impulsive and frequently acting to manipulate people's feelings. Since she was admitted to the hospital, she has spit at several staff members and alternated between sobbing and anger. She has no significant past medical history. The patient denies any history of smoking, alcohol use, or recreational drug use. Which of the following is the most likely diagnosis in this patient?

Answer Choices:

(A) Histrionic personality disorder
(B) Borderline personality disorder
(C) Dependent personality disorder
(D) Narcissistic personality disorder

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/62892665-f1d2-4c87-b00e-318eec9034ef

OpenEvidence Explanation

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The answer is **B. Borderline personality disorder (BPD)**.

This patient's presentation is classic for BPD, which is characterized by a **pervasive pattern of instability in interpersonal relationships, self-image, and affects, along with marked impulsivity**.[1][2] Several DSM-5 diagnostic criteria are clearly met in this vignette:

- **Self-harm/suicidal behavior** — wrist-cutting as a suicide gesture precipitated by threatened abandonment[2][3]
- **Frantic efforts to avoid abandonment** — the self-harm was explicitly motivated by preventing her boyfriend from leaving[4]
- **Unstable, intense interpersonal relationships** — a history of many turbulent romantic and family relationships[2][3]
- **Impulsivity** — described as "very impulsive" by family[2]
- **Inappropriate, intense anger** — alternating between sobbing and anger, spitting at staff[3]
- **Affective instability** — rapid shifts between emotional states[3]

Why not the other options?

- **Histrionic personality disorder (A):** While both can involve attention-seeking and manipulative behavior, BPD is distinguished by **self-destructiveness, angry disruptions in close relationships, and chronic feelings of emptiness**. Histrionic PD is characterized more by excessive emotionality and attention-seeking without the self-harm and abandonment fears seen here.[4]
- **Dependent personality disorder (C):** Dependent PD involves excessive need to be taken care of, resulting in submissive and clinging behavior — not the impulsivity, anger, and self-destructive behavior seen in this patient.[2]
- **Narcissistic personality disorder (D):** Narcissistic PD is characterized by **grandiosity, need for admiration, and lack of empathy**. The relative lack of self-destructiveness, impulsivity, and abandonment concerns distinguishes it from BPD.[2][4]

The key distinguishing feature in this case is the combination of **self-destructive behavior triggered by fear of abandonment** with unstable relationships and emotional lability — a hallmark triad of BPD.[4][5]

Would you like to explore the evidence-based psychotherapy options (e.g., DBT, MBT) for managing borderline personality disorder?

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Question 108

A 13-year-old boy presents to the emergency department with severe knee, hip, and groin pain. The patient has a past medical history notable only for obesity and asthma. His temperature is 98°F (36.7°C), blood pressure is 124/65 mmHg, pulse is 128/min, respirations are 14/min, and oxygen saturation is 99% on room air. Physical exam is notable for an inability of the patient to bear weight on his left leg and limited range of motion of the left hip. Which of the following is the best management for this patient?

Answer Choices:

(A) Casting and crutches
(B) Immobilization of the hip in a Pavlik harness
(C) Supportive therapy and observation
(D) Surgical pinning of the femoral head

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/9db645df-e0a1-4227-83da-3cdef55d3d34

OpenEvidence Explanation

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The correct answer is **D. Surgical pinning of the femoral head**.

This presentation is classic for **slipped capital femoral epiphysis (SCFE)** — the most common hip disorder in adolescents. The key features pointing to this diagnosis include the patient's age (13 years), **obesity**, hip/groin/knee pain, inability to bear weight, and limited hip range of motion.[1][2]

Why surgical pinning?

SCFE is treated surgically with **in situ screw fixation**, which is the standard of care for both stable and unstable SCFE.[2][3] This patient's inability to bear weight classifies this as **unstable SCFE**, which carries a significantly higher risk of avascular necrosis (up to 50%) and requires urgent surgical intervention, ideally within 24 hours.[2] A systematic review confirmed that the best evidence supports single screw in situ fixation for stable SCFE and urgent reduction with internal fixation for unstable SCFE.[3]

Why not the other options?

- **A (Casting and crutches):** Non-operative management is insufficient — SCFE always requires surgical intervention to prevent progression and complications such as avascular necrosis and chondrolysis.[2][4]
- **B (Pavlik harness):** This is used for developmental dysplasia of the hip in infants, not for SCFE in adolescents.
- **C (Supportive therapy and observation):** Observation alone risks further slippage and devastating complications including avascular necrosis and lifelong disability.[2][5]

Would you like to explore the differences in surgical approaches and outcomes between stable and unstable SCFE, including the role of the modified Dunn procedure?

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Question 110

A 51-year-old man is brought to the emergency department because of a 2-day history of fever, abdominal pain, and confusion. His wife states that he has been unable to recall his birthday or her name. He was diagnosed with hepatitis C 3 years ago but refused treatment. He has been treated twice in the past year for acute pancreatitis. There is no family history of serious illness. His only medication is a calcium supplement. He emigrated from India 15 years ago. He appears ill. His temperature is 38.3°C (100.9°F), pulse is 101/min, and blood pressure is 104/68 mm Hg. He is confused and oriented only to person. Examination shows scleral icterus and spider angiomas. There are fine tremors of the hands bilaterally. The abdomen is distended and shifting dullness is present. There is diffuse tenderness to palpation with no guarding. Bowel sounds are absent. Laboratory studies show:
Hemoglobin 12.6 g/dL
Leukocyte count 13,900/mm3
Platelet count 342,000/mm3
Serum
Albumin 2.6 g/dL
Total bilirubin 2.56 mg/dL
Alkaline phosphatase 54 U/L
AST 17 U/L
ALT 44 U/L
Paracentesis is performed. Ascitic fluid analysis shows an albumin concentration of 0.8 g/dL, glucose concentration of 62 mg/dL, and a leukocyte count of 1900/mm3 with 60% neutrophils. Which of the following is the most likely explanation for these findings?

Answer Choices:

(A) Aseptic peritoneal inflammation
(B) Neoplastic growth
(C) Bacterial translocation
(D) Perforated viscus

> **Correct Answer:**
>
> (C)
>
> **OpenEvidence Response:**
>
> (C) ✓

OpenEvidence Link: https://openevidence.com/ask/680cfbe6-06f6-4883-935b-6ca79bc4541d

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OpenEvidence Explanation

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The correct answer is **C. Bacterial translocation**.

This patient presents with decompensated cirrhosis (hepatitis C, scleral icterus, spider angiomas, ascites) complicated by **spontaneous bacterial peritonitis (SBP)**, which is caused by bacterial translocation from the gut.

Diagnosing SBP: The ascitic fluid shows a leukocyte count of 1,900/mm³ with 60% neutrophils, yielding an absolute neutrophil count of **1,140/mm³** — well above the diagnostic threshold of ≥250 neutrophils/mm³.[1][2] The serum-ascites albumin gradient (SAAG) is 2.6 − 0.8 = **1.8 g/dL** (≥1.1), confirming portal hypertension as the cause of ascites. The clinical picture — fever, confusion (hepatic encephalopathy), abdominal pain, absent bowel sounds (ileus), and leukocytosis — is classic for SBP.[2][3]

Why bacterial translocation: SBP is defined as infection of ascitic fluid without an identifiable intra-abdominal surgically treatable source.[3] Its pathogenesis involves **bacterial translocation** — the passage of gut bacteria (typically monomicrobial, gram-negative Enterobacteriaceae or Streptococcaceae) across a compromised intestinal barrier into mesenteric lymph nodes and the bloodstream, ultimately seeding the ascitic fluid.[2][4] Cirrhosis-associated immune dysfunction, portal hypertension, increased intestinal permeability, and gut dysbiosis all promote this process.[5][6]

Why not the other options:

- **A. Aseptic peritoneal inflammation** — The elevated PMN count with clinical signs of infection points to a bacterial process, not sterile inflammation.
- **B. Neoplastic growth** — Peritoneal carcinomatosis typically produces ascites with a low SAAG (<1.1), elevated protein, and lymphocyte predominance rather than neutrophil predominance.
- **D. Perforated viscus** — Secondary peritonitis from perforation typically shows ascitic fluid with very high protein, very low glucose (<50 mg/dL), elevated LDH, polymicrobial organisms on Gram stain, and often requires multiple criteria to distinguish from SBP. This patient's glucose of 62 mg/dL and the absence of guarding or rebound tenderness argue against perforation. Additionally, the clinical context of decompensated cirrhosis with no surgical abdomen strongly favors SBP.

Would you like to explore the empiric antibiotic regimens and albumin co-administration protocols recommended for SBP management?

Relevant images

(CONTENT OMITTED)

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Question 113

A 67-year-old man with chronic kidney disease comes to the physician because of worsening fatigue and shortness of breath on exertion for 6 months. He has a 20-year history of poorly-controlled type 2 diabetes mellitus. Current medications include metformin and insulin. His pulse is 105/min. Examination shows conjunctival pallor and bounding pulses. Laboratory studies show:
Hemoglobin 8.6 g/dL
Mean corpuscular volume 90 µm3
Reticulocyte count 0.5%
Serum
Ferritin 325 ng/mL
Urea nitrogen 45 mg/dL
Creatinine 2.2 mg/dL
The patient is prescribed a drug to treat the cause of his current symptoms. The drug's mechanism of action directly involves which of the following signaling pathways?

Answer Choices:

(A) PI3K/Akt/mTOR
(B) MAP kinase
(C) JAK/STAT
(D) IP3

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/dcace61b-3aac-459b-ab3c-fa600b371130

OpenEvidence Explanation

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The answer is **C. JAK/STAT**.

This patient presents with **anemia of chronic kidney disease** — normocytic anemia (MCV 90 μm³), low reticulocyte count (0.5%, indicating hypoproliferative anemia), elevated ferritin (ruling out iron deficiency), and elevated BUN/creatinine consistent with CKD. The cause is inadequate erythropoietin (EPO) production by the diseased kidneys.[1][2] The drug prescribed to treat this is an **erythropoiesis-stimulating agent (ESA)** such as epoetin alfa.[3][4]

EPO binds to the erythropoietin receptor (EPOR), a type I cytokine receptor, on erythroid progenitor cells. Upon EPO binding, EPOR homodimerizes and activates **JAK2 (Janus kinase 2)**, which phosphorylates tyrosine residues on the receptor's intracellular domain. This creates docking sites for **STAT5** (signal transducer and activator of transcription 5), which itself becomes phosphorylated, dimerizes, and translocates to the nucleus to activate genes promoting erythroid cell survival, proliferation, and differentiation.[5][6][7]

The following figure illustrates the EPO/EPOR-JAK2-STAT5 signaling pathway in erythroid progenitor cells:

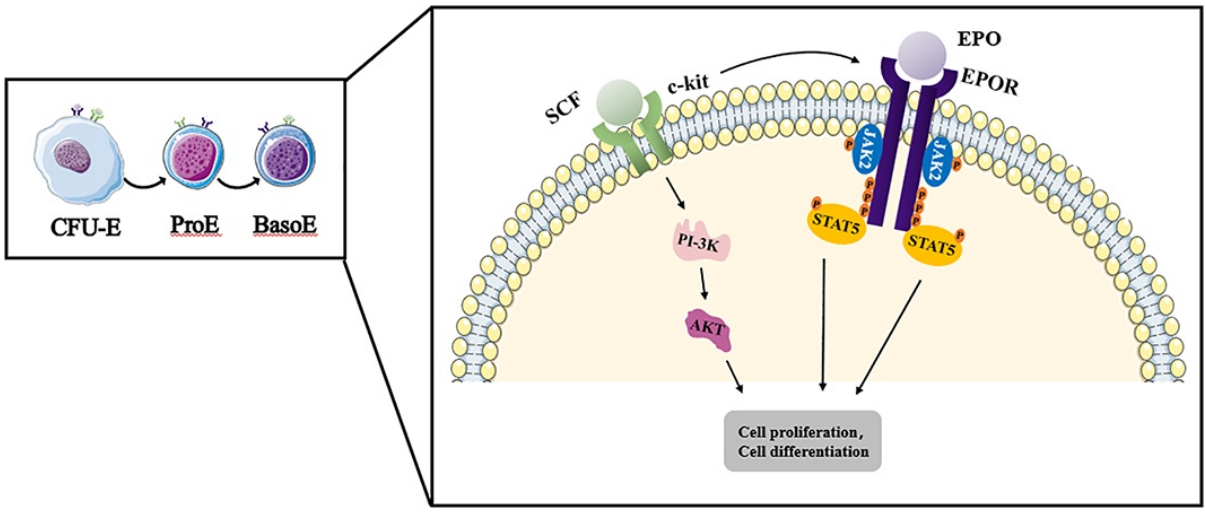


Figure 3. Signaling pathways involved in the regulation of erythrocyte maturation. After birth, signalling pathways involved in erythropoiesis. BasoE, basophilic erythroblast; CFU-E stands for colony-forming unit erythroid; EPO, erythropoietin; EPOR, the erythropoietin receptor; JAK2, tyrosine kinase 2; ProE, proerythroblast erythroblast; SCF, stem cell factor. STAT5, signal transducer and activator of transcription. The circled P represents phosphorylation.

While EPO signaling also activates secondary pathways including PI3K/Akt and MAPK, the[6][8] **JAK2/STAT5 pathway is the canonical and primary signaling mechanism** through which EPO exerts its erythropoietic effects.[5][7][9] Among the answer choices, JAK/STAT is the pathway most directly involved in the drug's mechanism of action.

Would you like to explore the comparative efficacy and safety of ESAs versus the newer HIF-prolyl hydroxylase inhibitors for managing anemia in CKD?

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Question 117

A 66-year-old man presents to the emergency department with abdominal pain, nausea, and vomiting. He endorses diffuse abdominal tenderness. His past medical history is notable for diabetic nephropathy, hypertension, dyslipidemia, depression, and morbid obesity. He also is currently being treated for an outbreak of genital herpes. His temperature is 99.0°F (37.2°C), blood pressure is 184/102 mmHg, pulse is 89/min, respirations are 18/min, and oxygen saturation is 98% on room air. Physical exam is notable for an obese man in no acute distress. A CT scan of the abdomen with contrast is performed and is unremarkable. The patient is admitted to the observation unit for monitoring of his pain. Notably, the patient's abdominal pain improves after an enema and multiple bowel movements. The patient's evening laboratory values are ordered and return as seen below.

Serum:
Na+: 141 mEq/L
Cl-: 99 mEq/L
K+: 4.8 mEq/L
HCO3-: 11 mEq/L
BUN: 20 mg/dL
Glucose: 177 mg/dL
Creatinine: 3.1 mg/dL

Which of the following is the most likely etiology of this patient's laboratory derangements?

Answer Choices:

(A) Acyclovir
(B) Atorvastatin
(C) Metformin
(D) Metoprolol

Correct Answer:

> (C)
>
> **OpenEvidence Response:**
>
> (C) ✓

OpenEvidence Link: https://openevidence.com/ask/fb460b36-604b-46ba-8db1-a0d1b68ccda8

OpenEvidence Explanation

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Let me calculate the anion gap to confirm the type of metabolic acidosis.

The answer is **C. Metformin**.

The laboratory values reveal a severe **anion gap metabolic acidosis** (AG = 31, with HCO_3^- of 11 mEq/L) in the setting of an **elevated creatinine (3.1 mg/dL)** in a patient with diabetic nephropathy. This constellation is classic for **metformin-associated lactic acidosis (MALA)**.

Why metformin? This patient has type 2 diabetes (implied by diabetic nephropathy and glucose of 177 mg/dL) and is likely on metformin as first-line therapy. Metformin is substantially excreted by the kidney, and in patients with significant renal impairment, drug accumulation leads to inhibition of mitochondrial complex I, shifting metabolism toward anaerobic glycolysis and impairing hepatic lactate clearance.[1][2] The resulting high anion gap metabolic acidosis with elevated lactate (>5 mmol/L) and pH <7.35 are hallmarks of MALA.[2] Notably, MALA is fundamentally an accumulation disorder precipitated by acute decline in kidney function rather than intrinsic toxicity at therapeutic concentrations.[2] This patient's baseline CKD from diabetic nephropathy, combined with a potential acute-on-chronic kidney injury (creatinine 3.1), creates the ideal setting for metformin accumulation. The ADA/KDIGO consensus report notes that metformin is contraindicated at eGFR <30 mL/min/

1.73 m^2 and that most episodes of MALA occur concurrent with acute illness when AKI contributes to reduced metformin clearance.[3]

Why not the other options?

- **Acyclovir (A):** While acyclovir can cause nephrotoxicity via crystal deposition in renal tubules, this typically presents with AKI alone (rising creatinine) rather than a high anion gap metabolic acidosis. Additionally, acyclovir-induced AKI is more commonly associated with IV administration rather than oral dosing for genital herpes.[4][5]
- **Atorvastatin (B):** Statins do not cause metabolic acidosis. Renal injury from statins is exceedingly rare and occurs almost exclusively through rhabdomyolysis-induced myoglobinuria.[6][7]
- **Metoprolol (D):** Metoprolol is primarily hepatically metabolized and does not cause metabolic acidosis or significant nephrotoxicity.[8][9]

Would you like to explore the current guidelines on metformin dosing adjustments and monitoring in patients with chronic kidney disease?

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Question 118

A 56-year-old man comes to the clinic for a check-up. He presents with a 1-year history of worsening shortness of breath and weight loss. He is a former construction worker, and worked in a steel mill when he was in high school. He is an active smoker with a 36-pack-year smoking history. The blood pressure is 130/78 mm Hg, pulse rate is 90/min, respiratory rate is 17/min, and the BMI is 31 kg/m2. The patient is afebrile and the oxygen saturation at rest is 95% on room air. The pulmonary examination reveals a mildly prolonged expiratory phase, and no wheezing or crackles are auscultated. A pulmonary function test is recommended for the patient, and 2 weeks later he returns with a report that shows an FEV1/FVC ratio of 60% and FEV1 of 50% of the predicted value. The lung volumes show a total lung capacity of 110% of predicted value, a residual volume of 115% of predicted value, and a DLCO of 60% of predicted value. Which of the following is the most likely diagnosis?

Answer Choices:

(A) Asbestosis
(B) Idiopathic pulmonary fibrosis
(C) Bronchiectasis
(D) Chronic obstructive pulmonary disease

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/494cc7e0-ee2b-4de8-9860-036d116adc13

OpenEvidence Explanation

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The most likely diagnosis is **D. Chronic obstructive pulmonary disease (COPD)**.

The pulmonary function test findings in this patient demonstrate a classic **obstructive pattern**: FEV1/FVC ratio of 60% (below 0.70), FEV1 of 50% predicted, increased total lung capacity (110% predicted), and increased residual volume (115% predicted) — all consistent with air trapping and hyperinflation seen in COPD.[1][2] The reduced DLCO at 60% predicted further supports emphysematous changes, which are common in COPD and associated with increased symptoms, decreased exercise capacity, and worse prognosis.[1]

Key distinguishing features from the other answer choices:

- **Asbestosis (A)** and **idiopathic pulmonary fibrosis (B)** produce a **restrictive** pattern on PFTs — decreased FVC, decreased TLC, low residual volume, and a normal or increased FEV1/FVC ratio. This patient's increased TLC and RV with a reduced FEV1/FVC ratio are the opposite of what would be expected in fibrotic lung disease. Additionally, asbestosis and IPF typically present with Velcro-like crackles on auscultation, which are absent here.[3][4]
- **Bronchiectasis (C)** can produce an obstructive pattern, but it typically presents with chronic productive cough, recurrent infections, and crackles on examination — none of which are described in this vignette.

This patient's 36-pack-year smoking history is the dominant risk factor. The prolonged expiratory phase on exam, progressive dyspnea, and obstructive PFT pattern with hyperinflation and reduced DLCO are hallmarks of COPD. Per GOLD severity staging, an FEV1 of 50% predicted classifies this as **GOLD Stage III (severe)** airflow obstruction.[2]

Would you like to explore the recommended initial management strategy for this patient, including pharmacotherapy and smoking cessation interventions per the 2026 GOLD guidelines?

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Question 119

A 25-year-old zookeeper presents to the office complaining of a dry cough, fever, and chills for the past month. He states that the symptoms come in episodes at the end of the workday and last a few hours. He also mentions that he is fatigued all the time. His job includes taking care of various types of birds. He is otherwise fine and denies recent travel or trauma. Medical history is unremarkable and he does not take any medications. He does not smoke cigarettes or drinks alcohol. Allergies include peanuts, dust, and pollen. Childhood asthma runs in the family. Chest X-ray reveals diffuse haziness in both lower lung fields. A PPD skin test is negative. What is the most appropriate treatment for this patient?

Answer Choices:

(A) Thoracocentesis
(B) Inhaled beclomethasone
(C) Avoid exposure to birds
(D) Isoniazid for 6 months

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/cd0195d2-418d-4266-9940-b9466df8ab3e

OpenEvidence Explanation

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The correct answer is **C. Avoid exposure to birds**.

This presentation is classic for **hypersensitivity pneumonitis (HP)**, specifically **bird fancier's lung** (also called bird breeder's lung). The key clinical features pointing to this diagnosis include:

- **Episodic dry cough, fever, and chills** occurring at the end of the workday (4–8 hours after antigen exposure is the typical latency for acute HP)[1]
- **Occupational exposure to birds** as a zookeeper caring for various bird species
- **Bilateral diffuse lower lung field haziness** on chest X-ray, consistent with ground-glass opacities seen in HP[2]
- **Negative PPD**, ruling out tuberculosis

Complete antigen avoidance is the mainstay of treatment for hypersensitivity pneumonitis.[3][4][5] The CHEST guidelines emphasize that surveillance for exposure and patient education focused on antigen avoidance at every visit is the "highest priority".[6] Studies demonstrate that antigen avoidance leads to symptomatic improvement in a majority of patients — in one cohort, 50% achieved normalization and 28% showed improvement in FVC after avian contact ceased.[6] Even in fibrotic HP, antigen identification and avoidance are associated with decreased all-cause mortality and transplantation (adjusted HR 0.47, 95% CI 0.31–0.71).[7]

Why the other options are incorrect:

- **A. Thoracocentesis** — There is no pleural effusion described; the diffuse bilateral haziness is parenchymal, not pleural.
- **B. Inhaled beclomethasone** — HP is not an asthma-equivalent condition. While systemic corticosteroids may accelerate initial recovery, they do not alter long-term prognosis, and inhaled corticosteroids are not the treatment for HP.[1][8]
- **D. Isoniazid for 6 months** — The PPD is negative, effectively excluding latent tuberculosis, making isoniazid unnecessary.

Would you like to explore the role of systemic corticosteroids as adjunctive therapy in cases of hypersensitivity pneumonitis where antigen avoidance alone is insufficient?

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Question 120

A 60-year-old female presents to her gynecologist with vaginal bleeding. She underwent menopause ten years prior. She has a past medical history of hypertension and diabetes mellitus. On physical examination, her uterus is uniformly enlarged. Ultrasound reveals a thickened endometrial stripe and tissue biopsy reveals neoplastic endometrial cells. A workup for metastatic disease is negative and the gynecologist recommends a laparoscopic hysterectomy. During the procedure, the surgeon ligates multiple vessels in order to remove the entire uterus. In the immediate postoperative period, the patient develops left-sided flank pain and oliguria. Serum creatinine is found to be 1.4 mg/dl whereas it was 1.0 mg/dl prior to the operation. Renal ultrasound is normal. Urinalysis is notable for hematuria. Ligation of which of the following vessels most likely contributed to this patient's condition?

Answer Choices:

(A) Artery of Sampson
(B) Ovarian artery
(C) Superior vesical artery
(D) Uterine artery

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/e9e18c6b-983c-46e9-af72-899c04e9cf8d

OpenEvidence Explanation

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The answer is **D. Uterine artery**. The clinical presentation — left-sided flank pain, oliguria, rising creatinine, and hematuria following hysterectomy — is consistent with **iatrogenic ureteral injury**, which most commonly occurs at the point where the **uterine artery crosses over the ureter**.

Anatomic basis: The ureter passes beneath the uterine artery approximately 2 cm lateral to the uterine cervix (classically remembered as "water under the bridge"). During hysterectomy, ligation of the uterine artery at this level places the ureter at risk for inadvertent ligation, kinking, transection, or thermal injury. A prospective study found that **80% of ureteral injuries during hysterectomy occurred at the junction of the ureter and the uterine artery**.[1] The average distance between the ureter and cervix is only 2 cm, and in 3.2% of the population it is as close as 0.5 cm.[2]

Clinical correlation: Ureteral obstruction or injury leads to ipsilateral flank pain, oliguria (especially if bilateral or if the contralateral kidney has limited reserve), rising serum creatinine, and hematuria — all present in this patient. Renal ultrasound may initially appear normal before hydronephrosis develops, as obstruction can take hours to manifest on imaging.[3] Unrecognized ureteral injury significantly increases the risk of acute renal insufficiency (aOR 23.8) and other serious complications.[4]

Why not the other options:

- **Artery of Sampson** (A) runs within the round ligament and supplies the round ligament; its ligation does not endanger the ureter.
- **Ovarian artery** (B) courses in the infundibulopelvic ligament at the pelvic brim, well above the typical site of ureteral injury during hysterectomy.
- **Superior vesical artery** (C) supplies the bladder and is not in close anatomic proximity to the ureter at the level where injuries typically occur during hysterectomy.

Would you like to explore the recommended strategies for intraoperative prevention and early detection of ureteral injuries during hysterectomy, including the role of prophylactic ureteral stenting?

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Question 121

A 40-year-old man presents to the physician with progressive weight loss for the last 3 months. He also says he frequently sweats profusely at night and has a recurring low-grade fever, for which he takes acetaminophen. The patient denies any symptoms like cough, breathlessness, or gastrointestinal symptoms. His temperature is 37.1°C (98.8°F), pulse is 76/min, blood pressure is 116/78 mm Hg, and respiratory rate is 13/min. On physical examination, he has generalized pallor. Bilateral cervical lymphadenopathy is present. Examination of his abdomen reveals non-tender hepatosplenomegaly in the right upper quadrant. Laboratory evaluation confirms the diagnosis of Hodgkin's lymphoma. Which of the following viral infections is most likely to have played a role in the pathogenesis of this patient's malignancy?

Answer Choices:

(A) Epstein-Barr virus
(B) Human T-cell leukemia virus type 1
(C) Human herpesvirus-8
(D) Human papillomavirus type 16

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/fc1aecec-c1a0-48d5-8e1a-231e803f896d

OpenEvidence Explanation

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The correct answer is **A. Epstein-Barr virus (EBV)**.

Epstein-Barr virus is the viral infection most strongly implicated in the pathogenesis of Hodgkin lymphoma. EBV is causally associated with approximately **25–40%** of classical Hodgkin lymphoma cases in developed countries and up to 80% in developing countries.[1][2] The EBV genome is detected within the malignant Hodgkin and Reed-Sternberg (HRS) cells, and the infection is clonal, confirming that infection precedes malignant transformation.[3]

The key oncogenic mechanism involves EBV's **latent membrane protein 1 (LMP-1)**, the principal viral oncoprotein, which mimics CD40 signaling and constitutively activates NF-κB, JAK-STAT, and JNK pathways, thereby rescuing proapoptotic germinal center B cells from programmed cell death and promoting their proliferation and survival.[1][4] LMP-2A similarly mimics B-cell receptor signaling, providing additional survival signals.[3] A landmark study in the NEJM demonstrated that infectious mononucleosis (caused by EBV) significantly increases the risk of EBV-positive Hodgkin lymphoma (relative risk 4.0), with a median incubation time of approximately 4 years.[5]

The other answer choices are associated with different malignancies:

- **HTLV-1** (B) → Adult T-cell leukemia/lymphoma
- **HHV-8** (C) → Kaposi sarcoma and primary effusion lymphoma[6]
- **HPV-16** (D) → Cervical, oropharyngeal, and anogenital carcinomas

Would you like to explore the specific molecular mechanisms by which EBV's latent proteins drive Reed-Sternberg cell formation and immune evasion in Hodgkin lymphoma?

Relevant images

(CONTENT OMITTED)

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Question 122

A 28-year-old gravida 1 at 32 weeks gestation is evaluated for an abnormal ultrasound that showed fetal microcephaly. Early in the 1st trimester, she had fevers and headaches for 1 week. She also experienced myalgias, arthralgias, and a pruritic maculopapular rash. The symptoms resolved without any medications. A week prior to her symptoms, she had traveled to Brazil where she spent most of the evenings hiking. She did not use any mosquito repellents. There is no personal or family history of chronic or congenital diseases. Medications include iron supplementation and a multivitamin. She received all of the recommended childhood vaccinations. She does not drink alcohol or smoke cigarettes. The IgM and IgG titers for toxoplasmosis were negative. Which of the following is the most likely etiologic agent?

Answer Choices:

(A) Dengue virus
(B) Rubella virus
(C) Toxoplasmosis
(D) Zika virus

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/cb93b851-5897-4a06-b2f2-7af081feefa5

OpenEvidence Explanation

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The answer is **D. Zika virus**.

The clinical presentation — travel to Brazil, mosquito exposure (evening hiking without repellent), a self-limited illness with **pruritic maculopapular rash, arthralgias, myalgias, low-grade fever, and headache** in the first trimester, followed by fetal **microcephaly** on ultrasound — is classic for congenital Zika virus syndrome.

Why Zika virus is most likely:

- The maternal symptoms match the typical ZIKV clinical presentation: a pruritic descending maculopapular rash, arthralgias, conjunctival injection, headache, and low-grade short-duration fever.[1]
- ZIKV is transmitted by Aedes mosquitoes, which are endemic in Brazil and bite primarily during dawn and dusk — consistent with her evening hiking without repellent.[2]
- First-trimester ZIKV infection carries the highest risk of fetal brain anomalies, including microcephaly, with a relative risk of approximately 16.8 for infection in the first or second trimester. The absolute risk of microcephaly ranges from 2.5–6.1% among ZIKV-positive pregnancies.[3][4]
- Negative toxoplasmosis serologies rule out that diagnosis.

Why the other options are less likely:

- **Dengue virus (A):** While also mosquito-borne and endemic in Brazil, dengue does not cause congenital microcephaly. ZIKV uniquely infects fetal endothelial cells via the AXL receptor with much greater efficiency than dengue.[5]
- **Rubella virus (B):** Congenital rubella can cause microcephaly, but the patient received all recommended childhood vaccinations (including MMR), making rubella immunity highly likely. Additionally, congenital rubella has been effectively eradicated in Brazil.[6]
- **Toxoplasmosis (C):** Explicitly ruled out by negative IgM and IgG titers.

Would you like to explore the recommended diagnostic workup and surveillance protocol for suspected congenital Zika syndrome, including the role of amniocentesis and serial imaging?

Relevant images

(CONTENT OMITTED)

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Question 124

A obstetrician is working in a developing country to help promote maternal health and fetal well being. While there, he delivers a baby who he suspects has congenital hypothyroidism, most likely caused by inadequate maternal iodine intake. Which of the following signs and symptoms would NOT be expected to be observed in this child?

Answer Choices:

(A) Hypotonia
(B) Diarrhea
(C) Umbilical hernia
(D) Macroglossia

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/c0d4f902-68b4-4397-9d1a-728c010a3f82

OpenEvidence Explanation

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The answer is **B. Diarrhea**.

Diarrhea is not a feature of congenital hypothyroidism; in fact, the opposite — **constipation** — is a classic gastrointestinal manifestation. Hypothyroidism slows

GI motility, leading to delayed bowel movements and constipation, not diarrhea.[1][2][3]

The other three options are all well-recognized signs of congenital hypothyroidism:

- **Hypotonia** — physical examination may reveal hypotonia with delayed reflexes.[2]
- **Umbilical hernia** — one of the most common signs, consistently listed across guidelines and reviews.[1][2][4]
- **Macroglossia** (large tongue) — also among the most common signs, resulting from myxedematous tissue infiltration.[2][4]

Additional classic features of untreated congenital hypothyroidism include prolonged jaundice, lethargy, poor feeding, hoarse cry, bradycardia, large posterior fontanelle, mottled skin, coarse facies, and hypothermia.[1][2][5] In the context of this question, iodine deficiency is a recognized environmental cause of congenital hypothyroidism, particularly in developing countries where iodine supplementation programs may be inadequate.[2]

Would you like to explore the recommended screening and treatment protocols for congenital hypothyroidism in resource-limited settings?

Relevant images

(CONTENT OMITTED)

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Question 127

A 67-year-old man with peripheral neuropathy comes to the physician for a follow-up examination after the results of serum protein electrophoresis showed monoclonal gammopathy. A complete blood count, serum creatinine, and serum electrolyte concentrations are within the reference ranges. A bone marrow biopsy shows 6% monoclonal plasma cells. Further analysis shows that class I major histocompatibility molecules are downregulated in these monoclonal plasma cells. The proliferation of these monoclonal plasma cells is normally prevented by a class of immune cells that lyse abnormal cells without the need for opsonization, priming, or prior activation. Which of the following best describes this class of immune cells?

Answer Choices:

(A) Bone marrow-derived macrophages
(B) CD4+ T lymphocytes
(C) Natural killer cells
(D) Band neutrophils

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/018ebaad-1135-4fc0-ac44-8308a25273e6

OpenEvidence Explanation

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The answer is **C. Natural killer cells**.

The question describes immune cells that lyse abnormal cells **without the need for opsonization, priming, or prior activation** — and that specifically target cells with **downregulated MHC class I molecules**. This is the hallmark of **natural killer (NK) cells** and their "missing-self" recognition mechanism.

NK cells are innate immune lymphocytes whose cytotoxic activity is governed by a balance between inhibitory and activating surface receptors. The dominant inhibitory signal arises from the interaction of killer immunoglobulin-like receptors (KIRs) and CD94/NKG2A with MHC class I molecules on healthy cells. [1][2] When MHC class I expression is reduced — as occurs in tumor cells or virally infected cells — this inhibitory signal is lost, and NK cells become activated to kill the target cell. This process is termed **"missing-self" recognition**.[1][3][4]

The following figure illustrates the mechanism of NK cell activation through missing-self recognition:

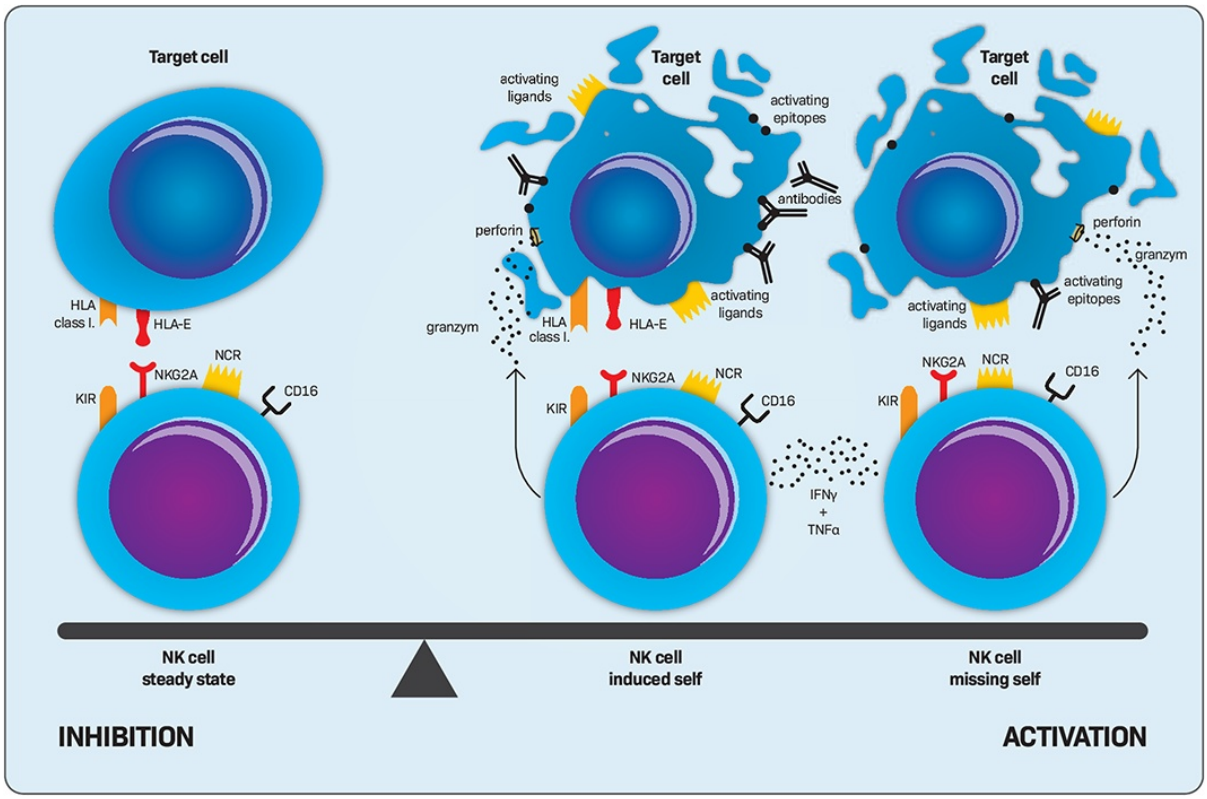


Figure 1. Schematic mechanism of action of NK cells. Under natural circumstances, a set of inhibitory receptors outbalance activating receptors which are missing their ligands. As a result, the NK cell remains in a steady state (left). If a cell is attacked by a virus, its DNA is damaged or changed by

tumorigenesis, it can express various sets of activating ligands which bind to activating receptors on NK cells. In addition, monoclonal antibodies bind to different epitopes expressed on the surface of affected cells, which leads to antibody-dependent cell cytotoxicity via the CD16 receptor on NK cells. This is called the self-induced activation theory (middle). Finally, tumor cells may try to escape T-cell surveillance through downregulation of human leukocyte antigen class I. In that case, NK cells are unable to bind their KIR receptors, become aware of a possible harmful event, and activating receptors initiate the effector functions (missing-self theory, right). Once activated, perforin and granzyme are released, ultimately leading to the lysis and death of the targeted cell. Concurrently, the NK cell produces a large amount of cytokines such as IFN- γ and TNF- α. Inhibitory receptors are represented here by KIR and NKG2A, and activating receptors are represented by the natural cytotoxicity receptor family (including NKp30, NKp44, and NKp46) and CD16. NK cell, natural killer cell; HLA, human leukocyte antigen; KIR, killer cell immunoglobulin-like receptor; NCR, natural cytotoxicity receptor; IFN-γ, interferon γ; TNF-α, tumor necrosis factor α

This is directly relevant to the clinical scenario presented. The monoclonal plasma cells in this patient have downregulated MHC class I molecules, which would normally make them susceptible to NK cell-mediated killing. Indeed, NK cells play a critical role in immunosurveillance against multiple myeloma, and progressive NK cell dysfunction is recognized as a determinant of myeloma progression from MGUS to active disease.[5][6][7]

Why the other options are incorrect:

- **Bone marrow-derived macrophages (A):** Macrophages require opsonization (e.g., antibody or complement coating) for efficient phagocytosis and do not use missing-self recognition.
- **CD4+ T lymphocytes (B):** These are helper T cells that require antigen presentation via MHC class II molecules and prior activation/priming; they do not directly lyse targets via missing-self recognition.
- **Band neutrophils (D):** These are immature granulocytes involved in acute inflammatory responses and require opsonization for phagocytosis; they do not perform missing-self surveillance.

Would you like to explore how NK cell dysfunction contributes to the progression from monoclonal gammopathy of undetermined significance (MGUS) to active multiple myeloma?

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Question 129

A 41-year-old man presents to the emergency room with sudden onset of blurry vision one hour ago. He states that he was resting at home when he noticed he had difficulty reading. Currently, he is also starting to see double, and is seeing two images on top of each other. Earlier today, he felt ill with nausea, vomiting, and watery diarrhea, which he attributed to food he had eaten at a picnic the day before. When asked which foods he ate, he lists potato salad, a hamburger, deviled eggs, and pickles made by his neighbor. He also heard that his friend who went to the picnic with him has developed similar symptoms and was seen in another hospital earlier. While in the emergency room, the patient's temperature is 98.4°F (36.9°C), pulse is 75/min, blood pressure is 122/84 mmHg, and respirations are 13/min. Cranial nerve exam is notable for fixed pupillary dilation, and difficulty depressing both eyes. The remainder of his exam is normal. Which of the following is the pathogenesis of this patient's presentation?

Answer Choices:

(A) Decreased acetylcholine release
(B) Overactivation of adenylate cyclase
(C) Release of interferon-gamma
(D) Inhibition of GABA release

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/db60bbde-1d17-4a64-bc11-ac1df5e1e53b

OpenEvidence Explanation

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A. Decreased acetylcholine release. This presentation is classic for **foodborne botulism**: GI symptoms after ingestion of likely contaminated food, clustered illness in another picnic attendee, then acute **cranial neuropathies with diplopia, blurred vision, ophthalmoplegia, and fixed dilated pupils**. Botulinum toxin acts at **presynaptic cholinergic nerve terminals**, where it cleaves **SNARE proteins** and thereby **blocks acetylcholine vesicle fusion/release** at the neuromuscular junction, producing a descending flaccid paralysis pattern.[1][2][3]

Why this fits:

- **Early GI symptoms** followed by **cranial nerve findings** are typical of foodborne botulism.[3][4]
- **Fixed dilated pupils** and ophthalmoplegia reflect autonomic and cranial nerve involvement, both common in botulism.[2][4]
- Home-preserved foods are classic exposures; the outbreak clue strongly supports a toxin-mediated foodborne illness.[5][6]

Why the other choices are wrong:

- **B. Overactivation of adenylate cyclase**: suggests cholera toxin or pertussis-related toxin mechanisms, not ophthalmoplegic descending paralysis.
- **C. Release of interferon-gamma**: more consistent with cell-mediated immune activation, not acute neuroparalysis.
- **D. Inhibition of GABA release**: suggests tetanospasmin, which causes **spastic** paralysis by blocking inhibitory interneurons, not flaccid paralysis with diplopia and mydriasis.

Would you like to explore the key bedside features that distinguish **botulism vs myasthenia gravis vs Miller Fisher syndrome** in the ED?

Relevant images

(CONTENT OMITTED)

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Question 130

A 4-week-old female newborn is brought to the physician because of increasing yellowing of her eyes and skin for 2 weeks. The mother has noticed that the girl's stools have become pale over the past week. She was breastfed since birth but her parents switched her to formula feeds recently after reading on the internet that breastfeeding could be the cause of her current symptoms. The patient was delivered vaginally at 38 weeks' gestation. Pregnancy and delivery were uncomplicated. She appears healthy. Vital signs are within normal limits. She is at the 50th percentile for length and at the 60th percentile for weight. Examination shows scleral icterus and jaundice. The liver is palpated 2 cm below the right costal margin. Cardiopulmonary examination shows no abnormalities. Neurologic examination shows no focal findings. Serum studies show:
Bilirubin
Total 15 mg/dL
Direct 12.3 mg/dL
Alkaline phosphatase 2007 U/L
AST 53 U/L
ALT 45 U/L
γ-glutamyl transferase 154 U/L
Blood group A positive
Which of the following is the most likely diagnosis?

Answer Choices:

(A) Galactosemia
(B) Biliary atresia
(C) Crigler–Najjar syndrome
(D) Breast milk jaundice

Correct Answer:

(B)

OpenEvidence Response:

> **(B)** ✓

OpenEvidence Link: https://openevidence.com/ask/f6dee7d6-9414-4195-90b7-b405ddbcd6d2

OpenEvidence Explanation

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The most likely diagnosis is **B. Biliary atresia**.

This presentation is classic for biliary atresia: a 4-week-old infant who appears otherwise healthy with progressive conjugated (direct) hyperbilirubinemia, **acholic (pale) stools**, hepatomegaly, markedly elevated alkaline phosphatase (2007 U/L), elevated GGT (154 U/L), and a predominantly **direct bilirubin** (12.3 of 15 mg/dL total). The key distinguishing features are:

- **Conjugated hyperbilirubinemia with acholic stools** — this combination is a "red flag" for biliary obstruction per NASPGHAN/ESPGHAN guidelines, which identify acholic stools, high-GGT cholestasis, and abnormal gallbladder on ultrasound as findings mandating evaluation for biliary atresia.[1]
- **Apparently well infant** — infants with biliary atresia typically appear healthy and grow normally, which can deceive parents and clinicians into attributing the jaundice to physiologic or breast milk causes.[1]
- **Markedly elevated ALP and GGT with only mildly elevated transaminases** — this obstructive pattern (high ALP/GGT, relatively low AST/ALT) is characteristic of extrahepatic biliary obstruction rather than hepatocellular injury.[2]

Why the other options are incorrect:

- **A. Galactosemia** — Infants with galactosemia typically present acutely ill with vomiting, poor feeding, hepatomegaly, coagulopathy, and often E. coli

sepsis after galactose exposure. This infant appears healthy and has an obstructive biochemical pattern rather than hepatocellular failure.[1]

- **C. Crigler-Najjar syndrome** — This is a disorder of bilirubin conjugation causing severe unconjugated (indirect) hyperbilirubinemia. This infant has predominantly direct hyperbilirubinemia (12.3 mg/dL direct), which rules out Crigler-Najjar.

- **D. Breast milk jaundice** — Breast milk jaundice causes unconjugated hyperbilirubinemia in otherwise well breastfed infants and does not cause acholic stools, hepatomegaly, or elevated direct bilirubin. Notably, the parents' switch to formula based on this assumption was misguided.

Clinical urgency: Timely diagnosis is critical because Kasai portoenterostomy performed before 30 days of life is associated with significantly better native liver survival (RR 1.22 for NLS comparing ≤30 vs >30 days), and each 10-day delay decreases the odds of bilirubin normalization by ~19%.[3][4] At 4 weeks of age, this infant needs urgent referral for abdominal ultrasound, liver biopsy, and likely intraoperative cholangiography.[5][6]

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Question 131

A 43-year-old man comes to the emergency department with nausea, abdominal discomfort, diarrhea, and progressive perioral numbness for the past 24 hours. 3 days ago, he underwent a total thyroidectomy for treatment of papillary thyroid cancer. His only medication is a multivitamin supplement. He appears fatigued. While measuring the patient's blood pressure, the nurse observes a spasm in the patient's hand. Physical examination shows a well-healing surgical wound on the neck. Which of the following ECG findings are most likely in this patient?

Answer Choices:

(A) Torsade de pointes
(B) QT prolongation
(C) Peaked T waves
(D) PR prolongation

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/ec6ba5b6-f6b9-476c-8a40-ee4387574b7a

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OpenEvidence Explanation

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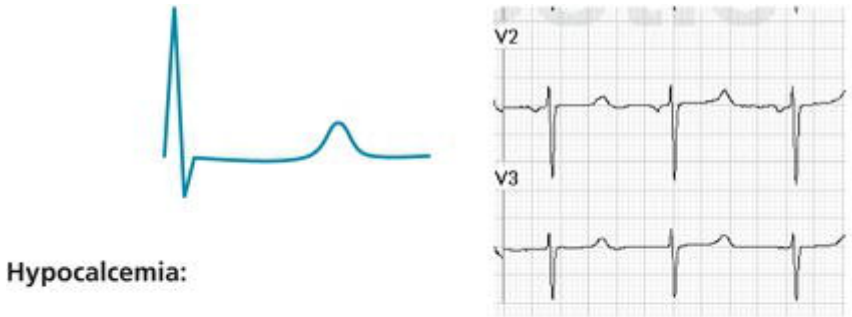
The answer is **B. QT prolongation**.

This patient is presenting with **post-thyroidectomy hypocalcemia** due to inadvertent injury to or devascularization of the parathyroid glands — the most common complication after total thyroidectomy, occurring in up to 19–38% of patients.[1][2] The clinical picture is classic:

- **Timing**: Symptoms developing within days of total thyroidectomy, with calcium nadir typically at 24–48 hours postoperatively[1]
- **Symptoms**: Perioral numbness, nausea, abdominal discomfort, and diarrhea — all consistent with hypocalcemia[3]
- **Trousseau sign**: The hand spasm observed during blood pressure measurement (carpal spasm induced by brachial artery occlusion from cuff inflation) is pathognomonic for hypocalcemia[3][4]

ECG findings in hypocalcemia are characterized by **QT prolongation** due to lengthening of the ST segment (phase 2 of the cardiac action potential). A systematic review demonstrated a statistically significant inverse correlation between corrected QT interval and serum calcium levels.[5] Notably, unlike other causes of QT prolongation (e.g., hypokalemia, drugs), hypocalcemia specifically prolongs the ST segment while preserving normal T-wave morphology.[6]

The following figure illustrates the characteristic ECG changes in calcium disorders:



Hypocalcemia:

Long QT that is due to a long ST segment, which is different from long QT secondary to drugs or hypokalemia. T wave is not wide, there is no T wave abnormality.



Hypercalcemia: short QTc <390 ms. No significant ST or T wave abnormality

Figure 70. Hypocalcemia and hypercalcemia.

Why not the other options?

- **A. Torsade de pointes** — While torsade can occur as a consequence of severe, progressive QT prolongation from hypocalcemia, it is a late and uncommon arrhythmia, not the "most likely" ECG finding.[3]
- **C. Peaked T waves** — This is the hallmark of **hyperkalemia**, not hypocalcemia.
- **D. PR prolongation** — PR prolongation is associated with AV conduction delays (e.g., from hyperkalemia, digoxin, or structural conduction disease), not hypocalcemia.

Would you like to explore the recommended management protocol for post-thyroidectomy hypocalcemia, including calcium and calcitriol supplementation strategies?

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Question 132

A 68-year-old woman presents with left lower quadrant pain that worsens with defecation. She describes the pain as 'crampy'. She also says she has suffered from mild constipation for the past few years. The patient denies any recent weight change or urinary symptoms. Her last menstrual period was 16 years ago. Her body temperature is 37.8°C (100.0°F), pulse is 102/min, respiratory rate is 16/min, and blood pressure is 133/87 mm Hg. On physical examination, tenderness to palpation in the left lower quadrant is present. The laboratory studies are presented as follows:
Hemoglobin 13.2 mg/dL
Hematocrit 48%
Leukocyte count 16,000/mm^3
Neutrophils 89%
Bands 5%
Eosinophils 0%
Basophils 0%
Lymphocytes 11%
Monocytes 0%
Platelet count 380,000/mm^3
Which of the following is the most likely diagnosis in this patient?

Answer Choices:

(A) Diverticulitis
(B) Hypothyroidism
(C) Adenocarcinoma of the colon
(D) Irritable bowel syndrome

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/08f88f03-ec69-472a-9918-d03c11827c57

OpenEvidence Explanation

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The most likely diagnosis is **A. Diverticulitis**.

This 68-year-old woman presents with the classic triad of acute diverticulitis: **left lower quadrant pain**, **low-grade fever** (37.8°C), and **leukocytosis with a left shift** (WBC 16,000/mm³ with 89% neutrophils and 5% bands). The crampy quality of the pain that worsens with defecation, along with her history of chronic constipation, further supports this diagnosis. Approximately 70% of patients with acute diverticulitis present with gradual-onset left lower quadrant pain, and leukocytosis is present in roughly 55% of febrile patients.[1]

Why the other options are less likely:

- **Adenocarcinoma of the colon (C):** While colon cancer can cause left-sided abdominal pain and altered bowel habits, it typically presents with alarm features such as hematochezia, iron deficiency anemia, unexplained weight loss, or change in stool caliber. This patient denies weight change, and the acute presentation with fever and marked leukocytosis with bandemia points toward an infectious/inflammatory process rather than malignancy.[2][3]
- **Irritable bowel syndrome (D):** IBS can cause crampy abdominal pain and altered bowel habits, but it does not cause fever or leukocytosis. IBS pain tends to be diffuse and short-lived, whereas diverticulitis-related pain is localized to the left lower quadrant and persists for more than 24 hours. The presence of systemic inflammatory signs effectively excludes IBS.[4]
- **Hypothyroidism (B):** While hypothyroidism can cause constipation, it does not explain the acute left lower quadrant tenderness, fever, or leukocytosis.

There are no other features suggestive of hypothyroidism (e.g., fatigue, cold intolerance, weight gain).

CT abdomen/pelvis with IV contrast is the recommended next step to confirm the diagnosis and evaluate for complications (sensitivity 98–99%, specificity 99–100%).[1] The World Society of Emergency Surgery specifically recommends against relying solely on clinical signs and laboratory tests in elderly patients with suspected diverticulitis.[5]

Would you like to discuss the management approach for this patient, including the role of antibiotics in uncomplicated diverticulitis?

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Question 134

A 55-year-old man with a history of chronic glomerulonephritis due to IgA nephropathy presents to your office with bone pain. Which of the following laboratory findings would you most expect upon analysis of this patient's serum?

> **Answer Choices:**
>
> (A) Increased PTH, decreased calcium, increased phosphate, decreased calcitriol
> (B) Decreased PTH, increased calcium, increased phosphate, increased calcitriol
> (C) Decreased PTH, decreased calcium, increased phosphate, decreased calcitriol
> (D) Normal PTH, normal calcium, normal phosphate, normal calcitriol

> **Correct Answer:**
>
> **(A)**
>
> **OpenEvidence Response:**
>
> **(A)** ✓

OpenEvidence Link: https://openevidence.com/ask/36f4f553-d7a4-4af8-bfc6-24431f629363

OpenEvidence Explanation

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The correct answer is **A: Increased PTH, decreased calcium, increased phosphate, decreased calcitriol**.

This patient with chronic glomerulonephritis from IgA nephropathy presenting with bone pain has **CKD-mineral and bone disorder (CKD-MBD)** driven by **secondary hyperparathyroidism**. The expected laboratory profile reflects the well-characterized pathophysiology of progressive renal failure:

1. **Decreased calcitriol (1,25-dihydroxyvitamin D)** — The failing kidney loses 1α-hydroxylase activity, reducing conversion of 25-hydroxyvitamin D to its active form. This begins declining as early as CKD stage 2.[1][2]

2. **Increased phosphate** — Impaired renal phosphate excretion leads to phosphate retention. Although compensatory mechanisms (elevated FGF23 and PTH) initially maintain normal serum phosphate, these fail as GFR declines further, resulting in frank hyperphosphatemia.[1][3]

3. **Decreased calcium** — Low calcitriol reduces intestinal calcium absorption, leading to hypocalcemia. This typically becomes apparent when GFR falls below ~50 mL/min/1.73 m^2.[2]

4. **Increased PTH** — Hypocalcemia, hyperphosphatemia, and low calcitriol all independently stimulate PTH synthesis and secretion, producing secondary hyperparathyroidism. Hyperparathyroidism is present in over half of patients with GFR <60 mL/min/1.73 m^2. The chronically elevated PTH drives excessive osteoclast activity, causing the **bone pain** described in this patient.[1][2][4][5]

The following figure illustrates the progressive changes in these mineral metabolism parameters across CKD stages:

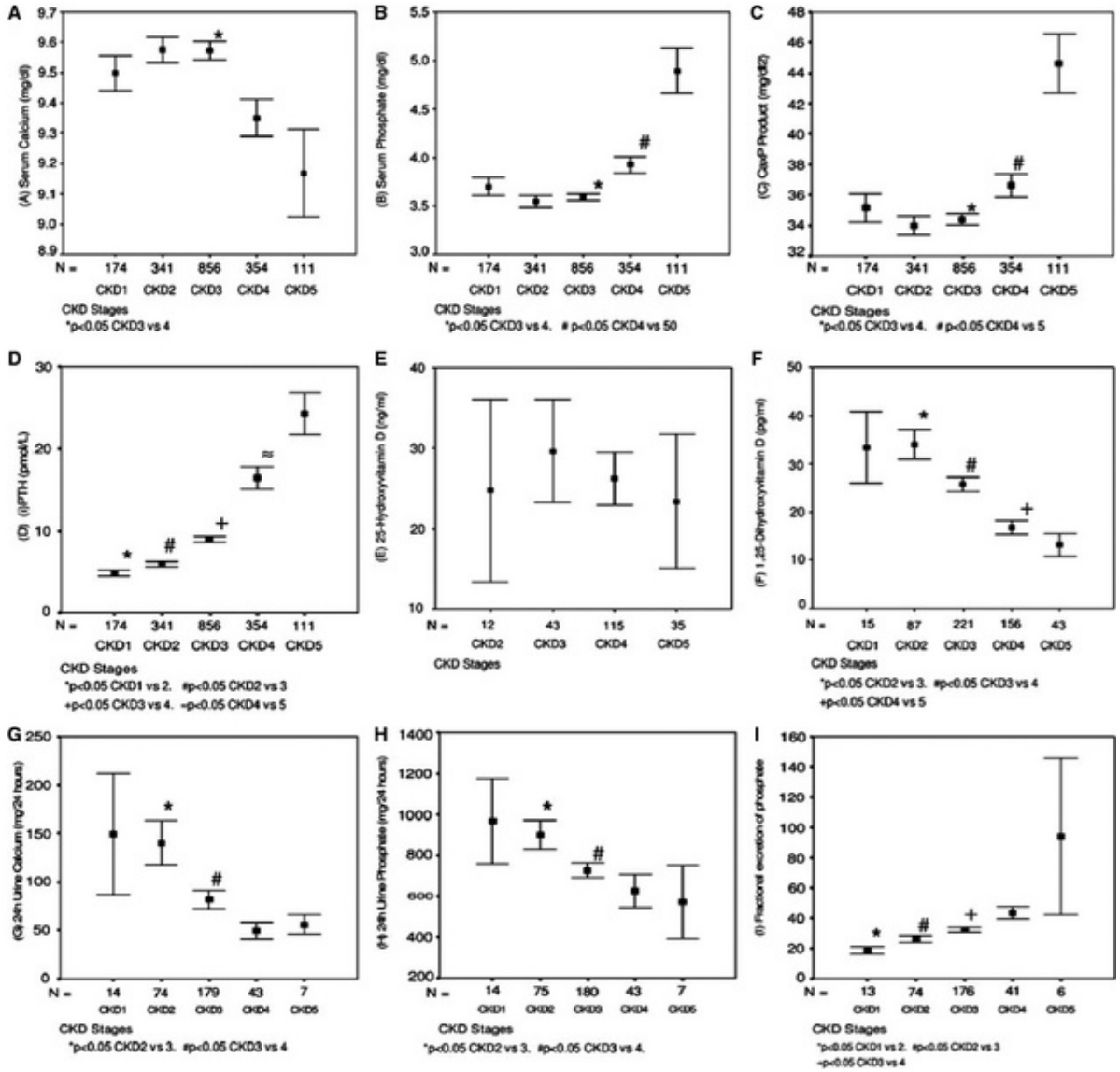


Figure 2. Shown is a cross-sectional representation of values for (A) serum calcium; (B) serum phosphate; (C) calcium-phosphate product; (D) PTH (E) 25 hydroxyvitamin D; (F) 1,25 dihydroxyvitamin D; (G) urine calcium (H) urine phosphate and (I) fractional excretion of phosphate in a large number of patients in stages 1 through 5 CKD (Published with permission from Nephrology, Dialysis, and Transplantation).

The other answer choices are incorrect because they do not reflect this pathophysiologic cascade. Option B (decreased PTH, increased calcium) would suggest hypoparathyroidism or vitamin D toxicity. Option C (decreased PTH) is inconsistent with the expected secondary hyperparathyroidism. Option D (all normal values) would not explain the patient's bone pain in the setting of chronic kidney disease.

Would you like to explore the management strategies for CKD-MBD, including the role of phosphate binders, calcimimetics, and vitamin D analogs in controlling secondary hyperparathyroidism?

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Question 136

A 61-year-old Caucasian male presents to your office with chest pain. He states that he is worried about his heart, as his father died at age 62 from a heart attack. He reports that his chest pain worsens with large meals and spicy foods and improves with calcium carbonate. He denies dyspnea on exertion and an ECG is normal. What is the most likely cause of this patient's pain?

> **Answer Choices:**
>
> (A) Partially occluded coronary artery
> (B) Umbilical hernia
> (C) Gastroesophageal junction incompetence
> (D) Intestinal metaplasia at the gastroesophageal junction

> **Correct Answer:**
>
> (C)
>
> **OpenEvidence Response:**
>
> (C) ✓

OpenEvidence Link: https://openevidence.com/ask/4de83f97-2f6b-43d4-ad85-9538879a27dd

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OpenEvidence Explanation

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The correct answer is **C. Gastroesophageal junction incompetence**.

This patient's presentation is classic for **gastroesophageal reflux disease (GERD)**, which results from incompetence of the lower esophageal sphincter at the

gastroesophageal junction. The key clinical features pointing to this diagnosis include:

- Chest pain that **worsens with large meals and spicy foods**
- **Relief with calcium carbonate** (an antacid)
- **No dyspnea on exertion** and a **normal ECG**, making a cardiac etiology less likely

The 2021 AHA/ACC Chest Pain Guidelines identify GERD as the most likely cause of recurring unexplained chest pain of esophageal origin, noting that it can mimic myocardial ischemia and often occurs after meals, with potential relief from antacids.[1] Symptoms suggestive of an esophageal cause include heartburn, regurgitation, and relief with antacid or antisecretory agents.[1] Up to 50% of patients with noncardiac chest pain have abnormal esophageal findings.[2]

Why the other answers are incorrect:

- **A. Partially occluded coronary artery** — While the family history raises concern, the absence of exertional symptoms, normal ECG, and meal/antacid-related pattern argue strongly against angina.
- **B. Umbilical hernia** — This would present as a periumbilical bulge, not chest pain with meal-related and antacid-responsive features.
- **D. Intestinal metaplasia at the gastroesophageal junction** — This describes Barrett's esophagus, a complication of chronic GERD. Barrett's itself is typically asymptomatic and is a histologic finding, not a cause of chest pain. The underlying mechanism causing this patient's symptoms is the GEJ incompetence (i.e., GERD), not the metaplasia.

Would you like to explore the diagnostic workup approach for distinguishing cardiac from esophageal chest pain in patients with significant cardiac risk factors?

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Question 138

A 7-year-old boy is brought to a pediatrician by his parents for evaluation of frequent bed wetting during the night. A detailed history reveals that there has been no history of urinary incontinence during the day since the boy was 4 years of age, but that he has never been dry at night continuously for 1 week. There is no history of urinary tract infections, urgency, frequency, or hesitancy. On physical examination, the boy's vital signs are stable. His neurologic and abdominal examinations are completely normal. His laboratory investigations are as follows:
Urine-specific gravity (first-morning sample) 1.035
Urine red blood cells Absent
Urine pus cells Absent
Urine culture Negative
Which of the following is the next step in the management of this patient?

Answer Choices:

(A) Magnetic resonance imaging (MRI) of the spine
(B) Reassuring the parents and use of an enuresis alarm
(C) Treatment with oral oxybutynin
(D) Treatment with oral imipramine

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/ab9f6ff6-6023-483a-bb54-5d0ff6e2f6a7

OpenEvidence Explanation

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The correct answer is **B. Reassuring the parents and use of an enuresis alarm**.

This child presents with **primary monosymptomatic nocturnal enuresis** — isolated nighttime bedwetting without daytime symptoms, no prior sustained dry period, normal physical examination, and a normal urinalysis. The high urine-specific gravity (1.035) effectively rules out diabetes insipidus, and the absence of pus cells, RBCs, and a negative culture exclude urinary tract infection.

Why an enuresis alarm is the correct first step:

First-line treatments for primary monosymptomatic nocturnal enuresis include **enuresis alarms and desmopressin**, with parental reassurance and behavioral modification as foundational components.[1] Enuresis alarms are typically offered in children older than 6 years and are highly effective — significantly reducing wet nights (mean deviation −2.68 nights), achieving 14 consecutive dry nights (RR 7.23), and maintaining dryness after discontinuation (RR 9.67) compared with no treatment.[1] Importantly, enuresis alarms have a **lower relapse rate** than desmopressin (46% vs. 65%).[1] The International Children's Continence Society gives alarm therapy a **Level 1, Grade A recommendation**.[2]

Why the other options are incorrect:

- **A (MRI of the spine):** There are no neurologic deficits, no daytime symptoms, and no abnormalities on examination to suggest spinal pathology such as tethered cord. Imaging is not indicated.
- **C (Oxybutynin):** Oxybutynin monotherapy is **not recommended** for monosymptomatic nocturnal enuresis. It is reserved as adjunctive therapy (with desmopressin or imipramine) when first-line treatments fail.[1]
- **D (Imipramine):** Imipramine is a second-line agent used when first-line therapies (alarm, desmopressin) are unsuccessful. It carries risks of cardiotoxicity and requires ECG screening before initiation.[1]

The following figure outlines the treatment algorithm for nocturnal enuresis in children.

FIGURE 1

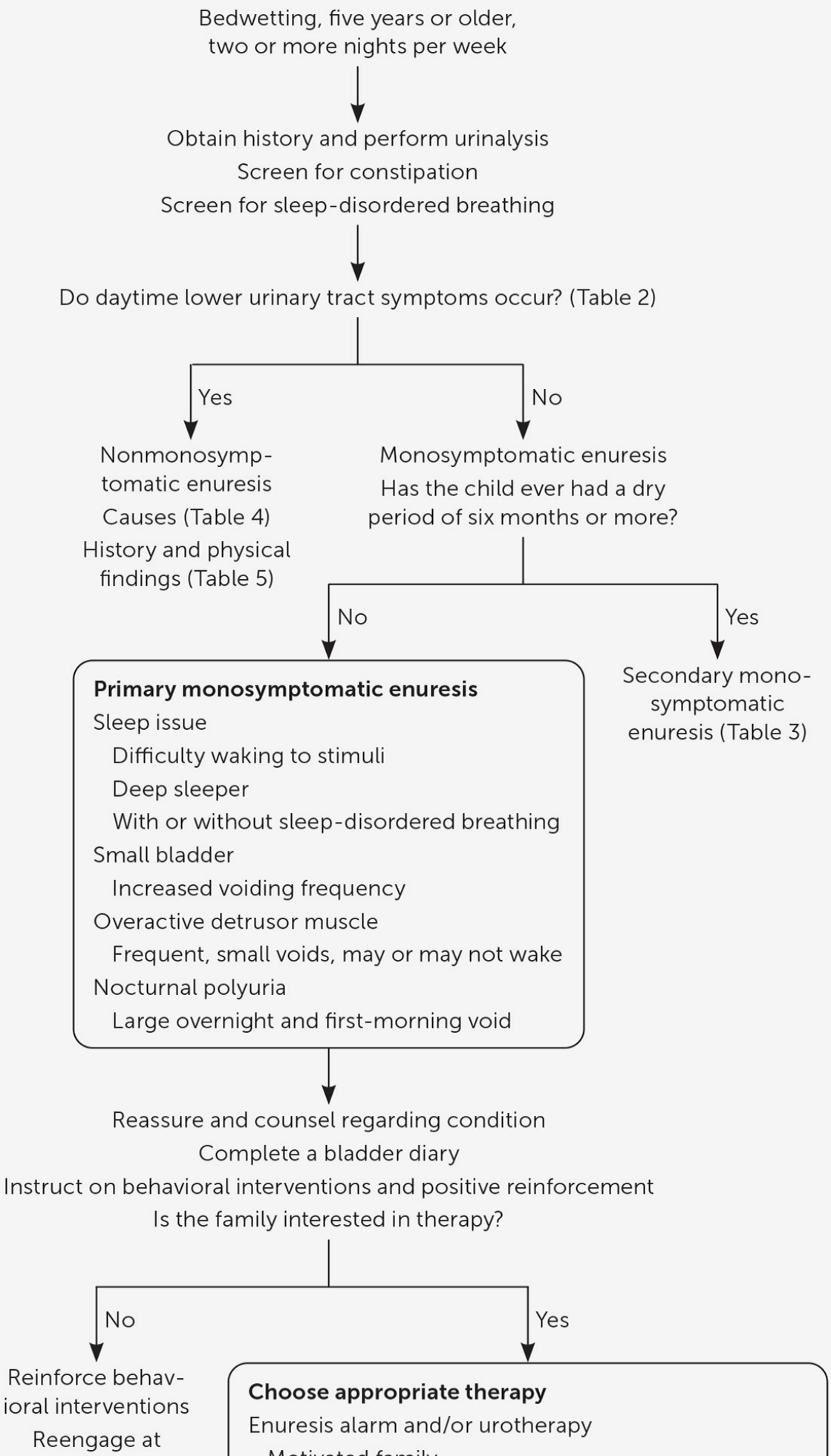

Bedwetting, five years or older, two or more nights per week
Obtain history and perform urinalysis
Screen for constipation
Screen for sleep-disordered breathing
Do daytime lower urinary tract symptoms occur? (Table 2)
Yes
No
Nonmonosymptomatic enuresis
Causes (Table 4)
History and physical findings (Table 5)
Monosymptomatic enuresis
Has the child ever had a dry period of six months or more?
No
Yes
Secondary monosymptomatic enuresis (Table 3)
Primary monosymptomatic enuresis
Sleep issue
Difficulty waking to stimuli
Deep sleeper
With or without sleep-disordered breathing
Small bladder
Increased voiding frequency
Overactive detrusor muscle
Frequent, small voids, may or may not wake
Nocturnal polyuria
Large overnight and first-morning void
Reassure and counsel regarding condition
Complete a bladder diary
Instruct on behavioral interventions and positive reinforcement
Is the family interested in therapy?
No
Yes
Reinforce behavioral interventions
Reengage at
Choose appropriate therapy
Enuresis alarm and/or urotherapy

Figure 1. Treatment of nocturnal enuresis in children. Information from references 1, 14–17, 21–24, and 27–32.

Would you like to explore the specific criteria for distinguishing monosymptomatic from nonmonosymptomatic enuresis and how the workup differs between them?

References

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Question 142

A 67-year-woman with non-Hodgkin lymphoma comes to the physician because of progressively increasing numbness and tingling in her fingers and toes. Her last cycle of chemotherapy with vincristine was 1 week ago. Physical examination shows decreased sensation to light touch in all distal extremities. Knee and ankle deep tendon reflexes are decreased. Which of the following is the most likely underlying mechanism of this patient's peripheral neuropathy?

Answer Choices:

(A) Inhibition of beta-tubulin polymerization
(B) Creation of free radicals that unwind DNA
(C) Inhibition of dihydrofolate reductase
(D) Incorporation of false pyrimidine analogues into DNA

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/2b6225d2-25a9-4ced-8cae-ffc63c56b122

OpenEvidence Explanation

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The correct answer is **A. Inhibition of beta-tubulin polymerization**.

Vincristine is a vinca alkaloid that causes peripheral neuropathy through its effects on the microtubule cytoskeleton. Vinca alkaloids bind to the **β-subunit of tubulin heterodimers, preventing their polymerization and incorporation into microtubules**.[1] This leads to cytoskeletal disorganization and microtubule disorientation within axons, which inhibits vesicle-mediated axonal transport and causes axonal degeneration — a process termed "dying back neuropathy".[1]

The clinical presentation described — distal sensory loss (numbness and tingling in fingers and toes), decreased light touch sensation, and diminished deep tendon reflexes — is classic for vincristine-induced peripheral neuropathy. The FDA label notes a characteristic sequence: sensory impairment and paresthesias appear first, followed by neuritic pain, and later motor difficulties with continued treatment.[2] This neuropathy is dose-dependent and length-dependent, consistent with the distal-predominant pattern seen here.[3][4]

The other answer choices correspond to different chemotherapeutic mechanisms:

- **B (Free radicals that unwind DNA)** — describes bleomycin
- **C (Inhibition of dihydrofolate reductase)** — describes methotrexate
- **D (Incorporation of false pyrimidine analogues into DNA)** — describes agents like 5-fluorouracil or cytarabine

Would you like to explore the evidence-based management strategies for vincristine-induced peripheral neuropathy, including dose modification thresholds and neuroprotective agents?

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Question 144

A 14-year-old girl comes to the physician with her father for evaluation of her short stature. She feels well overall, but is concerned because all of her friends are taller than her. Her birth weight was normal. Her father reports he had a short stature during his teenage years; he is currently 177 cm (5 ft 10 in) tall. She is at the 2ndpercentile for height and 35th percentile for weight. Breast development is Tanner stage 2. Pubic and axillary hair is absent. An x-ray of the left hand and wrist shows a bone age of 11 years. Which of the following is the most appropriate next best step in management?

Answer Choices:

(A) Pelvic ultrasound
(B) Measure serum dehydroepiandrosterone levels
(C) Reassurance and follow-up
(D) MRI of the brain

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/c9cb9680-dc76-4614-8a10-86a7743eb125

OpenEvidence Explanation

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The correct answer is **C. Reassurance and follow-up**.

This presentation is classic for **constitutional delay of growth and puberty (CDGP)**. The key features supporting this diagnosis include:

- **Family history**: The father reports having short stature during his teenage years but achieved a normal adult height of 177 cm, indicating a familial pattern of late growth and pubertal maturation.[1]
- **Delayed bone age**: Bone age of 11 years in a 14-year-old (3-year delay) is characteristic of CDGP, indicating remaining growth potential.[2][3]
- **Normal birth weight**: Rules out small-for-gestational-age as a cause of short stature.[1]
- **Early but present pubertal development**: Tanner stage 2 breast development indicates puberty has begun, albeit late. The absent pubic/axillary hair is consistent with delayed adrenarche accompanying the overall maturational delay.[4]
- **Otherwise well child**: No features suggesting pathologic causes such as chronic disease, GH deficiency, or Turner syndrome.

CDGP is a self-limited condition in which puberty starts later than usual but progresses normally, with catch-up growth occurring once puberty is fully underway.[2][5] When puberty has started and stature is not a major concern, reassurance with realistic adult height prediction is frequently sufficient.[4] Specialty referral is not typically warranted unless growth delay causes significant psychological distress, in which case low-dose estrogen therapy may be considered.[2]

Why the other options are incorrect:

- **A (Pelvic ultrasound)**: Would be indicated if there were concern for gonadal dysgenesis (e.g., Turner syndrome), but this patient has begun pubertal development and lacks stigmata of Turner syndrome.
- **B (Serum DHEA levels)**: Absent pubic/axillary hair reflects delayed adrenarche consistent with the overall constitutional delay; measuring DHEA is unnecessary in this context.

- **D (Brain MRI)**: Would be warranted if there were concern for a CNS lesion causing GH deficiency or hypogonadotropic hypogonadism, but the clinical picture is consistent with a benign variant of growth.

Would you like to explore the indications for initiating low-dose estrogen therapy in girls with CDGP who experience significant psychosocial distress from delayed puberty?

Relevant images

(CONTENT OMITTED)

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Question 147

A 35-year-old woman comes to the physician because she has been feeling very stressed over the past several months. During this period, she has found it difficult to relax. She states that her head is full of worries. She works at an accountant's office and reports difficulty in concentrating on her work. She has been working longer shifts because one of her coworkers is on vacation and reports feeling more tired than usual. She is married and frequently fights with her husband. The patient states that in order to deal with her stress, she goes shopping. While shopping, she steals small trivial items and feels immediately relieved thereafter. She discards the objects she steals and has feelings of shame and guilt about her actions. Her husband is concerned about her behavior, but she is unable to stop shoplifting. Her vital signs are within normal limits. On mental status examination, she is oriented to person, place, and time. She reports feeling anxious. Physical examination shows no abnormalities. Which of the following is the most appropriate next step in management?

Answer Choices:

(A) Administration of lithium
(B) Interpersonal therapy
(C) Psychodynamic psychotherapy
(D) Cognitive behavioral therapy

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/020fe5f2-83e1-4c50-b83f-f4b541d22136

OpenEvidence Explanation

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The correct answer is **D. Cognitive behavioral therapy (CBT)**.

This patient presents with classic features of **kleptomania** — an impulse control disorder characterized by the inability to resist the urge to steal items not needed for personal use or monetary value, with tension relief upon stealing, followed by guilt and shame.[1][2] The stolen items are trivial and discarded, and the behavior persists despite negative consequences, all consistent with DSM criteria.

Why CBT is the most appropriate next step:

CBT is the recommended first-line psychotherapeutic intervention for kleptomania. It addresses the maladaptive thought patterns and behavioral cycles underlying the impulse control disorder, and has been advocated across the literature as a core treatment modality.[1][3] Pharmacological agents such as SSRIs and opioid antagonists (naltrexone) have been studied as adjuncts to CBT, with naltrexone showing efficacy in reducing stealing urges and behavior in RCTs, but CBT remains the foundational behavioral treatment.[4][5] Exposure and response prevention (ERP), a CBT-based technique, has also shown treatment response in kleptomania.[6]

Why the other options are incorrect:

- **A. Lithium** — A mood stabilizer used for bipolar disorder. There is no indication for lithium in kleptomania, and this patient does not exhibit manic or hypomanic features.
- **B. Interpersonal therapy** — Primarily used for major depressive disorder and focuses on interpersonal relationships. It does not target the impulse control mechanisms central to kleptomania.
- **C. Psychodynamic psychotherapy** — While historically used for various psychiatric conditions, it lacks evidence for efficacy in kleptomania and does not directly address the behavioral reinforcement cycle of impulse control disorders.[1]

Notably, this patient also has significant anxiety symptoms that would benefit from CBT, as it is also the first-line behavioral treatment for anxiety disorders, making it an especially appropriate choice to address both conditions.[7]

Would you like to explore the role of naltrexone as adjunctive pharmacotherapy for kleptomania refractory to CBT alone?

References

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Question 148

A 65-year-old man presents to his primary care physician for a change in his behavior over the past few months. Initially, the patient was noted to be behaving inappropriately including using foul language and grabbing people unexpectedly. This has progressed to a worsening of his memory and trouble caring for himself. His temperature is 98.1°F (36.7°C), blood pressure is 162/103 mmHg, pulse is 83/min, respirations are 13/min, and oxygen saturation is 98% on room air. Physical exam is notable for an elderly man who laughs inappropriately at times and who is a poor historian. When he is engaged in conversation, he exhibits word finding difficulty and is rather inattentive. Which of the following is the most likely diagnosis?

Answer Choices:

(A) Alzheimer dementia
(B) Frontotemporal dementia
(C) Kluver-Bucy syndrome
(D) Vascular dementia

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/a737471b-e441-40ce-850b-d884b519a8b8

OpenEvidence Explanation

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The most likely diagnosis is **B. Frontotemporal dementia (FTD)**.

This presentation is classic for the **behavioral variant of frontotemporal dementia (bvFTD)**, which is characterized by early and prominent changes in personality and social conduct — including **disinhibition** (foul language, grabbing people), **inappropriate affect** (laughing inappropriately), and **loss of social awareness** — with cognitive decline developing later in the course.[1][2] Several features in this vignette strongly favor bvFTD over the other options:

- **Behavioral changes preceding memory loss**: The initial presentation was socially inappropriate behavior (disinhibition), which then progressed to memory impairment and functional decline. In Alzheimer dementia, episodic memory impairment is typically the earliest and most prominent feature, with behavioral changes occurring later. In bvFTD, behavioral and personality changes are the hallmark early manifestation.[1][2][3]
- **Word-finding difficulty and inattention with preserved insight deficits**: Executive dysfunction (including poor attention and verbal fluency impairment) is the characteristic cognitive profile of bvFTD, whereas visuospatial and memory deficits predominate in Alzheimer disease.[1]
- **Disinhibition and inappropriate social behavior**: These are core diagnostic criteria for bvFTD. The DSM-5 notes that the behavioral variant "typically first manifests with prominent changes in social behavior, such as disinhibition, apathy, or perseverative behavior".[2]

Why not the other options?

- **A. Alzheimer dementia** — Would present with early episodic memory loss (forgetting recent events, repeating questions) rather than behavioral disinhibition as the initial symptom.[1][4]
- **C. Klüver-Bucy syndrome** — Results from bilateral temporal lobe damage (e.g., herpes encephalitis) and features hyperorality, hypersexuality, visual agnosia, and placidity. This patient lacks these specific features, and the gradual progressive course is more consistent with neurodegeneration.
- **D. Vascular dementia** — Typically associated with a stepwise decline temporally related to cerebrovascular events, with focal neurological

deficits and corresponding vascular lesions on imaging. The insidious onset of behavioral symptoms is not characteristic.[2]

Would you like to explore the current diagnostic workup recommendations for distinguishing bvFTD from Alzheimer disease, including the role of biomarkers and neuroimaging?

Relevant images

(CONTENT OMITTED)

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Question 150

A 52-year-old man is brought to the emergency department with dry cough, shortness of breath, and low-grade fever that began 6 days ago. He also reports that he has had 3 episodes of watery diarrhea per day for the last 2 days. He appears slightly pale. His temperature is 38.0°C (100.4°F), pulse is 65/min, respirations are 15/min, and blood pressure is 140/78 mm Hg. Diffuse crackles are heard over bibasilar lung fields. Laboratory studies show:
Hemoglobin 13.8 g/dL
Leukocyte count 16,000/mm3
Platelet count 150,000/mm3
Serum
Na+ 131 mEq/L
Cl-
102 mEq/L
K+ 4.7 mEq/L
HCO3- 26 mEq/L
Urea nitrogen 18 mg/dL
Creatinine 1.2 mg/dL
An x-ray of the chest shows patchy infiltrates in both lungs. Which of the following is the most appropriate pharmacotherapy?

Answer Choices:

(A) Levofloxacin
(B) Trimethoprim/sulfamethoxazole
(C) Amoxicillin
(D) Rifampin

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/e3070e53-0649-4180-bfa2-724de630e0f8

OpenEvidence Explanation

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The most appropriate pharmacotherapy is **A. Levofloxacin**. This clinical presentation is classic for **Legionella pneumophila** pneumonia (Legionnaires' disease), and among the answer choices, levofloxacin is the only agent with activity against this intracellular pathogen.

Why Legionella is the leading diagnosis:

The combination of **dry cough**, **bilateral patchy infiltrates**, **watery diarrhea**, **hyponatremia** (Na^+ 131 mEq/L), **relative bradycardia** (pulse 65/min despite fever), and **leukocytosis** is a classic constellation for Legionnaires' disease.[1][2] Gastrointestinal symptoms (particularly watery diarrhea) occur in 19–47% of cases, and hyponatremia occurs more frequently in Legionella pneumonia than in other types of community-acquired pneumonia.[1][3] A multivariate analysis confirmed that diarrhea (OR 4.5) and hyponatremia (OR 5.6) are independent predictors distinguishing Legionella from pneumococcal pneumonia.[3]

Why levofloxacin is correct:

Legionella is an intracellular pathogen, making **β-lactams (including amoxicillin) ineffective**.[1][4] The recommended first-line agents are **fluoroquinolones (levofloxacin)** or **macrolides (azithromycin)**.[1][5] A systematic review of 3,525 patients found no difference in mortality between fluoroquinolones and macrolides for Legionella pneumonia.[5] The IDSA recommends levofloxacin 750 mg daily.[1] Among the answer choices, levofloxacin is the only appropriate option.

Why the other choices are incorrect:

- **Amoxicillin (C):** A β-lactam with no activity against intracellular Legionella[1]

- **Trimethoprim/sulfamethoxazole (B):** Not a recommended treatment for Legionella pneumonia
- **Rifampin (D):** Has in vitro activity against Legionella but is used only as adjunctive therapy in combination with a macrolide or fluoroquinolone in severe cases, never as monotherapy[2][6]

Would you like to explore the diagnostic approach to Legionella pneumonia, including the role of urinary antigen testing and its limitations?

Relevant images

(CONTENT OMITTED)

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Question 151

A transvaginal ultrasound shows an intrauterine heteroechoic mass with numerous anechoic spaces and no identifiable fetus or amniotic fluid. Both the ovaries are enlarged and have multiple thin-walled, septated cysts with clear content. Which of the following is the most likely cause of the ovarian findings?

> **Answer Choices:**
>
> (A) Chocolate cysts
> (B) Corpus luteum cysts
> (C) Yolk sac tumor
> (D) Theca leutein cysts

> **Correct Answer:**
>
> **(D)**
>
> **OpenEvidence Response:**
>
> **(D)** ✓

OpenEvidence Link: https://openevidence.com/ask/67f306cb-e0e3-4e86-97ee-9d6b0db60136

OpenEvidence Explanation

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The correct answer is **D. Theca lutein cysts**.

The ultrasound findings described — an intrauterine heteroechoic mass with numerous anechoic spaces and no identifiable fetus or amniotic fluid — are classic for a **complete hydatidiform mole** (complete molar pregnancy). The

anechoic spaces correspond to hydropic chorionic villi, and the absence of fetal tissue is characteristic of a complete (rather than partial) mole.[1][2]

The bilateral ovarian enlargement with multiple thin-walled, septated cysts containing clear fluid describes **theca lutein cysts**, which result from ovarian hyperstimulation by the markedly elevated β-hCG levels produced by the proliferating trophoblastic tissue.[3] These cysts are reported in **20–46%** of patients with complete molar pregnancies and are strongly associated with hCG levels >100,000 mIU/mL.[3][4] They typically regress spontaneously after molar evacuation as hCG levels decline, though they may persist for weeks to months.[5]

Why the other options are incorrect:

- **A. Chocolate cysts (endometriomas)** — These are thick-walled cysts with homogeneous low-level internal echoes ("ground glass" appearance), associated with endometriosis, not molar pregnancy.
- **B. Corpus luteum cysts** — These are typically unilateral, thick-walled cysts with a "ring of fire" Doppler pattern. They do not present as bilateral, multiple, thin-walled septated cysts.
- **C. Yolk sac tumor** — This is a germ cell tumor that presents as a solid or mixed solid-cystic ovarian mass, not bilateral thin-walled cystic enlargement. It is unrelated to the intrauterine findings described.

Theca lutein cysts are also a risk factor for the subsequent development of post-molar gestational trophoblastic neoplasia, particularly when bilateral, making their identification clinically important for surveillance planning.[4][5][6]

Would you like to explore the management algorithm for complete hydatidiform mole, including post-evacuation hCG surveillance and criteria for diagnosing persistent gestational trophoblastic neoplasia?

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Question 152

A 75-year-old woman is brought to the emergency department by her son because of a 2-day history of fever, headache, malaise, and dry cough. The patient lives with her son and his family and her son reports that other members of the family have had similar symptoms during the past week but that he has not had any symptoms. The result of a polymerase chain reaction test confirms that the woman is infected with a virus that has a helical capsid and a segmented genome. Which of the following is the most likely explanation for the son being free of symptoms?

Answer Choices:

(A) Serum antibodies against hemagglutinin
(B) Downregulation of ICAM-1 expression
(C) Protease-resistant antibodies in nasal secretions
(D) Homozygous mutation in the CCR5 gene

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/69f939a4-9a04-430a-afa4-b072e63f8919

OpenEvidence Explanation

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The answer is **A. Serum antibodies against hemagglutinin**.

The clinical scenario describes a virus with a **helical capsid** and **segmented genome** causing fever, headache, malaise, and dry cough spreading within a household — this is consistent with **influenza virus** (an orthomyxovirus with 8 segments of negative-sense RNA and a helical nucleocapsid). The son's lack of symptoms despite household exposure is best explained by pre-existing immunity.

Serum antibodies against hemagglutinin (HA) are the primary correlate of protection against influenza. HA mediates viral attachment to host cells via sialic acid receptors, and anti-HA antibodies neutralize the virus by preventing cell entry. The hemagglutination-inhibition (HAI) assay is the gold standard for measuring protective immunity, with higher HAI titers associated with increased protection against influenza infection and illness.[1][2][3] Both serum anti-HA and anti-neuraminidase antibodies independently predict immunity to influenza.[4]

Why the other options are incorrect:

- **B. Downregulation of ICAM-1 expression** — ICAM-1 is the receptor for rhinoviruses (major group), which have icosahedral (not helical) capsids and non-segmented genomes.
- **C. Protease-resistant antibodies in nasal secretions** — While mucosal IgA does contribute to influenza protection, the concept of "protease-resistant" antibodies in nasal secretions is not the established primary correlate of protection. This answer choice is a distractor; serum anti-HA antibodies remain the best-characterized and most clinically validated correlate.[5][6]
- **D. Homozygous mutation in the CCR5 gene** — CCR5 is a co-receptor for HIV, not influenza. The CCR5-Δ32 mutation confers resistance to HIV infection, which is unrelated to this clinical scenario.

Would you like to explore the differences between mucosal IgA and serum anti-HA antibodies in conferring protection against influenza, and how this distinction informs vaccine development strategies?

Relevant images

(CONTENT OMITTED)

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Question 153

A 71-year-old man comes to the physician for a routine visit. His psychiatric history is significant for major depression with psychotic features. He was diagnosed after his wife died from pancreatic cancer four years earlier. Three years ago, he deliberately overdosed on sleeping pills. Today, he feels well but still wakes up frequently at night and cannot sleep through the night. He lives alone in his apartment and has no children. He does not possess a firearm at home but has access to weapons at a local hunting club. The patient currently denies suicidal thoughts or thoughts of self-harm. He takes sertraline and olanzapine. He does not smoke or drink alcohol. Which of the following is the strongest risk factor for suicide in this patient?

Answer Choices:

(A) Previous suicide attempt
(B) History of psychosis
(C) Sleeping disorder
(D) Age

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/6f6ab52e-3360-43d2-903c-ffe44556a31c

OpenEvidence Explanation

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The answer is **A. Previous suicide attempt**.

A prior suicide attempt is consistently identified as the **strongest risk factor for completed suicide** across the literature. In a landmark Lancet review, a history of self-harm or suicide attempts was described as "the strongest factor" in most studies of suicide risk factors, present in at least 40% of cases.[1] A JAMA Psychiatry study found that the rate of suicide among individuals in the year after a suicide attempt was nearly **100-fold higher** than age- and sex-matched community controls.[2] In a study of late-life depression specifically, previous suicide attempts predicted the highest cumulative probability of dying by suicide over 24 years of follow-up.[3]

This patient's deliberate overdose on sleeping pills three years ago places him in the highest-risk category. While the other listed factors are all relevant contributors to suicide risk, none surpass a prior attempt in predictive strength:

- **History of psychosis (B):** Psychotic features in depression do increase risk, but psychosis alone is not as strong a predictor as a prior attempt.[4]
- **Sleep disorder (C):** Sleep disturbances are an independent but statistically **weak** risk factor for suicidal behavior (OR ~1.4–2.2), far less predictive than a prior attempt.[5][6]
- **Age (D):** Older age (≥70) does confer elevated risk, particularly in men, and is an important demographic factor, but it remains secondary to a history of suicidal behavior in risk stratification models.[7][8]

An NEJM review further categorized previous suicide attempts as having a "moderate" strength of association with high-quality evidence, while neuropsychiatric disorders had a "strong" association — however, the question asks about the *strongest single risk factor among the listed options*, and a prior attempt consistently outranks psychosis, sleep disturbance, and age alone.[4]

Would you like to explore evidence-based approaches to ongoing suicide risk mitigation in elderly patients with prior attempts, including means restriction counseling and safety planning interventions?

Relevant images

(CONTENT OMITTED)

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Question 156

A 22-year-old male presents to the emergency room complaining of neck stiffness. He reports that his neck started “locking” three hours ago. He is now unable to move it. His past medical history is notable for schizophrenia and asthma and he currently takes albuterol as well as another medication whose name he does not remember. His temperature is 99.0°F (37.2°C), blood pressure is 130/90 mmHg, pulse is 105/min, and respirations are 18/min. On physical examination, the patient appears anxious and diaphoretic. He speaks in full sentences and is oriented to person, place, and time. The patient’s neck is flexed and rotated to the right approximately 40 degrees. The right sternocleidomastoid and trapezius are firm and contracted. Extraocular movements are full and intact. Upon further questioning, he reports that he took more medication four hours ago because he was hearing voices. Which of the following should most likely be administered to this patient?

Answer Choices:

(A) Glycopyrrolate
(B) Benztropine
(C) Levodopa
(D) Dantrolene

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/70dcdb32-89de-4d3f-9553-6abc0758f378

OpenEvidence Explanation

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The answer is **B. Benztropine**. This patient is presenting with an **acute dystonic reaction** secondary to antipsychotic medication, and the treatment of choice is an anticholinergic agent such as benztropine.

Clinical Reasoning

This 22-year-old male with schizophrenia developed acute-onset cervical dystonia (neck flexed and rotated to the right with contracted sternocleidomastoid and trapezius) approximately one hour after taking an extra dose of his antipsychotic medication due to auditory hallucinations. This presentation is classic for an **antipsychotic-induced acute dystonic reaction**, which characteristically involves involuntary sustained muscle contractions bringing body parts into contorted positions, most commonly affecting the head and neck.[1][2] Acute dystonic reactions are more common in **young males** and develop rapidly after drug dosing, including after a single dose or dose increase.[2][3]

Why Benztropine?

Anticholinergic agents (benztropine 1–2 mg IV/IM, or diphenhydramine 25–50 mg IV/IM) are the standard treatment, producing relief within minutes.[2][3] Benztropine is FDA-indicated for the control of extrapyramidal disorders due to neuroleptic drugs.[4] A short oral course (4–7 days) may be necessary afterward, as dystonic reactions can recur hours after the initial injection.[3]

Why not the other options?

- **Glycopyrrolate** (A) is a peripheral anticholinergic that does not cross the blood-brain barrier and therefore would not treat a central nervous system–mediated dystonic reaction.
- **Levodopa** (C) is used for Parkinson disease, not acute drug-induced dystonia.
- **Dantrolene** (D) is a direct-acting skeletal muscle relaxant used for neuroleptic malignant syndrome (NMS) and malignant hyperthermia. While

this patient has some features of sympathetic activation (tachycardia, diaphoresis), the low-grade temperature, focal dystonia, intact mentation, and rapid onset after a dose increase are far more consistent with acute dystonia than NMS.

Would you like to explore how to differentiate acute dystonic reactions from neuroleptic malignant syndrome in the emergency setting?

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Question 159

A 9-year-old boy is brought to a physician by his mother for evaluation of generalized weakness, increased urination, and increased thirst. The mother mentions that her boy is always tired, and seems to be getting worse. He prefers watching television rather than going out and playing with other kids. Furthermore, he has had frequent episodes of constipation since birth. Except for frequent cravings for salty foods, the boy eats a regular diet. The patient was delivered healthy and is fully immunized. The medical history is unremarkable, and he takes no medications. He has no siblings. His father is a banker and his mother is a librarian. The pulse is 90/min, the blood pressure is 110/75 mm Hg, and the respiratory rate is 15/min. He is in the bottom 10th percentile for height and weight according to his age. The remainder of the physical examination is unremarkable. He recently had a urinalysis that showed elevated urinary calcium excretion.
Additional lab testing results are as follows:
Serum electrolytes
Sodium 135 mEq/L
Potassium 3.2 mEq/L
Chloride 95 mEq/L
Plasma renin activity 10 ng/mL/hr (normal, 0.5–3.3 ng/mL/hr)
Plasma aldosterone concentration 20 ng/dL (normal, 2–9 ng/dL)
What is the most likely diagnosis?

Answer Choices:

(A) Renal artery stenosis
(B) Bartter's syndrome
(C) Pheochromocytoma
(D) Gitelman's syndrome

Correct Answer:

(B)

OpenEvidence Response:

> **(B)** ✓

OpenEvidence Link: https://openevidence.com/ask/344be57f-19fc-44c3-bf26-a71d1e527fea

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OpenEvidence Explanation

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The most likely diagnosis is **B. Bartter's syndrome**.

This child presents with a classic constellation of findings that point to Bartter syndrome:

- **Hypokalemia** (K^+ 3.2 mEq/L) with **elevated plasma renin activity** and **elevated aldosterone** — indicating secondary hyperaldosteronism due to renal salt wasting, not a primary adrenal or renovascular process[1][2]
- **Hypercalciuria** — a hallmark that distinguishes Bartter syndrome from Gitelman syndrome, which characteristically presents with **hypocalciuria**[3][4]
- **Polyuria and polydipsia** (increased urination and thirst), **constipation since birth**, **salt craving**, **growth failure** (bottom 10th percentile), and **fatigue/weakness** — all classic features of Bartter syndrome presenting in childhood[1][5][6]
- **Normal blood pressure** (110/75 mmHg) — this effectively rules out renal artery stenosis and pheochromocytoma, both of which cause **hypertension** with elevated renin/aldosterone[1]

Why not the other options?

- **A. Renal artery stenosis** — Causes secondary hyperaldosteronism but presents with **hypertension**, not normotension. It would not explain hypercalciuria or the childhood presentation with salt craving and constipation.

- **C. Pheochromocytoma** — Presents with **hypertension**, episodic headaches, palpitations, and diaphoresis. The catecholamine-driven picture does not match this presentation.

- **D. Gitelman syndrome** — Shares many features with Bartter syndrome (hypokalemia, metabolic alkalosis, elevated renin/aldosterone, normotension), but is distinguished by **hypocalciuria** and **hypomagnesemia**, and typically presents **later in life** (adolescence or adulthood). This patient has **hypercalciuria**, which is characteristic of Bartter syndrome, not Gitelman syndrome.[3][4][7]

The following figure illustrates the transport defects in the thick ascending limb of the loop of Henle that underlie Bartter syndrome and explain the associated hypercalciuria — disruption of sodium-chloride reabsorption reduces the lumen-positive potential needed for paracellular calcium reabsorption.

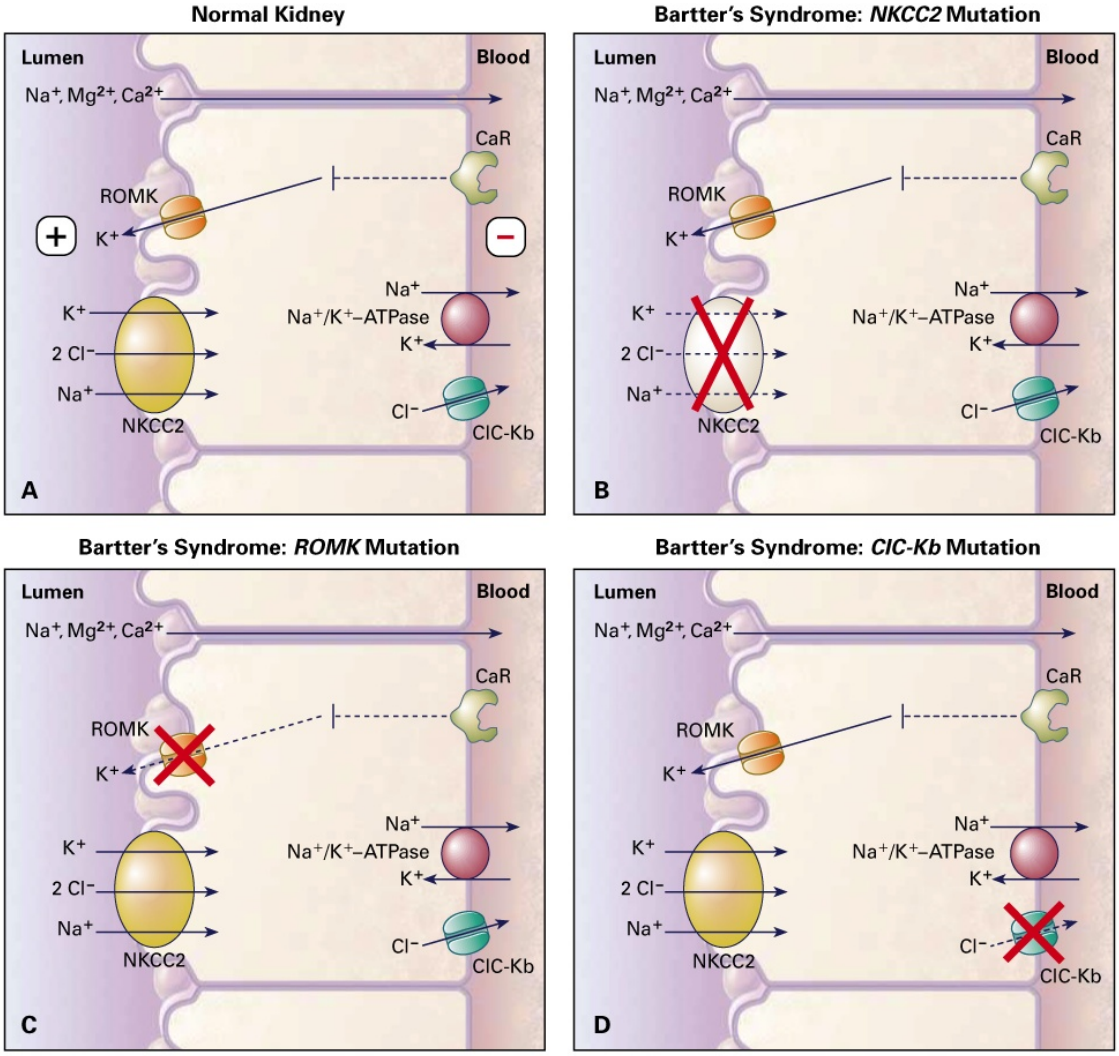


Figure 3. Transport Mechanisms in the Thick Ascending Limb of the Loop of Henle.

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Would you like to explore the specific treatment strategies for Bartter syndrome in pediatric patients, including the role of indomethacin and potassium-sparing diuretics?

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Question 161

A 51-year-old woman presents to her primary care physician complaining of months of dry mouth and dry eyes. She says the dryness has become so severe that she has difficulty swallowing food. She has a history of hypertension, for which she takes hydrochlorothiazide (HCTZ), but she has no other medical problems. Family history is significant for her grandmother having systemic lupus erythematosus. The vital signs include: blood pressure 118/76 mm Hg, heart rate 78/min, and respiratory rate 15/min. On physical exam, she has tender parotid glands bilaterally and dries mucous membranes. The presence of serum anti-Ro and anti-La autoantibodies is confirmed at high titers. In addition to her primary diagnosis, which of the following is this patient most at risk for developing in the future?

Answer Choices:

(A) Gastric carcinoma
(B) Non-Hodgkin lymphoma
(C) Invasive ductal carcinoma of the breast
(D) Adenocarcinoma of the lung

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/000c8dc1-1a35-4364-b478-3e48f857c21f

OpenEvidence Explanation

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The correct answer is **B. Non-Hodgkin lymphoma**.

This patient presents with classic features of **primary Sjögren syndrome** (pSS): dry mouth (xerostomia), dry eyes (xerophthalmia), bilateral parotid gland enlargement, and high-titer anti-Ro (SS-A) and anti-La (SS-B) autoantibodies. The most significant malignancy risk associated with pSS is **non-Hodgkin lymphoma (NHL)**, particularly of the mucosa-associated lymphoid tissue (MALT) type.

The risk of B-cell lymphoma is **15 to 20 times higher** in patients with primary Sjögren syndrome compared to the general population, with a lifetime risk of approximately 5–10%.[1] A meta-analysis of over 14,500 pSS patients confirmed a pooled relative risk of **13.76** for NHL.[2] This risk is the highest among all systemic autoimmune diseases, exceeding that of both SLE and rheumatoid arthritis.[2][3]

> "The risk of B-cell lymphoma is 15 to 20 times as high among patients with primary Sjögren's syndrome as in the general population (lifetime risk, 5 to 10%), a finding that has been attributed to the chronic B-cell activation in this condition."
>
> —Xavier Mariette, M.D., Ph.D. et al., Université Paris Sud and other institutions. Primary Sjögren's Syndrome. N Engl J Med. March 08, 2018.
>
> Used under license from The New England Journal of Medicine.

The predominant histologic subtype is **MALT lymphoma**, accounting for approximately 76% of Sjögren-associated lymphomas, followed by diffuse large B-cell lymphoma (11%).[4][5] These lymphomas frequently arise in the salivary glands — the very organs targeted by the autoimmune process.[1][6] Key risk factors for lymphoma development include parotid swelling (as seen in this patient), cryoglobulinemia, low complement levels, hypergammaglobulinemia, and rheumatoid factor positivity.[7][8]

The other answer choices — gastric carcinoma, invasive ductal carcinoma of the breast, and adenocarcinoma of the lung — are not classically associated with Sjögren syndrome. While some studies have noted modestly elevated risks for

certain solid tumors (thyroid, oral cavity), none approach the magnitude of the NHL association.[9]

Would you like to explore the recommended surveillance strategies and biomarkers used for lymphoma risk stratification in Sjögren syndrome patients?

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Question 162

A 59-year-old man presents to his primary care provider with fatigue, a progressively worsening cough with flecks of blood, shortness of breath, and dark urine. He reports feeling ill for the past 3 weeks. Past medical history is significant for hypertension and hyperlipidemia. He takes chlorthalidone and atorvastatin. Family history is noncontributory. He has smoked 20–30 cigarettes daily for the past 26 years. Anti-glomerular basement membrane serologies are positive. Which of the following is a specific feature for this patient's condition?

> **Answer Choices:**
>
> (A) Granulomatous inflammation and necrotizing vasculitis
> (B) Positive cryoglobulins
> (C) Linear IgG staining on immunofluorescence
> (D) Longitudinal splitting and thickening of the glomerular basement membrane

> **Correct Answer:**
>
> (C)
>
> **OpenEvidence Response:**
>
> (C) ✓

OpenEvidence Link: https://openevidence.com/ask/dec61d75-cf42-4b9d-a68a-a6911f132c33

OpenEvidence Explanation

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The answer is **C. Linear IgG staining on immunofluorescence**.

This patient presents with a pulmonary-renal syndrome — hemoptysis, dyspnea, and dark urine (hematuria) — with positive anti-glomerular basement membrane (anti-GBM) antibodies, consistent with **Goodpasture syndrome** (anti-GBM disease). The hallmark histopathologic finding specific to this condition is **linear deposition of IgG along the glomerular basement membrane** on immunofluorescence microscopy.[1][2][3]

Anti-GBM glomerulonephritis is defined by intense and diffuse linear staining for polyclonal IgG (frequently accompanied by C3) along the GBM, which distinguishes it from the granular capillary wall deposits seen in immune-complex glomerulonephritis and the pauci-immune pattern of ANCA-associated vasculitis.[1][3] The autoantibodies target the NC1 domain of the α3 (and α5) chain of type IV collagen, which is expressed in both glomerular and alveolar basement membranes — explaining the combined renal and pulmonary involvement.[2][4]

The following figure from Pedchenko et al. demonstrates the classic linear IgG immunofluorescence pattern along the GBM in Goodpasture disease:

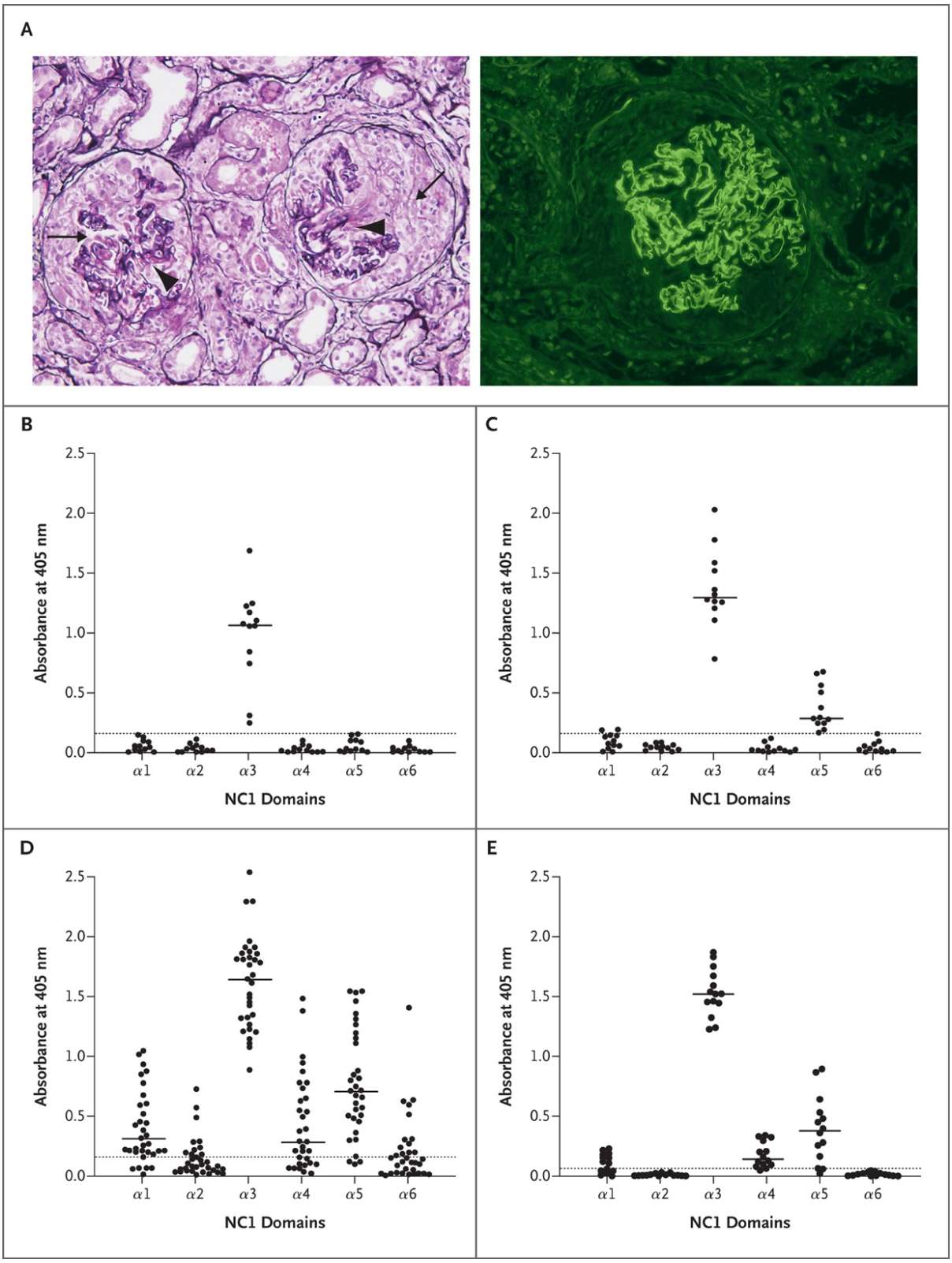


Figure 1. Classic Kidney Lesions in Goodpasture's Disease, and the Immunoreactivity of Circulating and Kidney-Bound Goodpasture Autoantibodies to Six Noncollagenous-1 Domain Monomers of Human Collagen IV.

Used under license from The New England Journal of Medicine.

Why the other options are incorrect:

- **A. Granulomatous inflammation and necrotizing vasculitis** — characteristic of granulomatosis with polyangiitis (GPA), an ANCA-associated vasculitis, not anti-GBM disease.[5]
- **B. Positive cryoglobulins** — associated with cryoglobulinemic vasculitis and certain immune-complex glomerulonephritides, not anti-GBM disease.[3]
- **D. Longitudinal splitting and thickening of the GBM** — characteristic of Alport syndrome, a hereditary collagen IV disorder, not Goodpasture syndrome.

Would you like to explore the treatment approach for anti-GBM disease, including the role of plasmapheresis and immunosuppression?

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Question 163

A 32-year-old man with HIV infection is brought to the emergency department by his roommate because of a 2-week history of progressively worsening headache and vomiting. Current medications include trimethoprim-sulfamethoxazole, dolutegravir, and tenofovir-emtricitabine. His temperature is 38.5°C (101.3°F). Physical examination shows nuchal rigidity. Kernig and Brudzinski signs are present. A lumbar puncture is performed and shows an opening pressure of 32 cm H2O (N: < 20). The pathogen isolated from the cerebrospinal fluid (CSF) can be cultured on Sabouraud agar. Further evaluation of this patient's CSF is most likely to show which of the following additional findings?

Answer Choices:

(A) Positive latex agglutination test
(B) Positive PCR for HSV-2 DNA
(C) Presence of tachyzoites
(D) Increased adenosine deaminase concentration

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/3ff0313b-8d17-4e9c-bc4c-954339475104

OpenEvidence Explanation

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The answer is **A. Positive latex agglutination test**.

The clinical scenario describes **cryptococcal meningitis** in an HIV-infected patient. The key clues are:

- **HIV infection** with subacute meningoencephalitis (2-week progressive headache, vomiting, meningeal signs)
- **Elevated CSF opening pressure** (32 cm H_2O; elevated in 60–80% of HIV-associated cryptococcal meningitis)[1]
- **Organism cultured on Sabouraud agar** — this is characteristic of fungi. *Cryptococcus neoformans* colonies are visible on **Sabouraud dextrose agar** plates, generally within 7 days[1]

The **latex agglutination test** detects cryptococcal capsular polysaccharide antigen (CrAg) in CSF and serum with sensitivity and specificity exceeding 90–99%.[2][3] In more than 90% of patients with cryptococcal meningitis, CrAg can be detected in CSF or serum by latex agglutination.[2] While the lateral flow assay has largely supplanted latex agglutination in clinical practice, both remain validated methods for CrAg detection.[3]

Why the other options are incorrect:

- **B. Positive PCR for HSV-2 DNA** — HSV meningitis presents acutely with temporal lobe involvement and would not grow on Sabouraud agar (HSV is a virus, not a fungus).
- **C. Presence of tachyzoites** — Toxoplasmosis in HIV typically causes ring-enhancing brain lesions (encephalitis), not meningitis, and *Toxoplasma* is a parasite that does not grow on Sabouraud agar.
- **D. Increased adenosine deaminase concentration** — Elevated CSF adenosine deaminase is associated with tuberculous meningitis; *Mycobacterium tuberculosis* is a bacterium and would not grow on Sabouraud agar.

Would you like to explore the current recommended induction therapy for HIV-associated cryptococcal meningitis, including the role of single-dose liposomal amphotericin B regimens?

Relevant images

(CONTENT OMITTED)

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Question 164

A 70-year-old woman comes to the physician for the evaluation of back pain. For the past six days, she has had a burning pain in her upper right back and chest. She cannot recall any recent injury and has no prior history of back pain. She has a history of hypertension and gastroesophageal reflux. The patient volunteers at an animal shelter three times a week. She does not smoke or drink alcohol. Current medications include ramipril and pantoprazole. The patient appears healthy and well nourished. Her temperature is 36.9°C (98.42°F), pulse is 76/min, and blood pressure is 145/92 mm Hg. Examination shows a long erythematous rash covered with multiple clear vesicles and crusty lesions extending from her back to below her right breast. Which of the following is the most likely underlying mechanism of the disease?

Answer Choices:

(A) Viral reactivation in dorsal root ganglia
(B) IgA deposits in the upper dermis
(C) Bacterial lymphatic infection of the epidermis
(D) Infestation with bloodsucking parasites

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/f997350b-a750-40b1-8970-cfdd54db26e7

OpenEvidence Explanation

(CONTENT OMITTED)

The answer is **A. Viral reactivation in dorsal root ganglia**.

This presentation is classic for **herpes zoster (shingles)**. The key features include:

- **Dermatomal distribution**: An erythematous rash with clear vesicles and crusted lesions extending from the back to below the right breast, following a unilateral thoracic dermatome.
- **Prodromal pain**: Six days of burning pain preceding or accompanying the rash, which is characteristic of the acute neuritis seen in zoster.
- **Age**: A 70-year-old patient — incidence of herpes zoster increases significantly with age due to waning cell-mediated immunity against varicella-zoster virus (VZV).

Why each other option is incorrect:

- **B. IgA deposits in the upper dermis** — This describes dermatitis herpetiformis, an autoimmune blistering condition associated with celiac disease. It typically presents with intensely pruritic, grouped papulovesicles on extensor surfaces (elbows, knees, buttocks) and is bilateral/symmetric, not dermatomal.
- **C. Bacterial lymphatic infection of the epidermis** — This describes erysipelas or cellulitis. These present with well-demarcated erythema, warmth, and swelling, often with systemic signs (fever, leukocytosis), but not with vesicles in a dermatomal pattern.
- **D. Infestation with bloodsucking parasites** — This could refer to conditions like scabies or pediculosis. These do not produce dermatomal vesicular eruptions.

Herpes zoster results from reactivation of latent VZV residing in **dorsal root ganglia** (or cranial nerve ganglia) after primary varicella infection, typically decades earlier. The virus travels anterogradely along sensory nerves to the skin, producing the characteristic painful, unilateral, dermatomal vesicular eruption.

Would you like to explore the indications for antiviral therapy and postherpetic neuralgia prevention in older adults with herpes zoster?

Question 166

A 60-year-old man presents to the office for shortness of breath. The shortness of breath started a year ago and is exacerbated by physical activity. He has been working in the glass manufacturing industry for 20 years. His vital signs include: heart rate 72/min, respiratory rate 30/min, and blood pressure 130/80 mm Hg. On physical exam, there are diminished respiratory sounds on both sides. On the chest radiograph, interstitial fibrosis with reticulonodular infiltrate is found on both sides, and there is also an eggshell calcification of multiple adenopathies. What is the most likely diagnosis?

Answer Choices:

(A) Berylliosis
(B) Silicosis
(C) Asbestosis
(D) Talcosis

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/aa29d3d2-f0aa-431b-a7e8-9c79619520a1

OpenEvidence Explanation

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The answer is **B. Silicosis**.

The combination of **eggshell calcification of hilar/mediastinal lymph nodes**, bilateral interstitial fibrosis with reticulonodular infiltrates, and a 20-year history of working in the **glass manufacturing industry** (a well-known source of silica exposure) is classic for silicosis. Eggshell calcification — peripheral calcification of lymph nodes — most commonly occurs in silicosis and coal workers' pneumoconiosis.[1] The Lancet review on silicosis confirms that hilar and mediastinal lymph nodes often enlarge and can calcify in a "characteristic eggshell pattern".[2]

Why not the other options:

- **Berylliosis (A):** Radiographically mimics sarcoidosis with small rounded or irregular opacities, not typically associated with eggshell calcification. It is also not a classic exposure in glass manufacturing.[3][4]
- **Asbestosis (C):** Produces small irregular/linear opacities predominantly in the lung bases (not reticulonodular upper-zone pattern) and is associated with pleural plaques rather than eggshell calcification of lymph nodes.[3][4]
- **Talcosis (D):** CT findings include centrilobular and subpleural nodules or heterogeneous conglomerate masses with foci of high attenuation from talc deposition, not eggshell calcification.[3]

Glass manufacturing involves cutting, grinding, and processing silica-containing materials, making it a high-risk occupation for silica dust inhalation. The 20-year exposure duration is consistent with chronic silicosis, which typically develops after decades of exposure.[5]

Would you like to explore the management approach and surveillance recommendations for patients with chronic silicosis?

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Question 167

A 43-year-old woman is brought to the emergency department by her brother for severe chest pain. The patient recently lost her husband in a car accident and is still extremely shocked by the event. On physical examination, her blood pressure is 105/67 mm Hg, the heart rate is 96/min and regular, breathing rate is 23/min, and the pulse oximetry is 96%. An S3 heart sound and rales in the lower right and left lung lobes are heard. A 12-lead ECG shows no significant findings. Echocardiography shows an enlarged left ventricle and left atrium. The patient is stabilized and informed about the diagnosis and possible treatment options. Which of the following is the most likely diagnosis?

Answer Choices:

(A) Atrial fibrillation
(B) Constrictive pericarditis
(C) Takotsubo cardiomyopathy
(D) Restrictive cardiomyopathy

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/3d958d90-1f85-4481-b175-bfa3c9c1ce62

OpenEvidence Explanation

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The answer is **C. Takotsubo cardiomyopathy**.

This presentation is classic for **Takotsubo cardiomyopathy** (also known as stress-induced cardiomyopathy or "broken heart syndrome"). The key features supporting this diagnosis include:

- **Profound emotional stressor**: The recent sudden death of her husband in a car accident is a classic emotional trigger.[1][2][3]
- **Acute heart failure signs**: The S3 gallop and bilateral rales indicate acute left ventricular dysfunction, consistent with the acute heart failure presentation of Takotsubo.[4][5]
- **Echocardiographic findings**: The enlarged left ventricle and left atrium reflect the increased LV end-diastolic volume characteristic of Takotsubo, where the Frank-Starling mechanism compensates for severely impaired contractility.[6]
- **No significant ECG findings**: While Takotsubo can present with ST-segment changes, the ECG may also be unremarkable, and the absence of ischemic changes helps distinguish it from acute coronary syndrome.[4][5]

Takotsubo cardiomyopathy is an acute, typically reversible LV dysfunction triggered by intense emotional or physical stress, mediated by a catecholamine surge causing myocardial stunning.[1][2] It predominantly affects postmenopausal women but can occur at any age, and it characteristically presents with chest pain mimicking acute coronary syndrome in the absence of culprit coronary artery disease.[4][5]

Why not the other options:

- **A. Atrial fibrillation** — The heart rate is described as regular, ruling out atrial fibrillation. Additionally, atrial fibrillation alone would not explain the acute LV enlargement and heart failure signs following emotional stress.
- **B. Constrictive pericarditis** — This presents with signs of right-sided heart failure (elevated JVP, peripheral edema, ascites) and would not typically show LV enlargement on echocardiography. It is also a chronic process, not an acute presentation triggered by emotional stress.

- **D. Restrictive cardiomyopathy** — This is a chronic condition with diastolic dysfunction and would present with biatrial enlargement but normal or small ventricular cavities, not an enlarged LV. It is not triggered by acute emotional stress.

Would you like to explore the acute management approach and complications to monitor for in Takotsubo cardiomyopathy?

Relevant images

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Question 168

A 56-year-old man is brought to the emergency department. He was found unconscious on the street. The staff recognizes him as a local homeless man with a long history of alcoholism. At the hospital, his pulse is 95/min, the blood pressure is 110/70 mm Hg, the respirations are 20/min, and the oxygen saturation is 98% on room air. On physical exam, the unconscious man is covered in bloody vomit with small clots and food particles. He smells of alcohol. A digital exam reveals black tarry stool in the rectal vault. The patient is given oxygen, IV fluids, and an NG-tube is placed and set to intermittent suction. Labs are sent and the patient is prepared for a procedure. Which of the following is the most appropriate next step in his management?

Answer Choices:

(A) Undergo colonoscopy
(B) Undergo upper GI endoscopy
(C) Proton pump inhibitors with anti-H.pylori regimen
(D) Surgery for peptic ulcer disease

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/c7c7757b-e59d-4a42-9f3f-44184e3d8bf4

OpenEvidence Explanation

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The answer is **B. Undergo upper GI endoscopy**.

This patient presents with classic signs of **acute upper gastrointestinal bleeding (UGIB)**: hematemesis (bloody vomit with clots and food particles) and melena (black tarry stool), in the setting of chronic alcoholism. The most appropriate next step after initial resuscitation (oxygen, IV fluids, NG tube) is **upper endoscopy (esophagogastroduodenoscopy)**, which serves as both the diagnostic and therapeutic procedure of choice.[1][2]

Why upper endoscopy is correct:

- Hematemesis and melena localize the bleeding source proximal to the ligament of Treitz, making this an upper GI bleed by definition. Upper endoscopy allows identification of the bleeding source — whether peptic ulcer disease, variceal hemorrhage (given his alcoholism and likely cirrhosis), Mallory-Weiss tear, or gastritis — and enables simultaneous hemostatic treatment.[1][2]

- The ACG guidelines recommend upper endoscopy within 24 hours of presentation for patients hospitalized with overt UGIB. Resuscitation should be initiated before endoscopy, which has already been started in this case.[3]

Why the other options are incorrect:

- **A. Colonoscopy** — Colonoscopy evaluates the lower GI tract and is not indicated when the clinical presentation clearly points to an upper GI source (hematemesis, coffee-ground emesis, melena).

- **C. PPI with anti-H. pylori regimen** — While PPIs may be started pre-endoscopy, an anti-H. pylori regimen is premature without first confirming the diagnosis endoscopically. H. pylori eradication is part of post-endoscopic management if peptic ulcer disease is confirmed.[4][5]

- **D. Surgery for peptic ulcer disease** — Surgery is reserved for patients who fail endoscopic and interventional radiologic hemostasis, not as a first-line intervention.[1]

Would you like to explore the differences in endoscopic management between variceal and non-variceal upper GI bleeding in patients with suspected cirrhosis?

Relevant images

(CONTENT OMITTED)

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Question 169

An 8-year-old girl comes to the physician because of a 2-day history of hematuria. Two weeks ago, she had a sore throat that resolved without treatment. Physical examination shows 1+ pitting edema of the lower legs and ankles. Urinalysis shows numerous RBCs and 3+ proteinuria. Her antistreptolysin O titer is elevated. Formation of which of the following is most likely involved in the underlying mechanism of this patient's symptoms?

Answer Choices:

(A) Antigen-specific IgE binding to mast cells
(B) Tissue-specific antibodies
(C) Antigen-antibody complexes
(D) Presensitized CD8+ cytotoxic T-cells

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/d49b8079-4a00-48db-ae36-a9b56705b6dd

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OpenEvidence Explanation

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The answer is **C. Antigen-antibody complexes**.

This clinical presentation — an 8-year-old with hematuria, edema, and proteinuria occurring **2 weeks after a streptococcal pharyngitis** with an elevated ASO titer — is classic for **post-streptococcal glomerulonephritis (PSGN)**, the prototype of **Type III hypersensitivity** (immune complex–mediated) disease.

The pathogenesis of PSGN centers on the formation and glomerular deposition of **antigen-antibody immune complexes**. Antibodies directed against streptococcal antigens (such as streptococcal pyrogenic exotoxin B and nephritis-associated plasmin receptor) form immune complexes either in the circulation or in situ within the glomerulus.[1][2] These deposited complexes activate complement (particularly the alternative pathway, reflected by low C3 with normal C4 levels), recruit inflammatory cells, and cause glomerular injury manifesting as hematuria, proteinuria, and edema.[3][4]

On biopsy, immunofluorescence reveals the characteristic coarse granular ("lumpy-bumpy") deposits of IgG and C3 in the mesangium and capillary loops, and electron microscopy shows subepithelial "humps" — all hallmarks of immune complex deposition.[4]

Why the other options are incorrect:

- **A (IgE binding to mast cells)** — This describes a Type I hypersensitivity reaction (e.g., anaphylaxis, allergic rhinitis), not glomerulonephritis.
- **B (Tissue-specific antibodies)** — This describes a Type II hypersensitivity reaction (e.g., Goodpasture syndrome with anti-GBM antibodies), where antibodies target antigens on host tissue directly.
- **D (Presensitized CD8+ T cells)** — This describes a Type IV (delayed-type) hypersensitivity reaction (e.g., contact dermatitis, transplant rejection), which is cell-mediated rather than antibody/immune complex–mediated.

Would you like to explore how PSGN is distinguished from other causes of nephritic syndrome in children, such as IgA nephropathy or C3 glomerulopathy?

Relevant images

(CONTENT OMITTED)

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Question 170

A 25-year-old man presents to the emergency department with altered mental status. He was found down in the middle of the street. His past medical history is unknown. His temperature is 99.0°F (37.2°C), blood pressure is 104/64 mmHg, pulse is 70/min, respirations are 5/min, and oxygen saturation is 91% on room air. The patient is being resuscitated in the trauma bay. Which of the following was most likely to be found on exam?

> **Answer Choices:**
>
> (A) Ataxia
> (B) Conjunctival injection
> (C) Miosis
> (D) Nystagmus

> **Correct Answer:**
>
> (C)
>
> **OpenEvidence Response:**
>
> (C) ✓

OpenEvidence Link: https://openevidence.com/ask/acf9632e-fec0-4486-a94b-af1cfd1387d0

OpenEvidence Explanation

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The answer is **C. Miosis**. This presentation — a young man found down with altered mental status, **respiratory rate of 5/min**, and oxygen saturation of 91% — is classic for **opioid overdose**.

The hallmark triad of opioid intoxication consists of **respiratory depression, stupor/altered mental status, and miosis (pinpoint pupils)**.[1] Respiratory depression is considered the sine qua non of opioid toxicity, and a respiratory rate of 12 breaths per minute or less in a patient not in physiologic sleep strongly suggests acute opioid intoxication, particularly when accompanied by miosis or stupor.[1] This patient's respiratory rate of 5/min with depressed consciousness is highly characteristic.

The other answer choices correspond to different toxidromes:

- **Ataxia** — more typical of ethanol intoxication, cerebellar lesions, or Wernicke encephalopathy, none of which characteristically produce this degree of respiratory depression.
- **Conjunctival injection** — associated with cannabis use or allergic reactions, not with the severe respiratory depression seen here.
- **Nystagmus** — seen with PCP intoxication, alcohol, or anticonvulsant toxicity, which would not typically present with this pattern of profound respiratory depression and bradypnea.[2]

The DSM-5 similarly characterizes opioid overdose as **unconsciousness, respiratory depression, and pinpoint pupils**.[3]

Would you like to explore the evidence-based approach to naloxone dosing and monitoring in suspected opioid overdose?

Relevant images

(CONTENT OMITTED)

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Question 172

An 83-year-old man is admitted to the hospital with fever, weakness, and decreased responsiveness. He is diagnosed with urosepsis based on urinalysis and culture and started on ceftriaxone and intravenous fluids. By hospital day 3, he is clinically improving. During the evening, the patient becomes irritable. He is talking to someone despite nobody being present in the room. He is easily agitated and attempts to strike a nurse with a remote control to his TV. Subsequently, the patient keeps getting out of bed and trying to walk away despite being a fall risk. Which of the following is the most appropriate next step in management?

Answer Choices:

(A) Diphenhydramine
(B) Lorazepam
(C) Olanzapine
(D) Physical restraints

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/cd83a44c-8523-4e59-aca3-320e4f61b28b

OpenEvidence Explanation

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The correct answer is **C. Olanzapine**. This patient is presenting with **hyperactive delirium** in the setting of urosepsis — characterized by acute onset of irritability, visual hallucinations (talking to someone not present), agitation, and dangerous behavior (striking at staff, attempting to leave bed). When pharmacologic intervention is needed for delirium with severe agitation posing risk of harm, second-generation antipsychotics such as olanzapine are the preferred agents.

Why olanzapine is appropriate: The AAFP guidelines recommend that when pharmacologic therapy for delirium is indicated (i.e., severe agitation with risk of harm to self or others and nonpharmacologic measures have failed), **second-generation antipsychotics such as olanzapine, risperidone, and quetiapine are preferred over haloperidol** due to faster onset of action and fewer adverse effects.[1] The lowest effective dose for the shortest duration is recommended.[1]

Why the other options are incorrect:

- **A. Diphenhydramine** — An anticholinergic antihistamine that is a well-known precipitant and exacerbator of delirium, particularly in elderly patients. It is listed on the AGS Beers Criteria as a medication to avoid in older adults.
- **B. Lorazepam** — Benzodiazepines may worsen or precipitate delirium and should be reserved for delirium caused by alcohol withdrawal, benzodiazepine withdrawal, or seizures. This patient's delirium is secondary to urosepsis, not substance withdrawal.[1][2][3]
- **D. Physical restraints** — The AGS Choosing Wisely campaign explicitly recommends against using physical restraints to manage behavioral symptoms of hospitalized older adults with delirium. Restraints are associated with increased injury, worsened delirium and agitation, longer hospital stays, and even death. Physical restraints on general medical wards should be minimized if not eliminated.[1][2][4]

Would you like to explore the evidence comparing specific second-generation antipsychotics (olanzapine vs. quetiapine vs. risperidone) for delirium management in elderly hospitalized patients?

Relevant images

(CONTENT OMITTED)

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Question 173

A 26-year-old woman comes to the physician because of fatigue, weight loss, and muscle aches during the past 2 months. There is no personal or family history of serious illness. Her only medication is a multivitamin. A metyrapone stimulation test is performed and the results rule out a diagnosis of adrenal insufficiency. Which of the following changes in laboratory findings are most likely to have been observed in this patient following the administration of the drug?

Answer Choices:

(A) Increase in serum ACTH
(B) Decrease in urinary 17-hydroxycorticosteroids
(C) Decrease in serum 11-deoxycortisol
(D) Increase in serum cortisol

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/507e9b19-efb4-456b-a4d8-2bb650452461

OpenEvidence Explanation

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The answer is **A. Increase in serum ACTH**.

Metyrapone inhibits **11β-hydroxylase**, the enzyme that converts 11-deoxycortisol to cortisol. In a patient with an **intact hypothalamic-pituitary-adrenal (HPA) axis** (i.e., adrenal insufficiency has been ruled out), the following cascade occurs after metyrapone administration:[1][2]

1. Cortisol synthesis is blocked → serum cortisol **falls** (not increases, eliminating option D)
2. The drop in cortisol removes negative feedback on the pituitary → **serum ACTH rises** (option A is correct)
3. Increased ACTH drives adrenal steroidogenesis, but because 11β-hydroxylase remains blocked, the cortisol precursor **11-deoxycortisol accumulates and increases** (not decreases, eliminating option C)
4. 11-deoxycortisol and its metabolites are measured as urinary 17-hydroxycorticosteroids (17-OHCS), so urinary 17-OHCS **increase** (not decrease, eliminating option B)[1]

The key distinction is that a normal (intact HPA axis) response to metyrapone — which is what this patient demonstrates since adrenal insufficiency was ruled out — includes a rise in ACTH, a rise in 11-deoxycortisol (>7 µg/dL), and an increase in urinary 17-OHCS.[1][3] Had the patient had adrenal insufficiency, ACTH and 11-deoxycortisol would fail to rise appropriately.

Would you like to explore how the metyrapone stimulation test compares to the cosyntropin (ACTH) stimulation test and insulin tolerance test for diagnosing adrenal insufficiency?

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Question 174

An investigator conducts a study to determine whether earlier detection of glioblastoma multiforme (GBM) in patients increases survival time. One subset of study participants consists of asymptomatic individuals who were diagnosed with GBM after undergoing a screening MRI of the brain. The other subset of study participants was diagnosed with GBM only after they developed symptoms. Results from the study show that the asymptomatic patients who were diagnosed with screening MRI had an average survival time that was 6 weeks longer than that of the patients who were diagnosed after symptom onset. Which of the following statistical biases is most likely to have occurred as a result of the endpoint selected for this study?

Answer Choices:

(A) Observer-expectancy bias
(B) Length-time bias
(C) Surveillance bias
(D) Lead-time bias

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/80de9f67-6039-4d6b-bc27-c3b1aab5a73d

OpenEvidence Explanation

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The answer is **D. Lead-time bias**.

In this study, the endpoint is **survival time measured from the time of diagnosis**. Because the screening MRI group was diagnosed earlier in the disease course (while still asymptomatic), their survival time from diagnosis to death appears longer — even if screening conferred no actual benefit in delaying death. This is the classic definition of **lead-time bias**: the apparent increase in survival attributable to the longer interval after a diagnosis made by screening compared with one made after symptom onset.[1][2][3]

The key distinction from the other answer choices:

- **Length-time bias** (B) refers to screening preferentially detecting slower-growing, more indolent tumors (which have a longer preclinical detectable phase), making screened patients appear to survive longer because their cancers are inherently less aggressive. This is less applicable here because GBM is a uniformly aggressive tumor with relatively little variability in growth rate.[2][4]
- **Surveillance bias** (C) refers to increased detection of disease in a group that is monitored more closely, leading to higher apparent incidence — not a spurious increase in survival time.
- **Observer-expectancy bias** (A) occurs when a researcher's expectations influence the outcome measurement, which is not the mechanism described here.

The study's fundamental flaw is using survival from diagnosis as the endpoint rather than overall mortality, which allows the earlier diagnosis in the screened group to artificially inflate apparent survival by exactly the amount of lead time gained.[1]

Would you like to explore how randomized controlled trials using mortality reduction as the endpoint can overcome lead-time and length-time biases in cancer screening studies?

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Question 175

A 23-year-old man is brought to the emergency department 25 minutes after being involved in a high-speed motor vehicle collision in which he was the restrained driver. On questioning by the paramedics, he reported severe chest pain and mild dyspnea. On arrival, he is confused and unable to provide a history. His pulse is 93/min, respirations are 28/min, and blood pressure is 91/65 mm Hg. Pulse oximetry on room air shows an oxygen saturation of 88%. He is able to move his extremities in response to commands. He opens his eyes spontaneously. Pupils are equal and reactive to light. Examination shows multiple bruises over the trunk and extremities. There is a 3-cm (1.2-in) wound at the left fifth intercostal space at the midclavicular line. There is jugular venous distention. Decreased breath sounds and hyperresonance on percussion are noted on the left. Which of the following is the most appropriate next step in management?

Answer Choices:

(A) CT scan of the chest
(B) Bronchoscopy
(C) Emergency thoracotomy
(D) Needle decompression

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/99856e89-292c-451e-ad8c-aad8a1c40b72

OpenEvidence Explanation

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The correct answer is **D. Needle decompression**.

This patient presents with classic findings of a **tension pneumothorax**: hypotension (91/65 mmHg), tachypnea, hypoxia (SpO_2 88%), jugular venous distention, decreased breath sounds, and hyperresonance on the left side — in the setting of a penetrating chest wound at the left 5th intercostal space. Tension pneumothorax is a clinical diagnosis that requires **immediate decompression** without waiting for imaging confirmation.[1][2]

Why needle decompression is correct:

Tension pneumothorax is a life-threatening emergency requiring emergent management. Per ATLS and WSES-AAST guidelines, the initial step is needle decompression at the 2nd intercostal space, midclavicular line (or 5th intercostal space, midaxillary line), followed by definitive tube thoracostomy.[1][2] Needle decompression serves as a temporizing bridge to chest tube placement and is the fastest bedside intervention to relieve tension physiology.[3]

Why the other options are incorrect:

- **A. CT scan of the chest** — Imaging is inappropriate in a hemodynamically unstable patient with a clinical diagnosis of tension pneumothorax. Delay for imaging risks cardiovascular collapse and cardiac arrest.[2]
- **B. Bronchoscopy** — Not indicated as an initial intervention for tension pneumothorax.
- **C. Emergency thoracotomy** — Reserved for patients in traumatic cardiac arrest or with specific indications (e.g., penetrating cardiac injury with loss of vital signs). This patient still has a pulse and blood pressure; decompression should be attempted first.[1]

The WSES-AAST guidelines emphasize that tension pneumothorax clinical findings — including hemodynamic instability, hypotension, tachycardia, jugular venous distension, and respiratory failure — require emergent decompression even in the prehospital setting.[1]

Would you like to explore the indications and technique for transitioning from needle decompression to definitive tube thoracostomy in penetrating chest trauma?

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Question 177

A 55-year-old man presents to a rheumatologist with bilateral wrist and knee pain that has been present for the last 10 years. The patient was a professional athlete who retired at age 50. He also notes morning stiffness in his joints that lasts approx. 50 minutes. He denies joint swelling, color changes in his digits, dryness of mucous membranes, and constitutional symptoms such as fever and chills. On physical exam, the physician notes several non-tender nodules on the left 1st, 3rd, and 4th distal interphalangeal joints. There is also tenderness with palpation at the base of both thumbs. The patient's knees are enlarged, bilaterally, and he has pain and crepitus on passive range of motion. Which of the following is the most likely diagnosis?

Answer Choices:

(A) Ankylosing spondylitis
(B) Gout
(C) Osteoarthritis
(D) Fibromyalgia

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/f5e20122-e4b0-4e4e-b4d1-9f9a2f60b74e

OpenEvidence Explanation

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The most likely diagnosis is **C. Osteoarthritis**.

This presentation is classic for osteoarthritis (OA), supported by several key features:

- **Non-tender nodules on the DIP joints** — these are **Heberden's nodes**, a hallmark of OA affecting the hands.[1][2]
- **Tenderness at the base of both thumbs** — involvement of the **first carpometacarpal (CMC) joint** is one of the most characteristic sites of hand OA.[1]
- **Bilateral knee enlargement with crepitus** — bony enlargement and crepitus on passive range of motion are cardinal signs of knee OA, and the knees are among the most commonly affected weight-bearing joints.[2]
- **Morning stiffness lasting ~50 minutes** — OA-related stiffness is typically **<60 minutes** (often <30 minutes), distinguishing it from inflammatory arthritides like rheumatoid arthritis, where stiffness usually exceeds 60 minutes.[1][2]
- **History as a professional athlete** — repetitive joint stress and prior mechanical loading are well-established risk factors for OA.[2]
- **Absence of systemic/inflammatory features** — no fever, no joint swelling suggestive of synovitis, and no color changes in digits all argue against inflammatory or autoimmune etiologies.

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The most likely diagnosis is **C. Osteoarthritis (OA)**.

This presentation is a textbook case of OA, with multiple classic features:

- **Heberden's nodes** — the non-tender nodules on the DIP joints are bony enlargements pathognomonic for OA, with a strong association with underlying radiographic OA changes.[3][4]
- **First CMC joint tenderness** — the base of the thumb is one of the most characteristic sites of hand OA.[1][5]

- **Bilateral knee enlargement with crepitus** — bony enlargement (95% specificity) and crepitus (89% sensitivity) are cardinal signs of knee OA on physical examination.[6]
- **Morning stiffness <60 minutes** — OA-related stiffness is typically brief (<30 minutes), whereas inflammatory arthritides such as rheumatoid arthritis cause stiffness lasting >1 hour. The 50-minute duration here is at the upper end but still within the OA range.[7][8]
- **History of professional athletics** — prior joint injury and repetitive mechanical loading are well-established OA risk factors.[8]
- **Absence of inflammatory or systemic features** — no joint swelling/warmth, no fever/chills, and no digit color changes effectively rule out inflammatory arthritides.[8][9]

Why the other options are incorrect:

- **A. Ankylosing spondylitis** — primarily affects the axial skeleton (sacroiliac joints, spine) in young men, with inflammatory back pain and prolonged morning stiffness. This patient has no axial symptoms.[10]
- **B. Gout** — presents with acute, episodic, intensely inflammatory monoarticular or oligoarticular flares (erythema, warmth, swelling), not a chronic 10-year insidious course with bony nodules.[11]
- **D. Fibromyalgia** — characterized by widespread pain, fatigue, and tenderness at specific tender points without objective joint findings such as crepitus, bony enlargement, or nodules.[10]

Would you like to explore the current evidence-based management approach for polyarticular osteoarthritis, including pharmacologic and non-pharmacologic strategies?

Relevant images

(CONTENT OMITTED)

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Question 179

A previously healthy 19-year-old man comes to the physician with right-sided, dull, throbbing scrotal pain for 12 hours. He has also had a burning sensation on urination and increased urinary frequency for the past 3 days. He has not had urethral discharge. He is sexually active with one female partner and does not use condoms. Vital signs are within normal limits. Physical examination shows a tender right testicle; lifting it provides relief. The penis appears normal, with no discharge at the meatus. Laboratory studies show a normal complete blood count; urinalysis shows 3 WBC/hpf. A Gram stain of a urethral swab shows polymorphonuclear leukocytes but no organisms. Testicular ultrasound shows increased blood flow to the right testicle compared to the left. Which of the following is the most likely cause of this patient's symptoms?

Answer Choices:

(A) Neisseria gonorrhoeae infection
(B) Testicular tumor
(C) Chlamydia trachomatis infection
(D) Varicocele

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/99c9615d-924e-4fe2-aac4-29ef18d77df5

OpenEvidence Explanation

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The answer is **C. Chlamydia trachomatis infection**.

This presentation is classic for **acute epididymitis** caused by *Chlamydia trachomatis*. Several features point to this diagnosis:

- **Age and sexual history**: In sexually active males aged 14–35, *C. trachomatis* and *N. gonorrhoeae* are the most common causes of epididymitis. *C. trachomatis* is the more common of the two.[1][2][3]
- **Gradual onset of scrotal pain with dysuria and urinary frequency**: This is the typical presentation of epididymitis, in contrast to the sudden onset seen with testicular torsion.[2]
- **Positive Prehn sign** (pain relief with testicular elevation): Characteristic of epididymitis.[2]
- **Increased blood flow on ultrasound**: Color Doppler showing hyperemia is a hallmark of epididymitis/epididymo-orchitis, in contrast to the decreased or absent flow seen in testicular torsion.[4][5]
- **Urethral Gram stain showing PMNs but no organisms**: This is the key distinguishing feature between *Chlamydia* and *Neisseria gonorrhoeae*. Gonococcal urethritis classically shows **intracellular gram-negative diplococci** on Gram stain. The absence of organisms on Gram stain with the presence of PMNs is characteristic of **nongonococcal urethritis**, most commonly caused by *C. trachomatis*. Chlamydia is an obligate intracellular organism that does not stain on Gram stain and requires NAAT for detection.[1][6][7]

Why not the other options?

- A. *N. gonorrhoeae*: **Would be expected to show gram-negative intracellular diplococci on urethral Gram stain.**[6]
- **B. Testicular tumor**: Typically presents as a painless mass, not with acute pain, dysuria, or increased blood flow pattern consistent with inflammation.[2]

- **D. Varicocele**: Presents as a painless "bag of worms" in the scrotum, most commonly on the left side, and is not associated with dysuria or inflammatory changes on ultrasound.[2]

Would you like to explore the recommended empiric antibiotic regimens for STI-related epididymitis per current CDC guidelines?

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Question 181

A 6-year-old boy is brought to the physician by his mother because of a 2-day history of dysuria and increased urinary frequency. Vital signs are within normal limits. Urinalysis shows cloudy, red urine. This patient's clinical presentation is best explained by an infection with a virus with which of the following features?

Answer Choices:

(A) Non-enveloped with linear, single-stranded DNA
(B) Non-enveloped with linear, single-stranded RNA
(C) Enveloped with linear, single-stranded RNA
(D) Non-enveloped with linear, double-stranded DNA

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/dda3091e-c243-4c72-a188-0c3442dab891

OpenEvidence Explanation

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The answer is **D. Non-enveloped with linear, double-stranded DNA**.

This clinical presentation — a young boy with dysuria, urinary frequency, and cloudy, red (hemorrhagic) urine — is classic for **adenovirus-associated**

hemorrhagic cystitis, which predominantly affects boys (male-to-female ratio ~2–3:1) and is most commonly caused by adenovirus serotypes 11 and 21.[1]

Adenoviruses are non-enveloped, icosahedral viruses with linear double-stranded DNA genomes (~25–48 kb).[2][3][4] These structural features make them remarkably resistant to detergents, acidic conditions, and moderate heating.[2] In immunocompetent children, adenovirus-related hemorrhagic cystitis is typically self-limited, lasting 4–14 days, and presents with gross hematuria, dysuria, and frequency.[1][5]

The other options correspond to different virus families:

- **A (non-enveloped, linear ssDNA)** — Parvoviruses (e.g., parvovirus B19)
- **B (non-enveloped, linear ssRNA)** — Picornaviruses (e.g., enteroviruses)
- **C (enveloped, linear ssRNA)** — Paramyxoviruses, Filoviruses, or others

None of these are classically associated with hemorrhagic cystitis in otherwise healthy children.

Would you like to explore the management approach and expected clinical course of adenovirus-associated hemorrhagic cystitis in immunocompetent pediatric patients?

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Question 185

A previously healthy 18-month-old boy is brought to the physician by his parents for evaluation of an abdominal mass noticed a few days ago. He appears markedly pale and lethargic. Examination shows a 6-cm, nonmobile mass in the left upper quadrant that crosses the midline. 24-hour urine collection shows elevated homovanillic acid and vanillylmandelic acid. Further evaluation including biopsy confirms the diagnosis of intermediate-risk neuroblastoma. The physician recommends the established standard treatment, which is initiation of neoadjuvant chemotherapy followed by surgical resection, if possible. After a thorough discussion of the risks and benefits of chemotherapy, the likelihood of unresectability without neoadjuvant treatment, and the prognosis without it, the patient's parents steadily refuse chemotherapy because they do not want their son to suffer the side effects. They prefer to take their son home for supportive care only. Which of the following is the most appropriate action by the physician?

Answer Choices:

(A) Help the parents to arrange supportive care at home
(B) Refer the patient to another oncologist
(C) Recommend for parents to take 2 weeks to think about decision
(D) Seek a court order for neoadjuvant chemotherapy

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/33c84dc1-1e55-400b-8813-b21798a7e80e

OpenEvidence Explanation

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The most appropriate action is **D. Seek a court order for neoadjuvant chemotherapy**.

This case involves an 18-month-old child — a minor without decision-making capacity — with a treatable, life-threatening malignancy. Intermediate-risk neuroblastoma has an **overall survival exceeding 90–95%** with standard chemotherapy-based treatment.[1][2][3] Parental authority, while generally respected, is not absolute when refusal of treatment places a child at significant risk of serious harm or death.

Why the other options are incorrect:

- **A (Arrange supportive care at home):** Acquiescing to the parents' refusal would constitute complicity in medical neglect. Without treatment, this child with a large, midline-crossing tumor and systemic symptoms (pallor, lethargy) faces a high likelihood of death from a disease that is highly curable with standard therapy.[1][4]
- **B (Refer to another oncologist):** While a second opinion can be part of the process, simply referring the patient does not fulfill the physician's obligation to protect the child. The diagnosis and treatment plan are already established and confirmed by biopsy; the issue is not a difference in medical opinion but parental refusal of clearly beneficial care.
- **C (Recommend 2 weeks to think):** Delaying treatment for a symptomatic child with an aggressive tumor is not appropriate. While shared decision-making and further discussion are important, the question states that a thorough discussion has already occurred and the parents "steadily refuse." Unnecessary delay could worsen the child's prognosis.

Legal and ethical basis for seeking a court order:

The AAP and ACEP guidelines establish that when parents decline a recommended intervention, physicians must determine whether the refusal incurs risk of harm to the child, and if so, physicians may be **legally obligated to**

seek state involvement and a court order authorizing treatment.[5][6][7] Courts have consistently upheld the principle of *parens patriae* — the state's authority to intervene to protect children from harm — and judges are more likely to override parental refusals when the prognosis with treatment is good.[8][9] Parental refusal of chemotherapy for a child with a potentially curable cancer is a well-recognized scenario in which legal intervention is appropriate as a last resort.[10][11]

Would you like to explore the ethical frameworks and stepwise approaches recommended for managing treatment refusal disputes in pediatric oncology?

Relevant images

(CONTENT OMITTED)

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Question 186

A laboratory primarily involved with studying cellular proofreading mechanisms is investigating the question of whether the ribosome can recognize a mischarged amino acid and still be incorporated into the growing peptide. In order to do so, they biochemically charge a Lys-tRNA with valine instead of lysine and insert the tRNA into the cell. They design an mRNA sequence that contains only codons for lysine. Which of the following will most likely occur?

Answer Choices:

(A) The ribosome will recognize the mischarged tRNA and prevent its incorporation by removing the valine
(B) The mischarged tRNA with valine will be incorporated in the codons that specificy for lysine
(C) The mischarged tRNA will be degraded by the proteasome
(D) The mischarged tRNA will be removed by the lysyl-tRNA synthetase

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/0dbc4c5e-a351-43a5-8ee6-909d1c0a62f2

OpenEvidence Explanation

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The answer is **B. The mischarged tRNA with valine will be incorporated in the codons that specify for lysine**.

The ribosome selects aminoacyl-tRNAs based solely on **codon-anticodon complementarity**, not by recognizing the amino acid attached to the tRNA.[1][2] During decoding, the ribosome monitors the geometry of the codon-anticodon duplex in the A site using conserved 16S rRNA nucleotides (G530, A1492, A1493), which assess whether the base pairing adopts proper Watson-Crick geometry.[1][3] The identity of the amino acid itself is invisible to the ribosome's decoding machinery.

In this experiment, the Lys-tRNA retains its **lysine anticodon**, so it will form a cognate codon-anticodon interaction with the lysine codons on the mRNA. Because the anticodon matches, the ribosome will accept the tRNA and incorporate valine into the growing peptide chain — even though valine is the "wrong" amino acid for those codons.[4][5] The ribosome is unable to correct misincorporations after they occur; it lacks any mechanism to proofread the amino acid itself.[6]

Why the other options are incorrect:

- **A (ribosome removes valine):** The ribosome has no mechanism to inspect or remove the amino acid attached to a tRNA. Its proofreading is limited to codon-anticodon geometry.[2][7]
- **C (proteasome degrades the tRNA):** The proteasome degrades proteins, not tRNAs. This answer conflates two unrelated quality control systems.
- **D (lysyl-tRNA synthetase removes it):** Aminoacyl-tRNA synthetases have editing domains that can hydrolyze misacylated amino acids, but lysyl-tRNA synthetase would not remove valine from a Lys-tRNA that has already been released and delivered to the ribosome. Moreover, the synthetase's editing function typically acts during or immediately after the charging reaction, not on free aminoacyl-tRNAs in the cytoplasm.[4]

This classic experiment demonstrates that the **genetic code is interpreted through the anticodon, not the amino acid**, and that translational fidelity depends critically on the accuracy of aminoacyl-tRNA synthetases in correctly charging tRNAs.

Would you like to explore how aminoacyl-tRNA synthetase editing domains prevent misacylation errors and the clinical consequences of mistranslation?

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Question 187

A 65-year-old man with metastatic lung cancer has been experiencing severe, unremitting pain. He has required escalating doses of oral morphine, but is now having dose limiting side-effects. His pain management team recommends using a medication that can reduce his opioid need through interaction with the NMDA-receptor. Which of the following was the most likely recommended agent?

Answer Choices:

(A) Propofol
(B) Ketamine
(C) Fentanyl
(D) Midazolam

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/f539b6b9-32da-4a66-b755-0352676e28ba

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OpenEvidence Explanation

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The correct answer is **B. Ketamine**.

Ketamine is a **noncompetitive NMDA receptor antagonist** that, at low subanesthetic doses, produces analgesia and modulates central sensitization,

hyperalgesia, and opioid tolerance.[1][2] It is the only agent among the answer choices that acts through the NMDA receptor to reduce opioid requirements.

Here is why the other options are incorrect:

- **A. Propofol** – A GABA-A receptor agonist used for sedation and anesthesia; it has no clinically relevant NMDA receptor activity.
- **C. Fentanyl** – A potent synthetic mu-opioid receptor agonist. Switching to fentanyl would not address the NMDA-mediated mechanism described in the question, and it would not reduce overall opioid need.
- **D. Midazolam** – A benzodiazepine acting on GABA-A receptors; it has no NMDA receptor antagonist properties.

The NCCN Adult Cancer Pain Guidelines list ketamine as a non-opioid analgesic adjunct, noting that low (subanesthetic) doses block glutamate at the NMDA receptor and can modulate opioid tolerance.[1] The American Society of Pain and Neuroscience (ASPN) guidelines similarly recommend considering ketamine for refractory cancer pain not responding to opioids and adjuvant analgesics.[2] A systematic review of 35 RCTs involving 2,279 cancer pain patients found that ketamine significantly reduced pain intensity and morphine dosage requirements.[3] Its primary mechanism — NMDA receptor blockade — reduces secondary hyperalgesia, the wind-up phenomenon, and opioid-induced hyperalgesia, thereby restoring opioid analgesic efficacy.[4][5]

Would you like to explore the practical dosing protocols and monitoring requirements for subanesthetic ketamine infusions in the palliative care setting?

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Question 190

A 23-year-old college student presents to the clinic with a history of intermittent chest discomfort. He reports that, about once per month for the past 8 or 9 months, he's had episodes of feeling like my chest is going to explode. During these episodes, he also feels shortness of breath, feels shakiness throughout his arms and legs, and sweats so heavily that he needs to change his shirt. He is unsure of any clear precipitating factors but thinks they may occur more often around important exams or when big school projects are due. He shares that, as these episodes continue to recur, he has had mounting anxiety about having one when he is in class or at a restaurant. As a result, he is leaving the house less and less. He has no past medical history; the physical exam is unremarkable. Which of the following is the best medication for the long-term management of this patient's condition?

Answer Choices:

(A) Citalopram
(B) Lithium
(C) Propranolol
(D) Quetiapine

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/bff60dfc-1997-4465-9a8a-eb40f785e8cb

OpenEvidence Explanation

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The best answer is **A. Citalopram**.

This patient presents with classic **panic disorder with developing agoraphobia**: recurrent, unexpected episodes of intense chest discomfort, shortness of breath, tremulousness, and diaphoresis occurring approximately monthly, with growing anticipatory anxiety and avoidance behavior (leaving the house less). The episodes may be more common around stressors but lack a consistent, identifiable trigger.

SSRIs are the first-line pharmacotherapy for long-term management of panic disorder. Citalopram is an SSRI, making it the correct choice among the options listed. Multiple guidelines and meta-analyses consistently recommend SSRIs (and SNRIs) as first-line treatment for both panic disorder and agoraphobia.[1][2][3] A network meta-analysis of 87 panic disorder RCTs (n = 12,800) found that SSRIs provided the best balance of high remission rates and low adverse event risk compared with other drug classes.[2][3] Treatment should be continued for at least 6–12 months to minimize relapse.[1][2]

Why the other options are incorrect:

- **B. Lithium** – A mood stabilizer used for bipolar disorder; it has no role in the treatment of panic disorder.
- **C. Propranolol** – A beta-blocker with limited evidence in anxiety disorders. A systematic review found insufficient evidence to support routine use of propranolol for panic disorder or other anxiety disorders. Its use is generally limited to as-needed management of performance anxiety (a subtype of social anxiety disorder).[2][4][5][6]
- **D. Quetiapine** – An atypical antipsychotic that, while showing some anxiolytic effect, is poorly tolerated with significant metabolic side effects (weight gain, hyperglycemia, hyperlipidemia) and high discontinuation rates, limiting it to refractory cases rather than first-line use.[2][7]

Would you like to explore the specific dosing and titration strategies for SSRIs in panic disorder, including how to manage the initial jitteriness that can occur during treatment initiation?

Relevant images

(CONTENT OMITTED)

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Question 193

During a Mycobacterium tuberculosis infection, Th1 cells secrete a factor capable of stimulating phagosome-lysosome fusion within macrophages. In addition, the secreted factors help activate macrophages to produce mediators such as NO, which are capable of destroying the invading pathogen. Furthermore, activation of the macrophages by the secreted factor eventually leads to the formation of a tubercle. Which of the following factors is secreted by Th1 cells and responsible for these actions?

Answer Choices:

(A) IL-4
(B) TNF-alpha
(C) IFN-gamma
(D) Histamine

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/7c81ccbd-d68a-4cfe-b4ed-a2ab56e00bfb

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OpenEvidence Explanation

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The correct answer is **C. IFN-gamma (interferon-gamma)**.

IFN-γ is the principal cytokine secreted by Th1 cells responsible for all three actions described in this question:

1. **Phagosome-lysosome fusion**: IFN-γ overcomes the phagosome maturation block that M. *tuberculosis* uses to survive within macrophages, inducing acidification and maturation of phagosomes into phagolysosomes.[1][2][3]

2. **Macrophage activation and NO production**: IFN-γ classically activates macrophages by upregulating inducible nitric oxide synthase (iNOS/NOS2), which metabolizes L-arginine to produce nitric oxide (NO) — a critical microbicidal effector against intracellular mycobacteria.[1][4][5]

3. **Granuloma (tubercle) formation**: IFN-γ-driven macrophage activation, along with TNF-α (which IFN-γ stimulates macrophages to release), leads to the organized cellular aggregation that forms the granuloma/tubercle characteristic of TB.[6][7]

The following figure illustrates the cytokine cascade in granuloma formation, highlighting the central role of IFN-γ produced by T cells in activating macrophages and driving granuloma development:

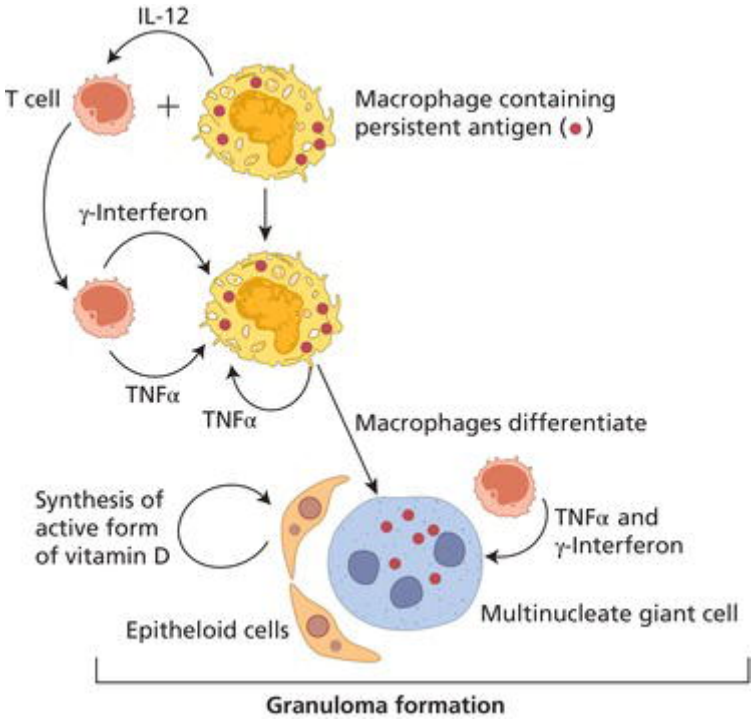


Figure 4. Mechanisms of T cell-dependent granuloma formation. IL, interleukin; TNF, tumour necrosis factor.

Why the other options are incorrect:

- **A. IL-4** — A Th2 cytokine that induces alternatively activated macrophages (via arginase-1 upregulation) and is considered inhibitory or redundant in TB defense.[4]
- **B. TNF-α** — Important for granuloma maintenance and is produced by macrophages (not primarily by Th1 cells); it works downstream of IFN-γ signaling.[6]
- **D. Histamine** — Released by mast cells and basophils in allergic/type I hypersensitivity reactions; it plays no role in Th1-mediated anti-mycobacterial immunity.

Would you like to explore how defects in the IL-12/IFN-γ axis lead to Mendelian susceptibility to mycobacterial disease (MSMD)?

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Question 195

A group of researchers conducted a study to determine whether there is an association between folic acid supplementation before pregnancy and autism spectrum disorder (ASD) in offspring. The researchers retrospectively surveyed 200 mothers with children diagnosed with ASD during the first 4 years of life and 200 mothers with healthy children. All participants were interviewed about their prenatal consumption of folic acid using standardized questionnaires. A 94% response rate was obtained from the surveys. The study ultimately found that folic acid supplementation was associated with lower rates of ASD in offspring (OR = 0.3, $p < 0.01$). Which of the following type of bias is most likely to have influenced these results?

Answer Choices:

(A) Interviewer bias
(B) Latency period
(C) Recall bias
(D) Survival bias

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/aa96296c-af6b-4f74-b5df-a7feedb8ae94

OpenEvidence Explanation

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The answer is **C. Recall bias**.

This study is a **retrospective case-control study** that relies on mothers' self-reported recall of prenatal folic acid use via standardized questionnaires. **Recall bias** is the most likely source of bias because mothers of children diagnosed with ASD (cases) are more motivated to search their memories for potential causes or protective factors they may have missed during pregnancy, compared to mothers of healthy children (controls) who have no such motivation.[1][2]

This differential recall is a well-documented phenomenon in retrospective studies of prenatal exposures. Mothers who have given birth to children with adverse outcomes tend to recall the course of their pregnancies differently — either remembering more exposures in an effort to understand what went wrong, or differentially reporting protective factors they did or did not take.[3] Studies have shown that the validity of questionnaire-based maternal recall decreases over time and that reporting differences between cases and controls can shift odds ratios by as much as 26% in either direction.[4] Registry-based studies specifically note that they "avoid recall biases associated with survey-based methods," underscoring that survey-based retrospective designs like the one described are particularly susceptible to this bias.[5]

Why not the other options:

- **Interviewer bias (A)** — While possible, the use of standardized questionnaires reduces this risk, and the question stem does not suggest differential interviewing between groups.
- **Latency period (B)** — This refers to the time between exposure and disease onset and is not a type of bias per se.
- **Survival bias (D)** — This would apply if the study systematically excluded participants who were lost to follow-up or died, which is not the primary concern here.

Would you like to explore how prospective cohort designs and registry-based studies have attempted to overcome recall bias in studying the folic acid–ASD association?

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Question 197

A 40-year-old woman presents to her primary care physician for a checkup. She has felt weaker lately and has lost some weight. She denies any urinary issues. Her BUN at her last visit 4 months ago was 45 mg/dL, and her creatinine was 2.0 mg/dL. Her laboratory studies this visit are seen below:

Hemoglobin: 8 g/dL
Hematocrit: 29%
Leukocyte count: 9,500/mm^3 with normal differential
Platelet count: 197,000/mm^3

Serum:
Na+: 139 mEq/L
Cl-: 100 mEq/L
K+: 5.9 mEq/L
HCO3-: 17 mEq/L
BUN: 59 mg/dL
Glucose: 99 mg/dL
Creatinine: 2.3 mg/dL
Ca2+: 9.0 mg/dL

Which of the following is the most likely diagnosis?

Answer Choices:

(A) Acute kidney failure
(B) Chronic kidney failure
(C) Obstructive uropathy
(D) Renal cell carcinoma

Correct Answer:

(B)

OpenEvidence Response:

> **(B)** ✓

OpenEvidence Link: https://openevidence.com/ask/0c6eaf7f-4b9c-4dcd-9693-94c7e144c3de

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OpenEvidence Explanation

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The most likely diagnosis is **B. Chronic kidney failure**.

This patient's presentation is classic for CKD based on several converging findings:

1. **Duration >3 months**: The KDIGO guidelines define CKD as abnormal kidney function present for ≥3 months. This patient had an elevated BUN (45 mg/dL) and creatinine (2.0 mg/dL) **4 months ago**, with further worsening now (BUN 59, Cr 2.3), confirming chronicity.[1]
2. **Anemia of CKD**: Hemoglobin of 8 g/dL is consistent with erythropoietin deficiency seen in CKD. Anemia is among the most common complications, affecting ~41% of CKD patients across global cohorts.[2]
3. **Metabolic acidosis**: Bicarbonate of 17 mEq/L reflects the impaired acid excretion characteristic of CKD. The prevalence of metabolic acidosis increases with declining GFR.[3]
4. **Hyperkalemia**: Potassium of 5.9 mEq/L is expected as the prevalence of hyperkalemia increases with declining kidney function.[4]
5. **Constitutional symptoms**: Weakness and weight loss are attributable to uremia and the catabolic state of CKD.

Why not the other options:

- **A. Acute kidney failure** — AKI is defined by an abrupt decline in function (creatinine rise ≥0.3 mg/dL within 48 hours or ≥1.5× baseline within 7 days).

This patient's renal dysfunction has been documented for >4 months with a gradual trajectory, meeting the definition of CKD rather than AKI.[5]

- **C. Obstructive uropathy** — The patient explicitly denies urinary symptoms, making obstruction unlikely. Obstructive uropathy typically presents with urinary complaints (hesitancy, retention, flank pain) and would require imaging confirmation such as hydronephrosis on ultrasound.[5][6]

- **D. Renal cell carcinoma** — While RCC can cause anemia and constitutional symptoms, it would not typically explain the hyperkalemia, metabolic acidosis, and progressive azotemia pattern seen here. The overall constellation is far more consistent with CKD.

Would you like to discuss the staging of this patient's CKD or the recommended workup for identifying the underlying etiology?

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Question 199

A 2-year-old girl with recurrent urinary tract infections is brought to the physician for a follow-up examination. Renal ultrasound shows bilateral dilation of the renal pelvis. A voiding cystourethrography shows retrograde flow of contrast into the ureters during micturition. Histologic examination of a kidney biopsy specimen is most likely to show which of the following findings?

Answer Choices:

(A) Glomerular crescents with macrophages
(B) Matrix expansion with mesangial proliferation
(C) Cortical thinning with tubular atrophy
(D) Thickened glomerular capillary loops

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/8b00386d-990d-4127-8cab-950fd1b5161d

OpenEvidence Explanation

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The answer is **C. Cortical thinning with tubular atrophy**.

This clinical scenario describes **vesicoureteral reflux (VUR)** — bilateral renal pelvis dilation on ultrasound and retrograde flow of contrast into the ureters on

voiding cystourethrography in a 2-year-old girl with recurrent UTIs. The characteristic renal histopathology of reflux nephropathy is **cortical thinning with tubular atrophy**, reflecting chronic tubulointerstitial damage from recurrent pyelonephritis and intrarenal reflux.

The hallmark histologic features of reflux nephropathy include interstitial fibrosis, chronic inflammatory cell infiltration, tubular atrophy, and cortical thinning — essentially the pattern of chronic pyelonephritis.[1][2][3] Morphologic studies in children with VUR have demonstrated lobar atrophy with variable **tubular atrophy** and glomerular sclerosis, with parenchymal destruction that can progress to complete loss of nephronic elements.[1] Recurrent pyelonephritic episodes are a major risk factor for this acquired renal scarring, particularly in girls.[4][5]

Why the other options are incorrect:

- **A. Glomerular crescents with macrophages** — This is characteristic of rapidly progressive (crescentic) glomerulonephritis, not reflux nephropathy.
- **B. Matrix expansion with mesangial proliferation** — While mesangial changes can occur late in reflux nephropathy as a secondary phenomenon, the primary and most characteristic finding is tubulointerstitial damage, not mesangial proliferation.[6]
- **D. Thickened glomerular capillary loops** — This pattern is seen in membranous nephropathy, not reflux nephropathy.

Would you like to explore the current guidelines on management of vesicoureteral reflux in children, including indications for surgical correction versus antibiotic prophylaxis?

References

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Question 200

An unconscious 55-year-old man is brought to the Emergency Department by ambulance. He had recently lost his job and his house was about to begin foreclosure. His adult children were concerned for his well being and called the police requesting a welfare check. He was found unresponsive in his gurague. There were several empty bottles of vodka around him and one half empty container of antifreeze. A review of his medical records reveals that he was previously in good health. Upon arrival to the ED he regains consciousness. His blood pressure is 135/85 mmHg, heart rate 120/min, respiratory rate 22/min, and temperature 36.5°C (97.7°F). On physical exam his speech is slurred and he has difficulty following commands. His abdomen is diffusely tender to palpation with no rebound tenderness. Initial laboratory tests show an elevated serum creatinine (Cr) of 1.9 mg/dL, and blood urea nitrogen (BUN) of 29 mg/dL. Which of the following findings would be expected in this patient's urine?

Answer Choices:

(A) Calcium oxalate crystals
(B) Hyaline casts
(C) Urine ketones
(D) Urate crystals

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/9f1bde54-2d81-4157-a7b8-1b291b309a3e

OpenEvidence Explanation

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The answer is **A. Calcium oxalate crystals**.

This clinical scenario describes **ethylene glycol (antifreeze) poisoning**, evidenced by the half-empty container of antifreeze found at the scene, combined with altered mental status, tachycardia, tachypnea, abdominal tenderness, and acute kidney injury (creatinine 1.9 mg/dL, BUN 29 mg/dL).

Ethylene glycol is metabolized by alcohol dehydrogenase to glycolaldehyde, then to glycolic acid (the primary cause of metabolic acidosis), and ultimately to **oxalic acid**, which precipitates with calcium to form **calcium oxalate crystals** in the urine and renal tubules.[1] Dihydrate crystals (envelope-shaped) appear early, while monohydrate crystals (needle-shaped) appear later.[2] This crystalluria is a hallmark laboratory finding of ethylene glycol poisoning and contributes directly to the acute kidney injury through proximal tubular necrosis.[3][4]

Why the other options are incorrect:

- **B. Hyaline casts** — nonspecific findings associated with concentrated urine or prerenal states, not characteristic of ethylene glycol toxicity.
- **C. Urine ketones** — would be expected with **isopropanol** (rubbing alcohol) ingestion, which is metabolized to acetone, producing ketonuria without significant metabolic acidosis.[1]
- **D. Urate crystals** — associated with hyperuricemia (e.g., tumor lysis syndrome, gout), not ethylene glycol poisoning.

Notably, the coingestion of ethanol (vodka) in this case may have partially delayed the onset of toxicity by competitively inhibiting alcohol dehydrogenase, but the elevated creatinine indicates that significant metabolism of ethylene glycol to its toxic metabolites has already occurred.[1]

Would you like to explore the management approach for ethylene glycol poisoning, including indications for fomepizole versus hemodialysis?

Relevant images

(CONTENT OMITTED)

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Question 204

A 10-year-old Caucasian female with Turner's syndrome underwent an abdominal imaging study and was discovered that the poles of her kidneys were fused inferiorly. Normal ascension of kidney during embryological development would be prevented by which of the following anatomical structures?

Answer Choices:

(A) Superior mesenteric artery
(B) Inferior mesenteric artery
(C) Celiac artery
(D) Splenic artery

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/62e917d4-13fe-463d-af42-d7fc40967b72

OpenEvidence Explanation

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The answer is **B. Inferior mesenteric artery**.

This clinical scenario describes a **horseshoe kidney**, the most common renal fusion anomaly, which is strongly associated with Turner syndrome (occurring in

approximately 10% of patients).[1][2] In horseshoe kidney, the lower poles of the two kidneys fuse across the midline, typically anterior to the great vessels.

During embryological development, the kidneys normally ascend from the pelvis to their final lumbar position. In a horseshoe kidney, the fused isthmus connecting the lower poles becomes trapped beneath the **inferior mesenteric artery (IMA)** as it attempts to ascend, preventing the kidneys from reaching their normal position at the L1–L2 level. The horseshoe kidney therefore remains lower than normal, typically at the **L3–L4 vertebral level**.[3][4]

The other arteries listed do not serve as the anatomical barrier to renal ascent:

- The **superior mesenteric artery** (A) arises at a higher level and is not the structure that impedes ascent of the fused isthmus.
- The **celiac artery** (C) and **splenic artery** (D) are located even more superiorly and are not relevant to this embryological process.

Turner syndrome patients should undergo baseline renal ultrasonography, as structural renal malformations (including horseshoe kidney, duplicated collecting systems, and ectopic kidneys) are found in **25–40%** of patients.[1][2]

Would you like to explore the clinical complications and long-term surveillance recommendations for horseshoe kidney in Turner syndrome patients?

Relevant images

(CONTENT OMITTED)

References

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Question 206

Researchers are studying the inheritance pattern of mutations in the cystic fibrosis transmembrane regulator (CFTR) gene, the gene responsible for cystic fibrosis. It is believed that, in addition to the commonly found ΔF508 mutation, a novel mutation in this gene is found in a particular population under study. Which of the following would most likely suggest that these two loci have a high probability of being closely linked?

Answer Choices:

(A) LOD Score < 1
(B) LOD Score < 2
(C) LOD Score > 3
(D) LOD Score = 0

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/9572d84b-4cbf-4d74-8d97-61751eb6d51b

OpenEvidence Explanation

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The correct answer is **C. LOD Score > 3**.

The **LOD (logarithm of the odds) score** is the standard statistical measure used to assess genetic linkage between two loci. A LOD score greater than 3 has been

the traditional threshold for declaring **significant evidence of linkage**, corresponding to odds of 1000:1 in favor of linkage (equivalent to $p \approx 0.0001$).[1][2]

Key LOD score interpretation thresholds:

- **LOD > 3**: Accepted as significant evidence that two loci are linked — meaning they are close enough on the same chromosome that they tend to be inherited together more often than expected by chance.[1][2][3]
- **LOD = 0**: Indicates equal likelihood of linkage versus no linkage (no evidence either way).[1]
- **LOD < −2**: Generally accepted as evidence **against** linkage between the two loci.[2]

In the context of this question, both the ΔF508 mutation and the novel mutation reside in the CFTR gene on chromosome 7. A LOD score > 3 would provide statistically significant evidence that these two loci cosegregate, consistent with their close physical proximity. This principle was applied in the original mapping of the CF locus, where LOD scores of 12–18 were obtained linking CFTR-region markers.[4]

The other answer choices (LOD < 1, LOD < 2, LOD = 0) would all fail to meet the threshold for declaring linkage and would either suggest no evidence or evidence against linkage.[1]

Would you like to explore how recombination fraction (θ) relates to physical distance between loci and its implications for genetic counseling in cystic fibrosis carrier screening?

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Question 208

A clinical researcher is interested in creating a new drug for HIV patients. Darunavir has been particularly efficacious in recent patients; however, some have experienced an increased incidence of hyperglycemia. A new drug called DN501 is developed with the same mechanism of action as darunavir but fewer side effects. Which of the following is the mechanism of action of DN501?

> **Answer Choices:**
>
> (A) Prevents viral transcription
> (B) Inhibits viral assembly
> (C) Inhibits viral entry
> (D) Prevents T-cell binding

> **Correct Answer:**
>
> **(B)**
>
> **OpenEvidence Response:**
>
> **(B)** ✓

OpenEvidence Link: https://openevidence.com/ask/bc37977d-a808-4558-806f-db77b4019d9f

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OpenEvidence Explanation

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The answer is **B. Inhibits viral assembly**.

Darunavir is an **HIV-1 protease inhibitor (PI)** that selectively inhibits the cleavage of HIV-1 encoded Gag-Pol polyproteins in infected cells, thereby

preventing the formation of mature virus particles.[1] This process — the proteolytic processing of viral polyproteins into functional structural and enzymatic components — is a critical step in viral assembly and maturation. Without proper cleavage by HIV protease, immature, non-infectious viral particles are produced.[2][3]

Since DN501 shares the same mechanism of action as darunavir, it would also function as a protease inhibitor that inhibits viral assembly.

The other options correspond to different antiretroviral drug classes:

- **A (Prevents viral transcription)** — This describes reverse transcriptase inhibitors (NRTIs, NNRTIs) or integrase inhibitors, depending on interpretation.
- **C (Inhibits viral entry)** — This describes entry inhibitors such as enfuvirtide (fusion inhibitor) or maraviroc (CCR5 antagonist).
- **D (Prevents T-cell binding)** — This would describe attachment or entry inhibitors targeting the CD4-gp120 interaction (e.g., fostemsavir), not protease inhibitors.

Would you like to explore the specific protease resistance-associated mutations that affect darunavir efficacy and how they inform the design of next-generation protease inhibitors?

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Question 210

An investigator is studying the effect of drug X on the retinoblastoma (Rb) gene on chromosome 13 in endometrial cells. Endometrial cells obtained from study participants are plated on growth media and the distribution of cell cycle phase is measured with flow cytometry. Drug X, which is known to activate cyclin-dependent kinase 4, is administered to all the cells, and the distribution of cell cycle phase is measured again 1 hour later. Which of the following is most likely to result from the action of drug X on the Rb gene?

> **Answer Choices:**
>
> (A) G1 phase arrest
> (B) Prophase I arrest
> (C) Initiation of S phase
> (D) Completion of G2 phase

> **Correct Answer:**
>
> (C)
>
> **OpenEvidence Response:**
>
> (C) ✓

OpenEvidence Link: https://openevidence.com/ask/580eb066-13d9-4967-a26e-a459c97406c5

OpenEvidence Explanation

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The answer is **C. Initiation of S phase**.

Drug X activates **CDK4**, which complexes with cyclin D to **phosphorylate the retinoblastoma protein (Rb)**, thereby inactivating its tumor-suppressive function. In its hypophosphorylated state, Rb binds and sequesters E2F transcription factors, preventing transcription of genes required for DNA synthesis and blocking the G1-to-S phase transition.[1][2] When CDK4 phosphorylates Rb, E2F is released, activating transcription of S-phase genes and driving cells from G1 into **S phase**.[3][4][5]

Here is why the other options are incorrect:

- **A. G1 phase arrest** — CDK4 activation promotes passage through G1, not arrest. CDK4 *inhibition* (e.g., by p16/INK4a or drugs like palbociclib) causes G1 arrest.[6]
- **B. Prophase I arrest** — Prophase I is a stage of meiosis, not the mitotic cell cycle. CDK4 regulates the G1/S transition in mitotic cells and has no role in meiotic arrest.
- **D. Completion of G2 phase** — G2 phase progression and the G2/M transition are regulated by cyclin B/CDK1 complexes, not CDK4.[1][7]

The following figure illustrates the canonical CDK4/6 pathway, showing how CDK4/6 complexes with cyclin D to phosphorylate Rb, releasing E2F to drive the G1-to-S phase transition.

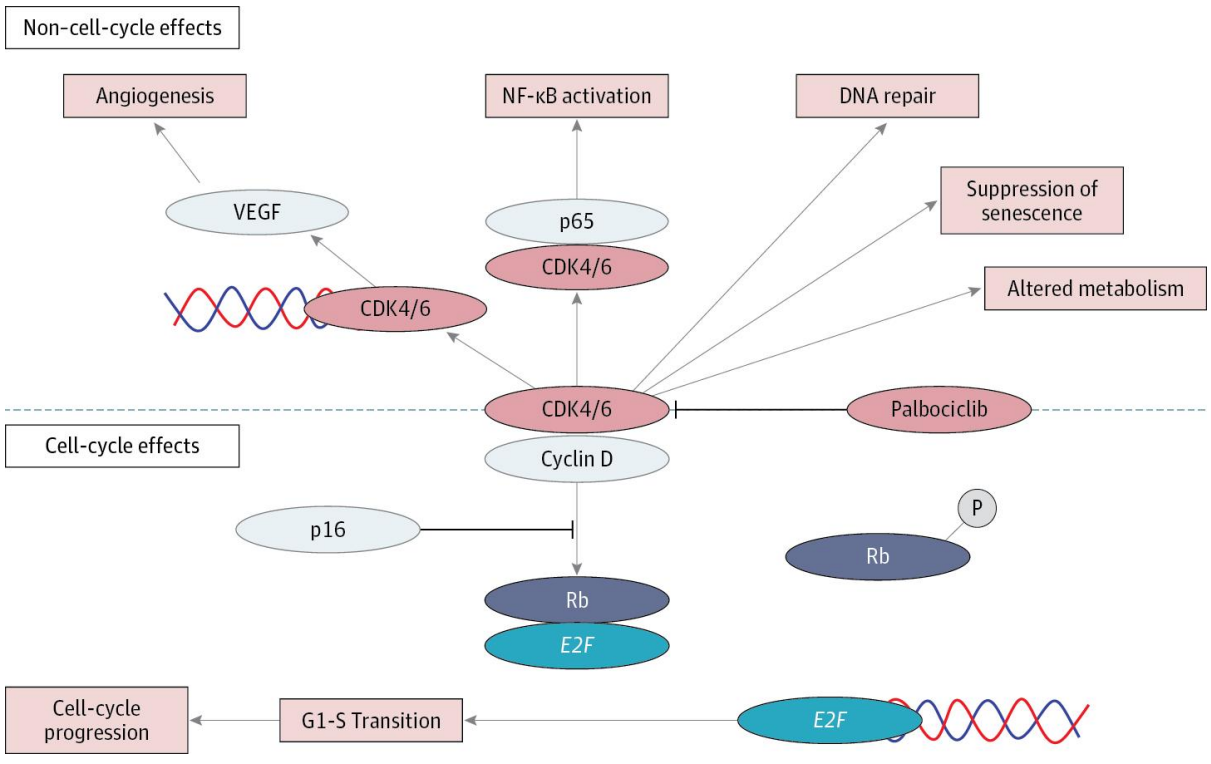


Figure 1. Biological Roles of CDK4/6

Used under license from JAMA Network.

Would you like to explore how CDK4/6 inhibitors like palbociclib exploit this pathway therapeutically in Rb-intact cancers?

References

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Question 213

A 67-year-old woman presents from home hospice with a change in her mental status. She has seemed more confused lately and is unable to verbalize her symptoms. Her temperature is 102°F (38.9°C), blood pressure is 117/65 mmHg, pulse is 110/min, respirations are 19/min, and oxygen saturation is 95% on room air. Physical exam is notable for a right upper quadrant mass that elicits discomfort when palpated. Ultrasound is notable for pericholecystic fluid and gallbladder wall thickening without any gallstones. Which of the following is the most likely diagnosis?

Answer Choices:

(A) Acalculous cholecystitis
(B) Calculous cholescystitis
(C) Choledocholithiasis
(D) Emphysematous cholecystitis

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/2627ed99-d049-48eb-b8bb-aa75ceb92794

OpenEvidence Explanation

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The correct answer is **A. Acalculous cholecystitis**.

This patient presents with the classic features of **acalculous cholecystitis**: fever, tachycardia, altered mental status, right upper quadrant tenderness, and ultrasound findings of **gallbladder wall thickening and pericholecystic fluid without gallstones**.[1][2] The clinical context is highly characteristic — she is a debilitated, elderly hospice patient, which places her at elevated risk for this condition.

Why acalculous cholecystitis?

Acalculous cholecystitis accounts for approximately 5–10% of all acute cholecystitis cases and occurs predominantly in critically ill, debilitated, or chronically immobilized patients.[1][3] The pathogenesis involves gallbladder ischemia and bile stasis, often precipitated by prolonged fasting, opioid use, and reduced oral intake — all common in the hospice setting.[4] The two most reliable ultrasound criteria are gallbladder wall thickness ≥3.5 mm and pericholecystic fluid, both present here.[2][4] Altered mental status may be the only presenting sign in debilitated patients who cannot verbalize symptoms.[3][5]

Why not the other choices?

- **B. Calculous cholecystitis** — This is the most common form of cholecystitis overall (90–95% of cases), but it requires gallstones, which are explicitly absent on ultrasound.[1]
- **C. Choledocholithiasis** — This refers to stones in the common bile duct and would not explain the gallbladder wall thickening and pericholecystic fluid pattern seen here. Additionally, no stones were identified on imaging.
- **D. Emphysematous cholecystitis** — This is a severe variant characterized by gas within the gallbladder wall, typically seen in diabetic or immunocompromised patients. Ultrasound would show intramural gas, which is not described here.[6]

Would you like to explore the management considerations for acalculous cholecystitis in patients receiving hospice care, including the role of percutaneous cholecystostomy versus comfort-focused measures?

Relevant images

(CONTENT OMITTED)

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Question 215

A 45-year-old man presents to the physician with complaints of increased urinary frequency and decreasing volumes for the past 2 months. He does not complain of any pain during urination. He is frustrated that he has to wake up 2 or 3 times per night to urinate even though he tried reducing the amount of water he consumes before bed and made some other dietary changes without any improvement. He has no family history of prostate disease. Physical examination is negative for any suprapubic mass or tenderness, and there is no costovertebral angle tenderness. Which of the following is the best next step in the management of this patient?

Answer Choices:

(A) Urinalysis and serum creatinine
(B) Reassurance
(C) Digital rectal examination
(D) Prostate-specific antigen

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/a56c23fc-12eb-4726-b9e9-3d3e00cbe534

OpenEvidence Explanation

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The best next step is **C. Digital rectal examination (DRE)**.

This 45-year-old man presents with classic **lower urinary tract symptoms (LUTS)** — urinary frequency, decreasing volumes, and nocturia — without dysuria, suggesting an obstructive or irritative process rather than infection. The physical examination has already addressed abdominal and flank pathology (no suprapubic mass, no CVA tenderness), but a **DRE has not yet been performed**, which is a core component of the physical examination for any man presenting with LUTS.

Why DRE before the other options:

- **DRE is part of the physical examination**, which should be completed before ordering laboratory tests. It assesses prostate size, consistency, and nodularity, helping to evaluate for BPH and screen for prostate cancer. International and AUA/EAU guidelines consistently recommend DRE as part of the initial evaluation of LUTS in men.[1][2][3][4][5]
- **Urinalysis and serum creatinine (A)** are appropriate parts of the workup, but they are laboratory investigations ordered after the physical examination is complete. The NEJM clinical practice review notes that a DRE should be performed alongside the history and physical, with urinalysis ordered subsequently to screen for UTI and hematuria.[3]
- **Reassurance (B)** is inappropriate given the 2-month duration, progressive symptoms, and failure of behavioral modifications.
- **PSA (D)** may be considered as part of the evaluation, but it is a laboratory test and not the immediate next step before completing the physical examination. PSA screening decisions also involve shared decision-making and are not universally recommended at age 45 without risk factors.[3]

In the stepwise approach to LUTS evaluation, completing the physical examination — including DRE — precedes ordering laboratory studies.[3][6]

Would you like to explore the full stepwise management algorithm for male LUTS, including when to initiate pharmacologic therapy versus referral to urology?

Relevant images

(CONTENT OMITTED)

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Question 218

A 17-year-old female accidentally eats a granola bar manufactured on equipment that processes peanuts. She develops type I hypersensitivity-mediated histamine release, resulting in pruritic wheals on the skin. Which of the following layers of this patient's skin would demonstrate histologic changes on biopsy of her lesions?

Answer Choices:

(A) Stratum corneum
(B) Stratum granulosum
(C) Stratum basale
(D) Dermis

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/5a48f4e1-804b-4820-befe-0fc5ca56c6a3

OpenEvidence Explanation

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The answer is **D. Dermis**.

Urticaria (wheals/hives) is a **dermal** process. The histologic changes occur in the dermis, not in the epidermal layers (stratum corneum, granulosum, or basale). In this patient's IgE-mediated type I hypersensitivity reaction to peanut allergen,

mast cells located in the **upper dermis** degranulate and release histamine and other mediators, producing the characteristic wheal.[1][2]

The EAACI/GA²LEN/EDF/WAO urticaria guideline specifies that wheals are histologically characterized by **edema of the upper and mid dermis**, with dilatation and increased permeability of postcapillary venules and lymphatic vessels, leading to serum leakage into the tissue.[1] Classic histopathologic features include dermal edema, capillary dilatation, and perivascular mixed inflammatory infiltrates (lymphocytes, eosinophils, neutrophils, and mast cells) within the superficial dermis.[3] The epidermis is notably spared — it maintains a normal stratum corneum and shows minimal to no changes.[4]

The other answer choices — stratum corneum (A), stratum granulosum (B), and stratum basale (C) — are all epidermal layers and would not demonstrate the characteristic histologic changes of urticaria.

Would you like to explore the immunologic cascade of IgE-mediated mast cell degranulation and how it differs from other hypersensitivity reaction types in terms of histopathology?

Relevant images

(CONTENT OMITTED)

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Question 219

A 4-year-old girl is brought to the emergency department with a persistent cough, fever, and vomiting. The past year the child has been admitted to the hospital 3 times with pneumonia. For the past 1 week, the child has been experiencing thick purulent cough and says that her chest feels 'heavy'. Her stools have been loose and foul-smelling over the past week. Her parents are also concerned that she has not gained much weight due to her frequent hospital visits. She was born at 39 weeks gestation via spontaneous vaginal delivery and is up to date on all vaccines and is meeting all developmental milestones. On physical exam, the temperature is 39.1°C (102.4°F). She appears lethargic and uncomfortable. Crackles are heard in the lower lung bases, with dullness to percussion. A small nasal polyp is also present on inspection. Which of the following is the most likely cause for the girl's symptoms?

Answer Choices:

(A) Dysfunction in a transmembrane regulator
(B) Inefficient breakdown of leucine, isoleucine, and valine
(C) Dysfunction in the motility of respiratory cilia
(D) Deficiency in lymphocytic activity

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/78dd252e-3b66-42f1-8e06-06979ed5d665

OpenEvidence Explanation

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The correct answer is **A. Dysfunction in a transmembrane regulator**, which refers to the **cystic fibrosis transmembrane conductance regulator (CFTR)** protein — the underlying defect in **cystic fibrosis (CF)**.

This child's presentation is classic for cystic fibrosis:

- **Recurrent pneumonia** (3 hospitalizations in one year) with thick purulent cough and lower lobe crackles — reflecting impaired mucociliary clearance due to thickened airway secretions caused by CFTR dysfunction[1][2]
- **Nasal polyp in a young child** — nasal polyps before age 16 should prompt investigation for CF; approximately 20% of CF patients develop nasal polyps[3]
- **Loose, foul-smelling stools (steatorrhea)** — resulting from exocrine pancreatic insufficiency, which affects ~80% of CF patients with severe CFTR variants[1][2]
- **Failure to thrive / poor weight gain** — a consequence of fat and protein maldigestion from pancreatic insufficiency[4]

Why the other options are incorrect:

- **B. Inefficient breakdown of leucine, isoleucine, and valine** — This describes maple syrup urine disease, a metabolic disorder presenting with neurological symptoms and a characteristic sweet-smelling urine, not recurrent pneumonia or nasal polyps.
- **C. Dysfunction in the motility of respiratory cilia** — This describes primary ciliary dyskinesia (PCD), which can cause recurrent sinopulmonary infections but is classically associated with situs inversus (Kartagener syndrome), neonatal respiratory distress, and chronic otitis media. PCD does not cause pancreatic insufficiency or steatorrhea, and nasal polyps are less characteristic.[5][6]

- **D. Deficiency in lymphocytic activity** — This describes a primary immunodeficiency. While immunodeficiency can cause recurrent infections, it would not explain the combination of nasal polyps, steatorrhea, and failure to thrive seen here.[7]

The diagnostic workup for CF involves **sweat chloride testing** (≥60 mEq/L is diagnostic) and/or **CFTR genetic testing**.[1]

Would you like to explore the current CFTR modulator therapies (e.g., elexacaftor-tezacaftor-ivacaftor) and their impact on outcomes in pediatric cystic fibrosis?

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Question 223

A 15-year-old girl comes to the physician because of episodic pelvic pain radiating to her back and thighs for 4 months. The pain occurs a few hours before her menstrual period and lasts for 2 days. She has been taking ibuprofen, which has provided some relief. Menses have occurred at regular 28-day intervals since menarche at the age of 12 years and last for 5 to 6 days. She is sexually active with two male partners and uses condoms inconsistently. Vital signs are within normal limits. Physical examination shows no abnormalities. Which of the following is the most likely cause of this patient's symptoms?

Answer Choices:

(A) Endometrial sloughing and uterine contractions mediated by prostaglandin
(B) Ascending infection of the uterus, fallopian tubes, ovaries, or surrounding tissue
(C) Fluid-filled sac within the ovary
(D) Hormone-sensitive smooth muscle tumor of the myometrium

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/1e8de677-42f0-494e-97f8-8571d5fbb0ac

OpenEvidence Explanation

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The answer is **A. Endometrial sloughing and uterine contractions mediated by prostaglandin**.

This presentation is classic for **primary dysmenorrhea**. The key features supporting this diagnosis include:

- **Cyclical pelvic pain** beginning a few hours before menses and lasting ~2 days, with radiation to the back and thighs
- **Regular menstrual cycles** since menarche
- **Partial relief with ibuprofen** (an NSAID/prostaglandin synthesis inhibitor)
- **Normal physical examination** with no abnormalities

Primary dysmenorrhea results from excessive prostaglandin production (particularly PGF2α and PGE2) by the endometrium during the secretory phase. As progesterone levels fall prior to menstruation, endometrial sloughing releases prostaglandins that cause **myometrial hypercontractility, vasoconstriction, and tissue ischemia**, producing the characteristic cramping pain. The radiation to the back and thighs reflects referred pain from uterine innervation.

Why not the other options:

- **B (PID/ascending infection):** While her inconsistent condom use is a risk factor, PID typically presents with constant (not cyclical) pain, cervical motion tenderness, adnexal tenderness, and often fever or discharge — none of which are present here.
- **C (Ovarian cyst):** Functional ovarian cysts can cause pelvic pain, but the pain is typically unilateral, not strictly timed to menses, and may present with adnexal fullness on exam.
- **D (Uterine leiomyoma):** Fibroids are exceedingly rare in a 15-year-old and would typically cause abnormal uterine bleeding, bulk symptoms, or an enlarged uterus on exam.

Would you like to explore the evidence comparing NSAIDs versus hormonal contraceptives as first-line treatment for primary dysmenorrhea in adolescents?

Question 224

A 25-year-old male is hospitalized for acute agitation, photophobia, and dysphagia. His parents report that he has been experiencing flu-like symptoms for one week prior to hospital admission. Five weeks ago, the patient was in Mexico, where he went on several spelunking expeditions with friends. The patient ultimately becomes comatose and dies. Autopsy of brain tissue suggests a viral infection. The likely causal virus spreads to the central nervous system (CNS) in the following manner:

Answer Choices:

(A) Hematogenous dissemination to the meninges
(B) Retrograde migration up peripheral nerve axons
(C) Reactivation of virus previously latent in dorsal root ganglia
(D) Infection of oligodendrocytes and astrocytes

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/406bc5b8-d073-4eda-a619-386ecf38d307

OpenEvidence Explanation

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The answer is **B. Retrograde migration up peripheral nerve axons**.

The clinical presentation — acute agitation, photophobia, dysphagia (pharyngeal spasms), flu-like prodrome, spelunking exposure (bat contact in caves), and rapid progression to coma and death — is classic for **rabies encephalitis**. Spelunking is a well-recognized risk factor for rabies exposure, as bat bites or even aerosolized bat saliva in caves can transmit the virus.[1][2]

Mechanism of CNS spread: Rabies virus (RABV) is a neurotropic rhabdovirus that reaches the CNS exclusively via **retrograde axonal transport** through peripheral nerves.[2][3][4] After inoculation (typically via bite), the virus replicates briefly in muscle tissue, then binds nicotinic acetylcholine receptors at the neuromuscular junction and enters motor nerve terminals. It is then transported retrogradely along axonal microtubules via dynein motor complexes to the spinal cord and subsequently to the brain.[2][4] Viremia does not occur — the virus never disseminates hematogenously.[2]

The following figure illustrates the complete pathogenic journey of RABV from initial transmission through retrograde axonal transport to CNS infection:

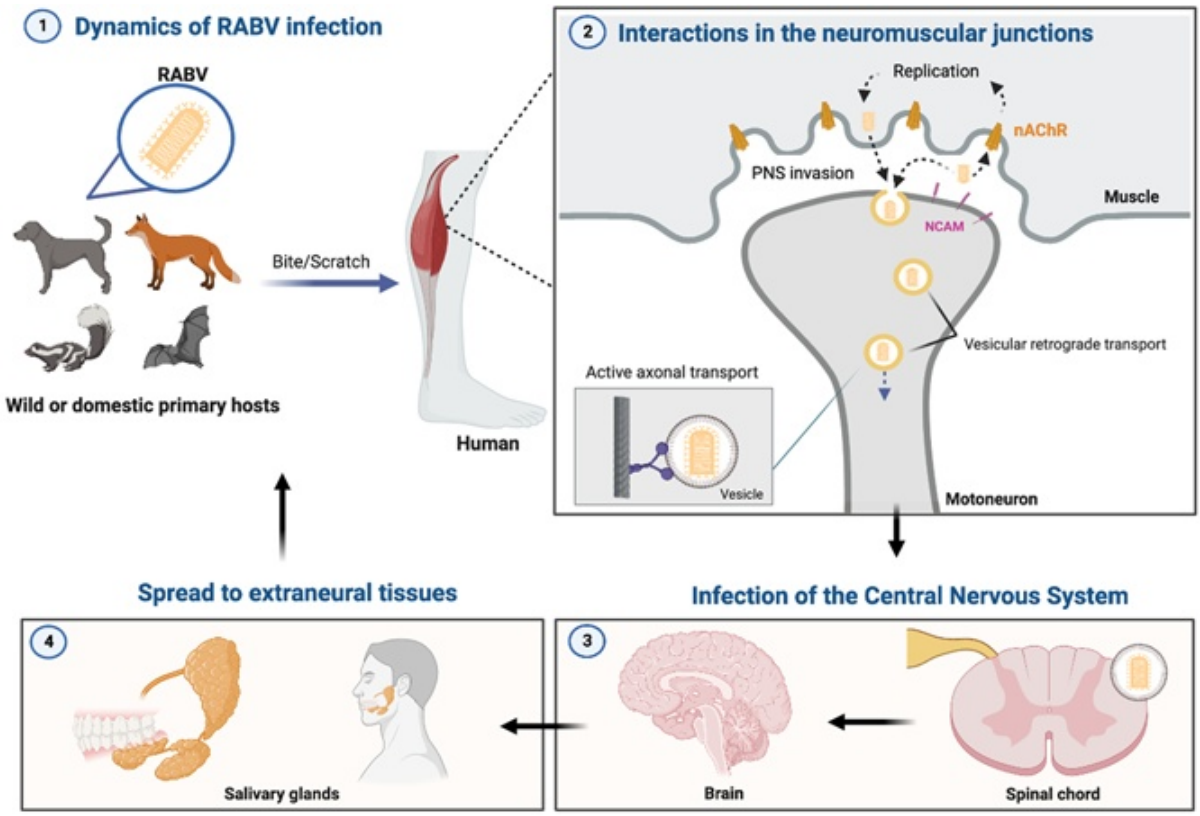


Figure 1. Rabies lyssavirus (RABV) dynamics: from the initial infection to neuroinvasion in the host organism. From 1 to 4, it shows that once inoculated, RABV replicates in the muscles after the interaction with nicotinic receptors (nACh) and invades the peripheral nerves that transport the virus toward the central nervous system (CNS). RABV also infects extraneural tissues, such as the salivary

glands, facilitating its spread to other naive hosts. nAChR, nicotinic receptors; NCAM, neural cell adhesion molecule. Created with biorender.com .

Why the other options are incorrect:

- **A (Hematogenous dissemination to the meninges):** RABV does not cause viremia; spread is entirely neural.[2]
- **C (Reactivation from dorsal root ganglia):** This describes varicella-zoster virus reactivation, not rabies. Dorsal root ganglia become infected during rabies, but this occurs secondarily via transneuronal spread from motor neurons — not from prior latency.[2]
- **D (Infection of oligodendrocytes and astrocytes):** This pattern is characteristic of JC virus (progressive multifocal leukoencephalopathy). RABV primarily infects neurons, not glial cells.[2][3]

Would you like to explore the current evidence on post-exposure prophylaxis protocols and the Milwaukee Protocol for treatment of symptomatic rabies?

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Question 225

A 19-year-old Caucasian male presents to your office with hypopigmented skin. He undergoes a skin biopsy and is found to have an absence of melanocytes in the epidermis. Which of the following is the most likely diagnosis?

Answer Choices:

(A) Tinea versicolor
(B) Albinism
(C) Vitiligo
(D) Melanoma

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/f878d4c5-9a62-4388-94bb-948458e76934

OpenEvidence Explanation

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The correct answer is **C. Vitiligo**.

The key histopathological finding that distinguishes vitiligo from the other answer choices is the **absence of melanocytes** in the epidermis. Vitiligo is an acquired autoimmune depigmenting disorder characterized by the destruction and loss of epidermal melanocytes, resulting in well-circumscribed depigmented

macules.[1][2] Immunohistochemical studies using melanocyte-specific markers have confirmed that melanocytes are indeed absent — not merely inactive — in vitiligo lesions.[3]

This finding is critical for differentiating vitiligo from the other options:

- **Albinism** — Melanocytes are **present** in the epidermis but are dysfunctional due to defective or absent tyrosinase, resulting in little or no melanin production. The melanocyte population density is normal.[4]
- **Tinea versicolor** — This is a superficial fungal infection caused by Malassezia species. Hypopigmentation results from interference with melanin synthesis by the organism, not from melanocyte loss. Biopsy would show fungal hyphae and spores ("spaghetti and meatballs" pattern), with melanocytes still present.
- **Melanoma** — This is a malignant proliferation of melanocytes, which would show increased (not absent) atypical melanocytes on biopsy.

Would you like to explore the autoimmune mechanisms underlying melanocyte destruction in vitiligo and how they inform current treatment strategies?

Relevant images

(CONTENT OMITTED)

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Question 226

A 51-year-old man presents for a routine check-up. He has no complaints. At his last annual visit, his physical and laboratory tests were unremarkable. His past medical history is significant for hypercholesterolemia, well managed with rosuvastatin, and hypertension, well managed with hydrochlorothiazide. His current medications also include aspirin. The patient is afebrile, and his vital signs are within normal limits. Physical examination is unremarkable. His laboratory tests are significant for the following:
WBC 29,500/mm3
Hematocrit 26.1%
Hemoglobin 9.1 g/dL
Platelet count 298,000/mm3
A peripheral blood smear and differential shows 92% small normocytic lymphocytes. The patient's diagnosis in confirmed by bone marrow biopsy and flow cytometry. He is monitored through regular follow-up visits. Three years after the initial diagnosis, the patient presents with swollen cervical and axillary lymph nodes, unintentional weight loss of 4.5 kg (approx. 10 lb), and "rib pain" on his right side. On physical examination, there is palpable, firm, non-tender cervical and axillary lymphadenopathy bilaterally. He also has moderate splenomegaly, which, when palpated, elicits pain. Which of the following is the best treatment for this patient's most likely diagnosis?

Answer Choices:

(A) Bleomycinrn
(B) Imatinib
(C) Fludarabinern
(D) Vincristinern

Correct Answer:

(C)

OpenEvidence Response:

> **(C)** ✓

OpenEvidence Link: https://openevidence.com/ask/7f493071-920e-45e4-87f2-76ec1e97fba6

OpenEvidence Explanation

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The correct answer is **C. Fludarabine**.

This question describes a two-stage clinical scenario. The initial presentation — a 51-year-old asymptomatic man with marked leukocytosis (WBC 29,500), anemia (Hgb 9.1), and a peripheral smear showing **92% small normocytic lymphocytes**, confirmed by bone marrow biopsy and flow cytometry — is classic for **chronic lymphocytic leukemia (CLL)**. The patient was initially monitored (consistent with a watch-and-wait approach for CLL).

Three years later, the development of rapidly enlarging cervical and axillary lymphadenopathy, unintentional weight loss, rib pain, and splenomegaly strongly suggests **Richter transformation** — the histologic transformation of CLL into diffuse large B-cell lymphoma (DLBCL), which occurs in approximately 5–10% of CLL patients.[1][2] Clinical features suggestive of Richter transformation include rapid lymph node enlargement, B symptoms (weight loss, fever, night sweats), elevated LDH, and new organomegaly.[3][4]

Among the answer choices, **fludarabine** is the only agent with an established role in treating both CLL and Richter transformation. Fludarabine is a component of the **OFAR regimen** (oxaliplatin, fludarabine, cytarabine, rituximab), which is one of the NCCN-recommended chemoimmunotherapy regimens for Richter transformation.[1][5] Fludarabine is also a cornerstone of CLL treatment as part of the FCR regimen.[6]

The other options are not appropriate:

- **Bleomycin (A)** — used in Hodgkin lymphoma (ABVD regimen) but not a standard treatment for CLL or Richter transformation
- **Imatinib (B)** — a tyrosine kinase inhibitor used for CML (BCR-ABL positive), not CLL
- **Vincristine (D)** — while vincristine is a component of CHOP and other regimens used in Richter transformation, it would not be used as monotherapy; fludarabine is the more specific and directly correct answer for this question's context

Would you like to explore the current optimal sequencing of targeted therapies versus chemoimmunotherapy for Richter transformation in the era of BTK inhibitors and checkpoint inhibitors?

Relevant images

(CONTENT OMITTED)

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Question 227

A 62-year-old woman is evaluated because of a 3-day history of headache, nausea, and decreased urination. Laboratory studies show:
Serum
Na+ 136 mEq/L
K+ 3.2 mEq/L
Cl- 115 mEq/L
Mg2+ 1.4 mEq/L
Urine
pH 7.0
Arterial blood gas analysis on room air shows a pH of 7.28 and a HCO3- concentration of 14 mEq/L. Prolonged treatment with which of the following drugs would best explain this patient's findings?

Answer Choices:

(A) Trimethoprim-sulfamethoxazole
(B) Eplerenone
(C) Amphotericin B
(D) Heparin

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/e378b4be-4222-4eed-bc8e-050055443136

OpenEvidence Explanation

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The answer is **C. Amphotericin B**.

This patient presents with a **non-anion gap (hyperchloremic) metabolic acidosis** (pH 7.28, HCO_3^- 14 mEq/L, Cl^- 115 mEq/L), **hypokalemia** (K^+ 3.2 mEq/L), **hypomagnesemia** (Mg^{2+} 1.4 mEq/L), an **alkaline urine pH** (7.0), and decreased urination — a constellation classic for **amphotericin B-induced distal (type 1) renal tubular acidosis (RTA)**.

Why Amphotericin B?

Amphotericin B inserts into renal tubular cell membranes, disrupting membrane permeability. This causes increased back-diffusion of hydrogen ions across the collecting duct, impairing distal acidification and producing a **type 1 (distal) RTA**.[1][2][3] The hallmark findings include:

- **Hyperchloremic, normal anion gap metabolic acidosis** with an inappropriately **high urine pH** (>5.5 despite systemic acidemia), indicating failure to acidify the urine distally
- **Hypokalemia** from urinary potassium wasting[1][4]
- **Hypomagnesemia** from urinary magnesium wasting[1][5]
- **Decreased renal function** (azotemia, oliguria) from afferent arteriolar vasoconstriction and direct tubular toxicity[1]
- Symptoms of headache and nausea, which are common adverse effects[4]

The FDA label for amphotericin B specifically lists **hypokalemia, renal tubular acidosis, hypomagnesemia**, and azotemia as recognized adverse effects.[4]

Why not the other options?

- **Trimethoprim-sulfamethoxazole (A):** Trimethoprim blocks ENaC in the collecting duct, causing **hyperkalemia** (not hypokalemia), and can cause a type 4 RTA pattern.
- **Eplerenone (B):** A mineralocorticoid receptor antagonist that causes **hyperkalemia** and type 4 RTA — the opposite potassium pattern seen here.

- **Heparin (D):** Inhibits aldosterone synthesis, leading to **hyperkalemia** and type 4 RTA — again inconsistent with the hypokalemia in this case.

The key distinguishing feature is the **hypokalemia with alkaline urine pH**, which points to a distal (type 1) RTA rather than a type 4 RTA. Among the listed drugs, only amphotericin B causes this pattern.[2][6]

Would you like to explore the mechanisms distinguishing the different types of renal tubular acidosis and their associated drug causes in more detail?

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Question 230

An 11-year-old child complains of pain in the leg while playing. Blood pressure in the upper limb is 140/90 mm Hg and lower limbs are 110/70 mm Hg. There is a brachiofemoral delay in the pulse. Auscultation shows a loud S1, loud S2, and S4. There is a presence of an ejection systolic murmur in the interscapular area. Chest X-ray reveals the notching of the ribs. What is the most likely diagnosis in this patient?

> **Answer Choices:**
>
> (A) Pulmonic stenosis
> (B) Coarctation of the aorta
> (C) Aortic stenosis
> (D) Transposition of great vessels

> **Correct Answer:**
>
> **(B)**
>
> **OpenEvidence Response:**
>
> **(B)** ✓

OpenEvidence Link: https://openevidence.com/ask/838aca0b-c975-4bdb-bccf-16d373db6ce1

OpenEvidence Explanation

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The most likely diagnosis is **B. Coarctation of the aorta**.

This presentation is classic for coarctation of the aorta, with every finding pointing to this diagnosis:

- **Upper-to-lower extremity blood pressure gradient**: The upper limb BP (140/90) is significantly higher than the lower limb BP (110/70), reflecting obstruction to aortic flow distal to the left subclavian artery. Normally, lower extremity systolic BP is equal to or slightly higher than upper extremity BP.
- **Brachiofemoral delay**: A hallmark physical exam finding in coarctation — the femoral pulse is delayed and diminished relative to the radial/brachial pulse due to the narrowed aortic segment.
- **Ejection systolic murmur in the interscapular area**: This reflects turbulent flow across the coarctation site, which is typically located just distal to the left subclavian artery (juxtaductal). The murmur radiates to the back.
- **Rib notching on chest X-ray**: A classic radiographic sign caused by dilated intercostal arteries serving as collateral pathways to bypass the coarctation. This finding typically develops after age 5–6 years, consistent with this 11-year-old patient.
- **S4 gallop**: Indicates left ventricular hypertrophy from chronic pressure overload proximal to the coarctation.

Why not the other options?

- **Pulmonic stenosis (A)**: Would produce an ejection systolic murmur at the left upper sternal border, not the interscapular area, and would not cause upper-lower extremity BP discrepancy.
- **Aortic stenosis (C)**: Produces a murmur at the right upper sternal border radiating to the carotids, with a narrow pulse pressure but no upper-lower limb gradient.
- **Transposition of great vessels (D)**: A cyanotic congenital heart disease presenting in the neonatal period, not at age 11 with hypertension.

Would you like to explore the management approach and indications for surgical versus catheter-based intervention in coarctation of the aorta?

Question 235

A 32-year-old man comes to the physician for a pre-employment examination. He recently traveled to Guatemala. He feels well but has not seen a physician in several years, and his immunization records are unavailable. Physical examination shows no abnormalities. Serum studies show:
Anti-HAV IgM Positive
Anti-HAV IgG Negative
HBsAg Negative
Anti-HBs Positive
HBcAg Negative
Anti-HBc Negative
HBeAg Negative
Anti-HBe Negative
Anti-HCV Negative
Which of the following best explains this patient's laboratory findings?

Answer Choices:

(A) Active hepatitis A infection
(B) Previous hepatitis A infection
(C) Chronic hepatitis B infection
(D) Chronic hepatitis C infection

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/c9dab3a2-621e-44f1-b485-7b5241d4ee6e

OpenEvidence Explanation

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The correct answer is **A. Active hepatitis A infection**.

The key serologic finding is a **positive anti-HAV IgM with negative anti-HAV IgG**, which is the hallmark of **acute (active) hepatitis A infection**. IgM anti-HAV becomes detectable 5–10 days before symptom onset and peaks within one month of illness, while IgG anti-HAV appears later during the convalescent phase and persists for life.[1][2] The absence of IgG with presence of IgM indicates the patient is in the early acute phase of infection, consistent with recent acquisition during travel to Guatemala, an endemic area.

The following figure illustrates the typical serological course of acute HAV infection, showing the temporal relationship between IgM and total anti-HAV antibodies:

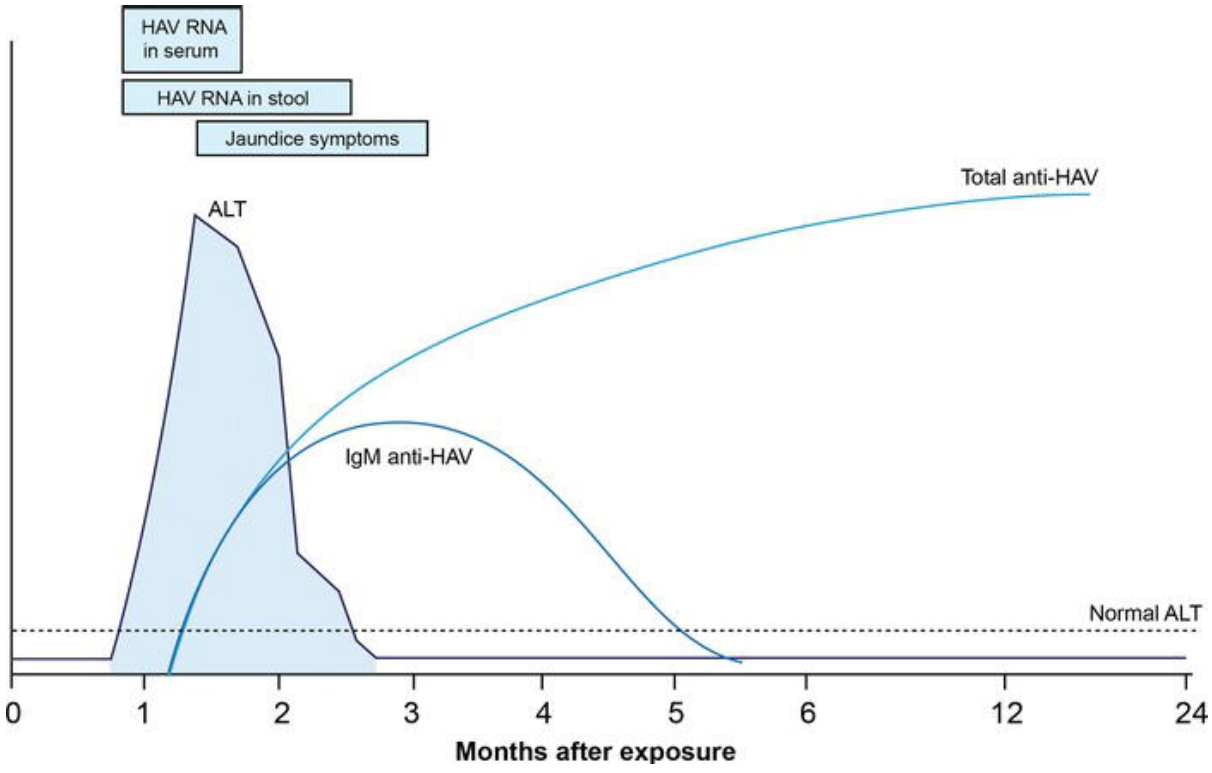


Figure 13. Typical serological course of acute hepatitis A virus (HAV) infection. ALT, alanine aminotransferase; IgM, immunoglobulin M.

Importantly, this patient is **asymptomatic**, which is common — approximately 70% of adults with acute HAV infection may have subclinical presentations.[4]

Previous hepatitis A infection (option B) would show positive anti-HAV IgG (with or without IgM), not isolated IgM positivity.

Regarding the hepatitis B serologies: the pattern of **negative HBsAg, positive anti-HBs, and negative anti-HBc** is consistent with **immunity from prior hepatitis B vaccination** rather than natural infection. Vaccination produces only anti-HBs, whereas resolved natural infection produces both anti-HBs and anti-HBc.[5][6] This rules out chronic hepatitis B (option C). The negative anti-HCV rules out hepatitis C (option D).[7]

Would you like to explore the recommended post-exposure prophylaxis and vaccination strategies for hepatitis A in travelers to endemic regions?

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Question 236

A 7-month-old male infant is brought to the pediatrician by his mother. She reports that the child develops severe sunburns every time the infant is exposed to sunlight. She has applied copious amounts of sunscreen to the infant but this has not helped the problem. On examination, there are multiple areas of reddened skin primarily in sun exposed areas. The child's corneas appear irritated and erythematous. Which of the following processes is likely impaired in this patient?

> **Answer Choices:**
>
> (A) Nucleotide excision repair
> (B) Non-homologous end joining
> (C) Homologous recombination
> (D) Mismatch repair

> **Correct Answer:**
>
> **(A)**
>
> **OpenEvidence Response:**
>
> **(A)** ✓

OpenEvidence Link: https://openevidence.com/ask/306866fe-7085-46b8-9d22-0454acd86e90

OpenEvidence Explanation

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The answer is **A. Nucleotide excision repair**.

This clinical presentation — an infant with **severe sunburns on minimal sun exposure**, erythema in sun-exposed areas, and **corneal/ocular irritation** — is classic for **xeroderma pigmentosum (XP)**, an autosomal recessive disorder caused by defective **nucleotide excision repair (NER)**.[1][2]

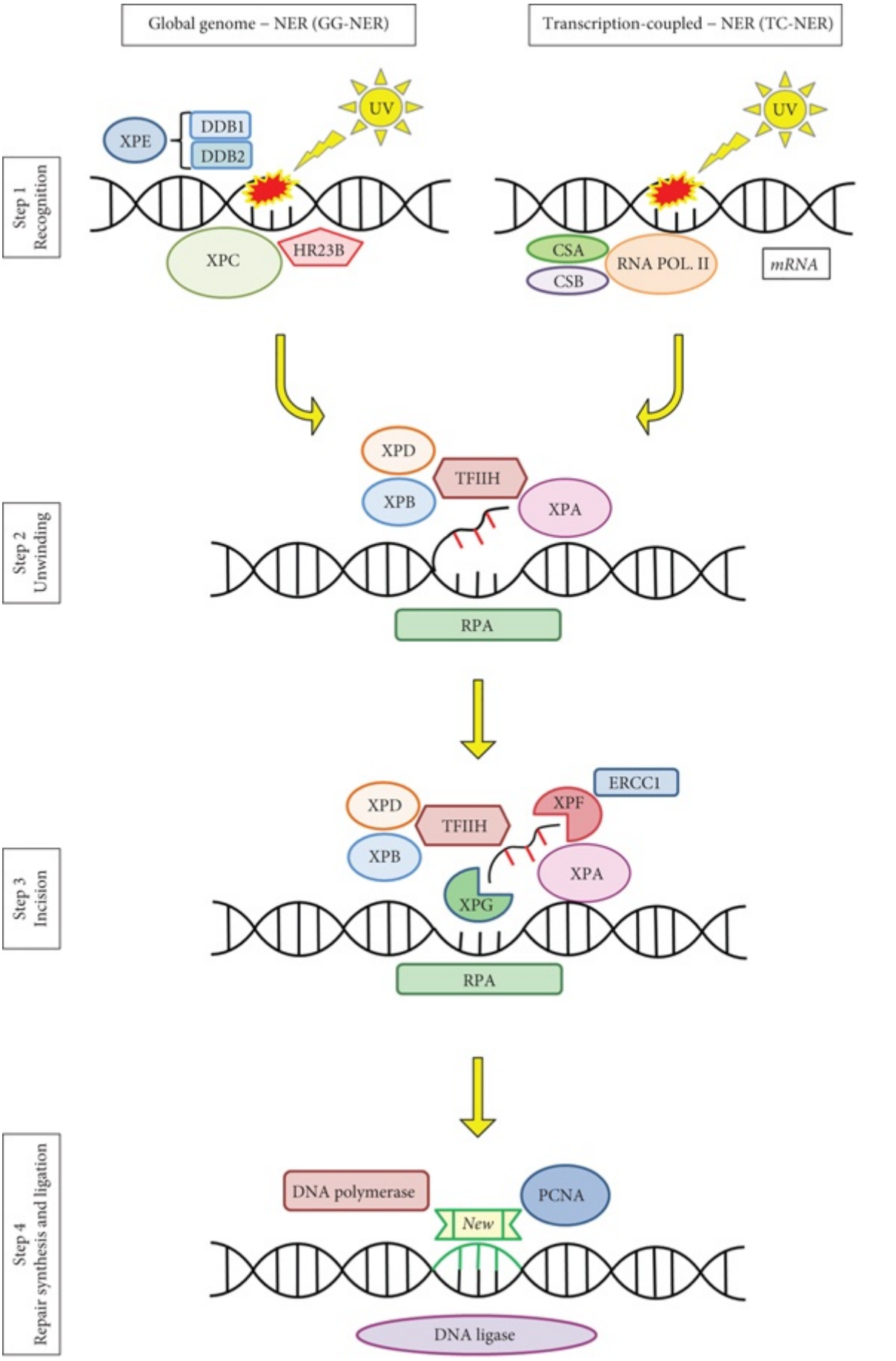
NER is the primary pathway responsible for repairing UV-induced DNA damage, specifically bulky helix-distorting lesions such as pyrimidine dimers and 6-4 photoproducts.[3] Mutations in any of the seven XP genes (XPA–XPG) involved in NER result in an inability to repair this damage, leading to extreme photosensitivity.[4][5] Approximately 60% of XP patients present with severe sun sensitivity (dermatitis solaris) in the first weeks to months of life, and sunscreen alone is insufficient because even minimal UV exposure causes disproportionate DNA damage that cannot be repaired.[6]

The ocular findings are also characteristic — XP predominantly affects UV-exposed ocular surfaces, causing conjunctivitis, keratitis, corneal neovascularization, and eventually ocular surface neoplasms.[2][7] In one large series, 91% of XP patients had at least one ocular abnormality.[7]

Why the other options are incorrect:

- **Non-homologous end joining (B)** and **homologous recombination (C)** repair double-strand DNA breaks (e.g., from ionizing radiation), not UV-induced damage. Defects in these pathways are not associated with photosensitivity.
- **Mismatch repair (D)** corrects base-pair mismatches during DNA replication and is associated with Lynch syndrome (hereditary nonpolyposis colorectal cancer), not photosensitivity.[3]

The following figure illustrates the NER pathway and the roles of the various XP proteins in damage recognition, excision, and repair:



(T. Brambullo 2020)

Figure 1. The nucleotide excision repair (NER) pathway. Step 1: DNA damage recognition through two different ways: global genome (GG-NER) or transcription-coupled (TC-NER). Step 2: DNA unwinding. Step 3: DNA damage excision. Step 4: missing strand synthesis and ligation.

Would you like to explore the specific complementation groups of xeroderma pigmentosum and how genotype-phenotype correlations influence clinical severity and cancer risk?

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Question 240

A 46-year-old man presents to the physician with a complaint of a cough for 6 months. He has been taking over-the-counter cough medications, but they have not helped much. He adds that he expectorated bloody sputum the previous night. He denies breathlessness but mentions that he frequently experiences fatigue after little physical exertion. There is no past history of any specific medical disorder. His father died of lung cancer at the age of 54 years. His temperature is 37.0°C (98.6°F), the pulse rate is 82/min, the blood pressure is 118/80 mm Hg, and the respiratory rate is 18/min. Auscultation of his chest reveals the presence of localized rhonchi over the interscapular region. A plain radiograph of the chest shows a coin-like opacity in the right lung. Further diagnostic evaluation confirms the diagnosis of small cell carcinoma of the lung. If his blood were to be sent for laboratory evaluation, which of the following proteins is most likely to be elevated in his serum?

Answer Choices:

(A) Bence-Jones protein
(B) Calcitonin
(C) CA 15-3
(D) Neuron-specific enolase

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/9d266ea3-f0ed-4703-a377-d3f77063736f

OpenEvidence Explanation

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The correct answer is **D. Neuron-specific enolase (NSE)**.

Neuron-specific enolase is the most likely protein to be elevated in the serum of a patient with small cell lung carcinoma (SCLC). SCLC is a poorly differentiated **neuroendocrine carcinoma**, and NSE — the gamma subunit of the glycolytic enzyme enolase — is highly concentrated in neurons and neuroendocrine cells, making it a well-established tumor marker for this malignancy.[1]

NSE is elevated in approximately **69–81% of all SCLC patients** at diagnosis, with higher rates in extensive-stage disease (83–91%) compared to limited-stage disease (39–59%).[2][3][4] Its level correlates with tumor burden, number of metastatic sites, and response to treatment.[1] A meta-analysis of 33 studies (9,546 samples) confirmed a pooled sensitivity of 68.8% and specificity of 92.1% for SCLC detection.[5]

Why the other options are incorrect:

- **A. Bence-Jones protein** — This is a monoclonal immunoglobulin light chain found in the urine of patients with multiple myeloma, not lung cancer.
- **B. Calcitonin** — While calcitonin can be mildly elevated in some SCLC patients, it is classically associated with **medullary thyroid carcinoma**, not SCLC. It is not the most likely elevated marker in this scenario.[6]
- **C. CA 15-3** — This tumor marker is associated with **breast cancer**, not small cell lung cancer.

The NCCN Guidelines for SCLC note that SCLC is characterized by neuroendocrine differentiation, with the majority of tumors reactive to neuroendocrine markers including CD56/NCAM, synaptophysin, and chromogranin A.[7] NSE remains the most widely used serum biomarker for clinical monitoring of SCLC, though ProGRP (pro-gastrin-releasing peptide) has emerged as a complementary marker with potentially superior specificity.[8][9]

Would you like to explore the role of NSE and other neuroendocrine markers in monitoring treatment response and predicting relapse in SCLC?

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Question 245

A 70-year-old woman is brought to the emergency department for the evaluation of abdominal pain, nausea, and vomiting for 1 day. Computed tomography shows a small bowel perforation. The patient is prepared for emergent exploratory laparotomy. She is sedated with midazolam, induced with propofol, intubated, and maintained on nitrous oxide and isoflurane for the duration of the surgery. A single perforation in the terminal ileum is diagnosed intraoperatively and successfully repaired. The patient is transferred to the intensive care unit. The ventilator is set at an FiO2 of 50%, tidal volume of 1000 mL, respiratory rate of 12/min, and positive end-expiratory pressure of 2.5 cm H2O. Her temperature is 37.3°C (99.1°F), pulse is 76/min, and blood pressure is 111/50 mm Hg. She is responsive to painful stimuli. Lung examination shows bilateral rales. Abdominal examination shows a distended abdomen and intact abdominal surgical incisions. The remainder of the physical examination shows no abnormalities. Arterial blood gas analysis shows:
pH 7.44
pO2 54 mm Hg
pCO2 31 mm Hg
HCO3- 22 mm Hg
Which of the following is the best next step in the management of this patient?

Answer Choices:

(A) Increase the FiO2
(B) Increase the tidal volume
(C) Increase PEEP
(D) Increase the respiratory rate

Correct Answer:

(C)

OpenEvidence Response:

> (C) ✓

OpenEvidence Link: https://openevidence.com/ask/025ea81a-d300-4211-a0db-f15738e0b967

OpenEvidence Explanation

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The best next step is **C. Increase PEEP**.

This patient has significant **postoperative hypoxemia** (PaO2 of 54 mmHg on 50% FiO2, yielding a P/F ratio of 108) with bilateral rales following emergent abdominal surgery. The clinical picture — use of nitrous oxide and high FiO2 intraoperatively, supine positioning during surgery, and bilateral rales — is most consistent with **postoperative atelectasis** with intrapulmonary shunting.

Why increasing PEEP is the correct answer:

The current PEEP of **2.5 cm H2O is inadequately low**. PEEP recruits collapsed alveoli, reduces intrapulmonary shunt fraction, and improves oxygenation in the setting of atelectasis.[1][2] PEEP directly combats the underlying pathophysiology — alveolar collapse — rather than simply compensating for it. Standard ICU practice recommends initial PEEP of at least 5 cm H2O, and higher levels (8–12 cm H2O) are commonly used in hypoxemic patients.[3][4]

Why the other options are less appropriate:

- **A. Increase FiO2** — When hypoxemia is driven by true shunt (collapsed, non-ventilated alveoli), increasing FiO2 has limited efficacy because the shunted blood never contacts ventilated alveoli. Additionally, high FiO2 can worsen absorption atelectasis.[5]
- **B. Increase tidal volume** — The tidal volume of 1000 mL is already excessive (likely >12 mL/kg predicted body weight for a 70-year-old woman). Increasing it further would risk ventilator-induced lung injury.

Lung-protective ventilation recommends 6–8 mL/kg predicted body weight.[3]

- **D. Increase respiratory rate** — The ABG shows a pH of 7.44 and pCO2 of 31 mmHg, indicating the patient is already adequately ventilated (even slightly hyperventilated). Increasing the respiratory rate would worsen the respiratory alkalosis without addressing the oxygenation problem.

Would you like to explore the optimal PEEP titration strategy and lung-protective ventilation parameters for postoperative patients with suspected atelectasis?

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Question 247

A 42-year-old man with AIDS comes to the physician for intermittent fever, nonproductive cough, malaise, decreased appetite, abdominal pain, and a 3.6-kg (8-lb) weight loss over the past month. He has not seen a doctor since he became uninsured 2 years ago. His temperature is 38.3°C (100.9°F). Abdominal examination shows mild, diffuse tenderness throughout the lower quadrants. The liver is palpated 2–3 cm below the right costal margin, and the spleen is palpated 1–2 cm below the left costal margin. His CD4+ T-lymphocyte count is 49/mm3 (N ≥ 500 mm3). Blood cultures grow acid-fast organisms. A PPD skin test shows 4 mm of induration. Which of the following is the most appropriate pharmacotherapy for this patient's condition?

Answer Choices:

(A) Voriconazole
(B) Amphotericin B and itraconazole
(C) Erythromycin
(D) Azithromycin and ethambutol

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/ff074736-6fe2-43ca-aa83-6b9435486c89

OpenEvidence Explanation

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The correct answer is **D. Azithromycin and ethambutol**.

This patient presents with disseminated **Mycobacterium avium complex (MAC)** infection, evidenced by the combination of AIDS with a profoundly low CD4+ count (49/mm³), systemic symptoms (fever, weight loss, malaise), hepatosplenomegaly, and **acid-fast bacilli** growing from blood cultures. The negative PPD (4 mm induration, below the 5 mm threshold for HIV-positive patients) argues against M. tuberculosis, and disseminated MAC is the most common mycobacterial blood culture isolate in patients with CD4 counts <50/mm³.

Why azithromycin and ethambutol?

Per the NIH/IDSA/CDC Guidelines for Prevention and Treatment of Opportunistic Infections in Adults with HIV, the preferred initial treatment for disseminated MAC disease consists of at least two drugs:[1]

- **Clarithromycin 500 mg PO twice daily plus ethambutol 15 mg/kg PO daily** (AI recommendation), or
- **Azithromycin 500–600 mg PO daily plus ethambutol 15 mg/kg PO daily** (AII recommendation) when drug interactions or intolerance preclude clarithromycin

The FDA-approved labeling for azithromycin specifically indicates a daily dose of 600 mg in combination with ethambutol for treatment of disseminated MAC infections.[2] Ethambutol is the recommended second agent based on randomized trials showing its inclusion is associated with lower relapse rates.[1]

Why not the other options?

- **A (Voriconazole)** and **B (Amphotericin B and itraconazole)** are antifungal agents with no role in mycobacterial infections.
- **C (Erythromycin)** is a macrolide but lacks the antimycobacterial potency of azithromycin or clarithromycin against MAC and is not recommended. Additionally, monotherapy is contraindicated due to rapid emergence of resistance.[3]

Would you like to explore the indications for adding a third or fourth agent (e.g., rifabutin) in patients with severe disseminated MAC disease and CD4 counts below 50?

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Question 250

A 35-year-old woman is brought into the clinic by a concerned neighbor who says that the patient is often seen setting up bear traps all around her property because of an impending 'invasion of the mole people.' The patient has come to the clinic wearing a garlic necklace. She vaguely explains that the necklace is to mask her scent from the moles tracking her. She has no past psychiatric history and she denies hearing voices or seeing objects. No significant past medical history. Although she has lived in the same community for years, she says she usually keeps to herself and does not have many friends. She holds a regular job at the local hardware store and lives alone. Which of the following is the best initial course of treatment for this patient?

Answer Choices:

(A) Cognitive behavioral therapy (CBT)
(B) The patient does not require any intervention
(C) Electroconvulsive therapy (ECT)
(D) Refer to outpatient group therapy

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/e4ffc1d2-e13d-4db4-979a-ca6f6315f929

OpenEvidence Explanation

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The best initial course of treatment is **A. Cognitive behavioral therapy (CBT)**.

This patient's presentation is consistent with **delusional disorder** (persecutory type) — she holds a fixed, non-bizarre-to-bizarre belief about "mole people" invading, takes elaborate protective measures (bear traps, garlic necklace), but otherwise maintains relatively intact functioning (holds a regular job, lives independently), has no hallucinations, and has no prior psychiatric history. The key distinction from schizophrenia is the absence of hallucinations, disorganized speech/behavior, or significant functional decline beyond the circumscribed delusional system.

Among the answer choices, **CBT** is the most appropriate initial intervention for several reasons:

- While antipsychotic medications are considered the pharmacological mainstay of delusional disorder treatment, they are not listed among the options. CBT has demonstrated efficacy for delusions, with meta-analytic evidence showing small but significant reductions in delusional conviction (SMD = -0.31) and paranoia severity (SMD = -0.29). CBT for psychosis has shown superiority over treatment-as-usual for delusions (g = 0.37) across cumulative meta-analyses.[1][2][3][4]

- CBT can serve as a useful adjunctive or initial approach, particularly in patients who may resist pharmacotherapy — a common challenge in delusional disorder given poor insight. Expert opinion has noted that CBT may have a role in modifying delusional beliefs.[1][5]

- **The patient does not "not require intervention"** (option B) — her behavior (setting bear traps) poses a safety risk to others, and the delusions are clearly impairing her social functioning.

- **ECT** (option C) is not a first-line treatment for delusional disorder and is generally reserved for treatment-resistant cases or those with severe comorbid depression.

- **Group therapy** (option D) would be poorly suited as an initial intervention given her social isolation, paranoid ideation, and the nature of her delusions, which could make group settings counterproductive.

Would you like to explore the evidence for combining CBT with low-dose antipsychotic therapy in delusional disorder for optimizing treatment outcomes?

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Question 252

A 30-year-old man presents to his primary care provider complaining of drowsiness at work for the past several months. He finds his work as a computer programmer rewarding and looks forward to coming into the office every day. However, he often falls asleep during meetings even though he usually gets a good night sleep and has limited his exposure to alcohol and caffeine in the evening. His past medical history is noncontributory. His vital signs are within normal limits. Physical examination is unremarkable. The primary care provider recommends keeping a sleep journal and provides a questionnaire for the patient's wife. The patient returns one month later to report no changes to his condition. The sleep journal reveals that the patient is getting sufficient sleep and wakes up rested. The questionnaire reveals that the patient does not snore nor does he stop breathing during his sleep. A sleep study reveals mean sleep latency of 6 minutes. Which of the following is the best course of treatment for this patient's condition?

Answer Choices:

(A) Methylphenidate
(B) Sodium oxybate
(C) Imipramine
(D) Increase daytime naps

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/72a7ed13-7181-42be-bbf6-5454dc3662cf

OpenEvidence Explanation

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The best course of treatment is **A. Methylphenidate**.

This patient presents with **narcolepsy type 2** (NT2) — excessive daytime sleepiness for several months, a mean sleep latency of **6 minutes** on the multiple sleep latency test (MSLT, ≤8 minutes is diagnostic), adequate nighttime sleep, no snoring or apneas (ruling out obstructive sleep apnea), and no cataplexy.[1][2] Among the answer choices, **methylphenidate** is the appropriate pharmacologic treatment for excessive daytime sleepiness in narcolepsy.

Why methylphenidate is correct:

Methylphenidate is **FDA-approved for narcolepsy** and is recommended by the American Academy of Sleep Medicine (AASM) as a treatment option for narcolepsy in adults.[3][4] It promotes wakefulness by blocking dopamine and catecholamine reuptake, and is effective for reducing excessive daytime sleepiness.[5][6]

Why the other options are less appropriate:

- **Sodium oxybate (B):** While also recommended for narcolepsy, sodium oxybate is primarily used when cataplexy is present or when nighttime sleep is disrupted — neither of which applies here. It carries a black box warning for CNS depression and respiratory depression and is available only through a REMS program. It would not be the best first-line choice for isolated EDS without cataplexy.[3]
- **Imipramine (C):** Tricyclic antidepressants are used off-label to treat **cataplexy**, not excessive daytime sleepiness. This patient has no cataplexy.[5]
- **Increase daytime naps (D):** While scheduled naps can be a helpful adjunctive behavioral strategy, the AASM found insufficient evidence to recommend scheduled naps alone, and this patient's symptoms are significant enough to warrant pharmacotherapy.[3][7]

Would you like to explore the differences in first-line treatment selection between narcolepsy type 1 and type 2, including when modafinil versus stimulants are preferred?

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Question 254

A 62-year-old man presents to the physician because of incomplete healing of a chest wound. He recently had a triple coronary artery bypass graft 3 weeks ago. His past medical history is significant for type 2 diabetes mellitus and hypertension for the past 25 years. Clinical examination shows the presence of wound dehiscence in the lower 3rd of the sternal region. The wound surface shows the presence of dead necrotic tissue with pus. Computed tomography (CT) of the thorax shows a small fluid collection with fat stranding in the perisurgical soft tissues. What is the most appropriate next step in the management of the patient?

Answer Choices:

(A) Surgical debridement
(B) Negative pressure wound management
(C) Sternal wiring
(D) Sternal fixation

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/26e0442e-d9d3-4ba4-903b-1a43327e95ec

OpenEvidence Explanation

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The most appropriate next step is **A. Surgical debridement**. In a patient with sternal wound dehiscence showing dead necrotic tissue and purulent discharge after CABG, **aggressive surgical debridement** is the primary and initial intervention, as recommended by both the ACCF/AHA and the American Association for Thoracic Surgery (AATS) guidelines.

The 2011 ACCF/AHA CABG guidelines state as a **Class I recommendation** (Level of Evidence B) that "a deep sternal wound infection should be treated with aggressive surgical debridement in the absence of complicating circumstances".[1] The AATS guidelines similarly emphasize that the standard principles of treatment for deep sternal infections include **debridement of all devitalized and necrotic tissue**, drainage of all infected spaces, antibiotic therapy, and techniques to achieve closure of the sternal space.[2]

Why not the other options?

- **Negative pressure wound therapy (NPWT)** is an important adjunctive therapy but is used *after* debridement, not as the initial step when necrotic tissue and pus are present. The AATS guidelines recommend NPWT be initiated in patients in whom delayed sternal closure is anticipated *following* debridement (Class IIa). NPWT can serve as a bridge to flap closure or as standalone therapy, but the wound must first be debrided.[1][2][3]
- **Sternal wiring and sternal fixation** are reconstruction/closure techniques that may be considered later in the management sequence — only after the infection has been controlled and the wound bed is clean. Immediate closure can be performed only if deep mediastinal tissues are free of infection and there is enough sternum to reapproximate.[2]

The management sequence is therefore: surgical debridement → wound management (NPWT or dressing changes) → eventual sternal reconstruction/closure once infection is controlled.[4]

Would you like to explore the risk factors and preventive strategies for deep sternal wound infection in patients with diabetes undergoing cardiac surgery?

References

1. 2011 ACCF/AHA Guideline for Coronary Artery Bypass Graft Surgery. A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Developed in Collaboration With the American Association for Thoracic Surgery, Society of Cardiovascular Anesthesiologists, and Society of Thoracic Surgeons. Hillis LD, Smith PK, Anderson JL, et al.. Journal of the American College of Cardiology. 2011;58(24):e123-210. doi:10.1016/j.jacc.2011.08.009.

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Question 255

The Kozak sequence for the Beta-globin gene has a known mutation which decreases, though does not abolish, translation of the Beta-globin mRNA, leading to a phenotype of thalassemia intermedia. What would the blood smear be expected to show in a patient positive for this mutation?

Answer Choices:

(A) Macrocytic red blood cells
(B) Hyperchromic red blood cells
(C) Microcytic red blood cells
(D) Bite cells

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/b176bb4f-324b-477a-af2b-201b96febc47

OpenEvidence Explanation

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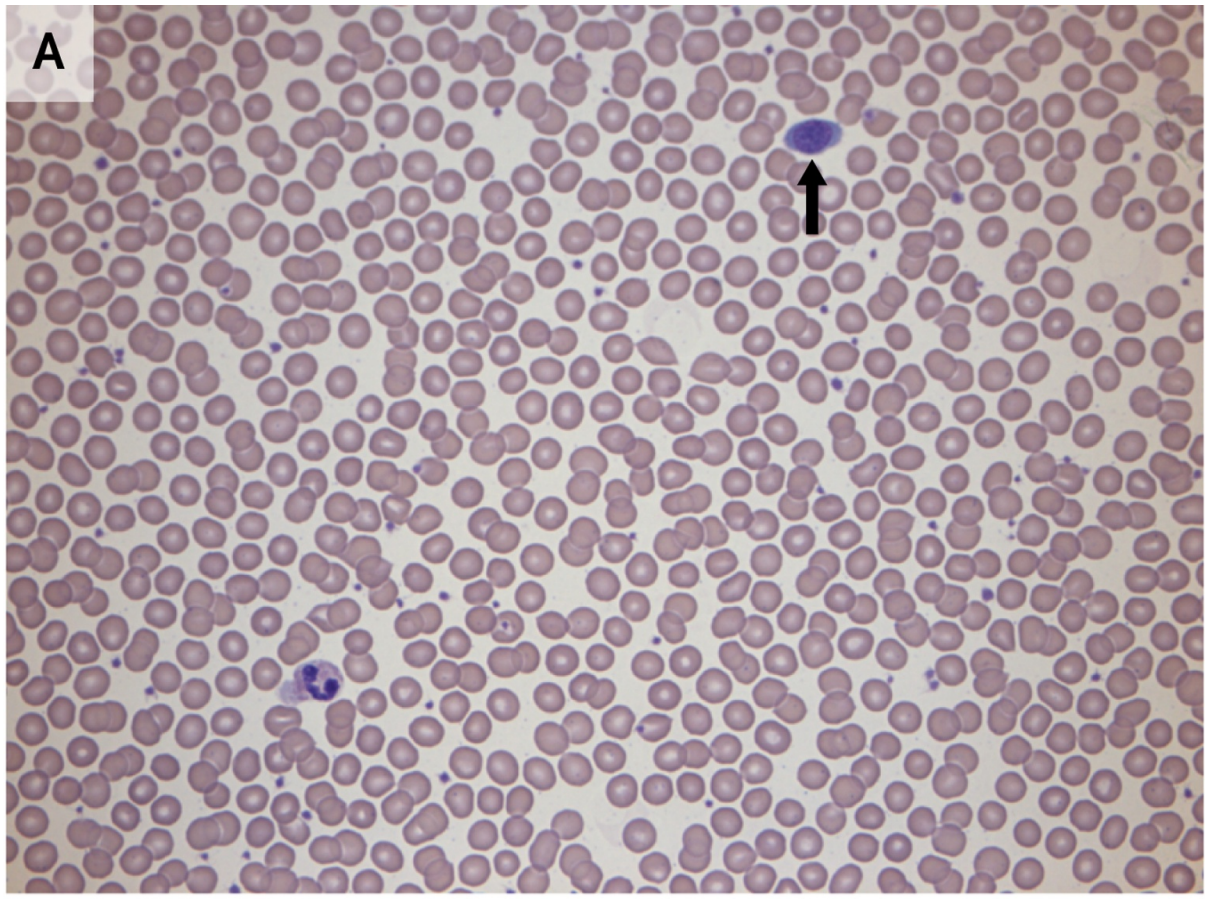
The answer is **C. Microcytic red blood cells**.

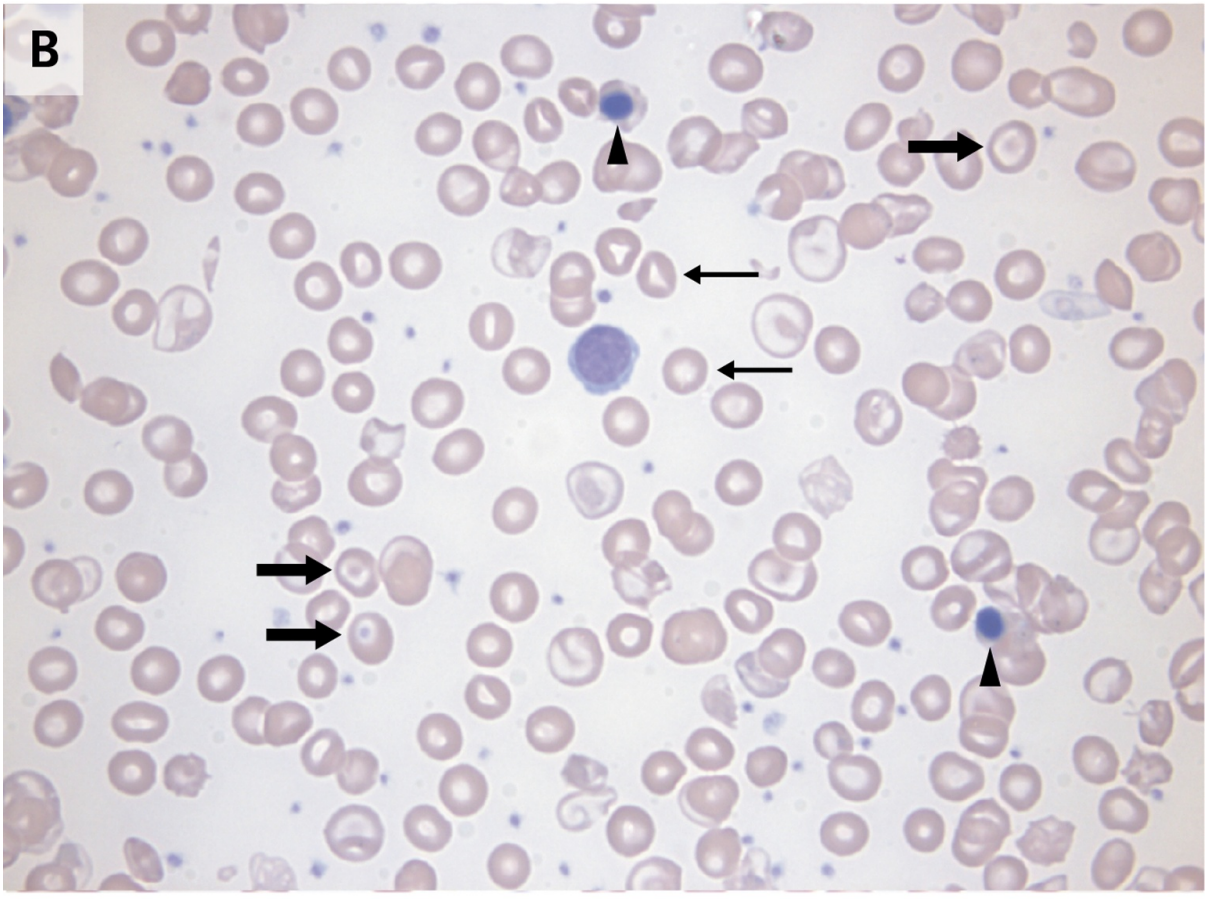
The Kozak sequence (GACACCATGG) of the beta-globin gene plays a critical role in translation initiation. A mutation at this site (e.g., the β+45 G→C substitution) **decreases but does not abolish** beta-globin chain translation — approximately a 30% reduction in translation efficiency — producing a β+-thalassemia

phenotype.[1] When compounded with other beta-thalassemia mutations or alpha-globin gene triplications, this can manifest as **thalassemia intermedia**.[1]

The peripheral blood smear in beta-thalassemia intermedia characteristically shows **microcytosis, hypochromia**, anisocytosis, poikilocytosis, and target cells.[2][3] GeneReviews notes that peripheral blood smear findings in beta-thalassemia intermedia are similar to those in beta-thalassemia major, with red blood cell indices showing microcytic anemia (MCV typically <75 fL).[2][3] This microcytosis results from the reduced beta-globin production leading to decreased hemoglobin content per red cell.

The following figure illustrates the characteristic blood smear morphology seen in beta-thalassemia compared to other microcytic anemias:


A


B

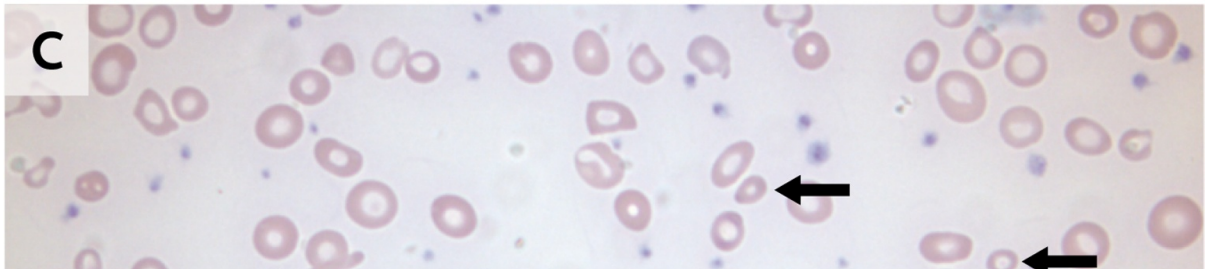

C

Figure 3. Blood-Smear Features of Microcytic Anemias.

Used under license from The New England Journal of Medicine.

The other answer choices can be eliminated:

- **Macrocytic RBCs (A)** — Thalassemias produce microcytic, not macrocytic, anemia.
- **Hyperchromic RBCs (B)** — Thalassemias cause hypochromia (reduced hemoglobin per cell), not hyperchromia.
- **Bite cells (D)** — These are characteristic of G6PD deficiency and oxidative hemolysis, not thalassemia.

Would you like to explore how different beta-thalassemia genotype combinations (e.g., compound heterozygosity with various β+ and β0 mutations) influence the clinical severity and determine whether a patient manifests as intermedia versus major?

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Question 259

A 23-year-old woman is referred to a genetic counselor. She is feeling well but is concerned because her brother was recently diagnosed with hereditary hemochromatosis. All first-degree relatives were encouraged to undergo genetic screening for any mutations associated with the disease. Today, she denies fever, chills, joint pain, or skin hyperpigmentation. Her temperature is 37.0°C (98.6°F), pulse is 85/min, respirations are 16/min, and blood pressure is 123/78 mm Hg. Her physical examination is normal. Her serum iron, hemoglobin, ferritin, and AST and ALT concentrations are normal. Gene screening will involve a blood specimen. Which of the following genes would suggest hereditary hemochromatosis?

Answer Choices:

(A) BCR-ABL gene
(B) BRCA gene
(C) FA gene
(D) HFE gene

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/15dad21f-8076-418e-897f-53523df1fb3e

OpenEvidence Explanation

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The answer is **D. HFE gene**.

Hereditary hemochromatosis (HH) is most commonly caused by mutations in the **HFE gene**, located on chromosome 6p. The most clinically significant mutation is **C282Y (p.Cys282Tyr)**, with **H63D** being another recognized variant. Homozygosity for C282Y accounts for the vast majority of classic HFE-related hemochromatosis cases.

Why the other options are incorrect:

- **A. BCR-ABL gene** — This is the fusion gene product of the Philadelphia chromosome translocation t(9;22), associated with **chronic myelogenous leukemia (CML)** and some cases of acute lymphoblastic leukemia.
- **B. BRCA gene** — BRCA1 and BRCA2 are tumor suppressor genes associated with **hereditary breast and ovarian cancer syndromes**.
- **C. FA gene** — FA (Fanconi anemia) genes (e.g., FANCA, FANCC) are associated with **Fanconi anemia**, a bone marrow failure syndrome with congenital anomalies and cancer predisposition.

In this clinical scenario, the asymptomatic sister of a patient with hereditary hemochromatosis is appropriately undergoing **HFE genotyping**, which is the recommended screening approach for first-degree relatives of affected individuals. Normal iron studies at this stage are expected, as iron overload in HH typically develops over years and manifests later in life — particularly later in women due to menstrual iron losses.

Would you like to explore the recommended management and surveillance strategy for asymptomatic individuals found to be homozygous for HFE C282Y?

Question 261

A 30-year-old male presents to the emergency department with a complaint of abdominal pain. The patient states he was at a barbecue around noon. Lunch was arranged as a buffet without refrigeration. Within 2 to 3 hours, he had abdominal pain with 3 episodes of watery diarrhea. On exam, vital signs are T 99.1, HR 103, BP 110/55, RR 14. Abdominal exam is significant for pain to deep palpation without any rebounding or guarding. There is no blood on fecal occult testing (FOBT). What is the most likely cause of this patient's presentation?

> **Answer Choices:**
>
> (A) Salmonella enteritidis
> (B) Listeria monocytogenes
> (C) Staphylococcus aureus
> (D) Vibrio cholerae

> **Correct Answer:**
>
> (C)
>
> **OpenEvidence Response:**
>
> (C) ✓

OpenEvidence Link: https://openevidence.com/ask/f83c2ee7-ba90-41bd-934f-5b01d26a174d

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OpenEvidence Explanation

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The answer is **C. Staphylococcus aureus**.

The key clinical features pointing to **Staphylococcus aureus** food poisoning are the **rapid onset of symptoms (2–3 hours)** after consuming food from an **unrefrigerated buffet**. S. aureus produces a **heat-stable preformed enterotoxin** in improperly stored food, causing an intoxication (not an infection) with a characteristic incubation period of **1–7 hours** (typically 2–7 hours).[1][2] Symptoms include abdominal cramping, nausea, vomiting, and watery diarrhea, and the illness is typically self-limiting, resolving within 24–48 hours.[2]

Why the other options are incorrect:

- **A. Salmonella enteritidis** — Causes inflammatory diarrhea with a longer incubation period (typically 6–72 hours), often with fever and potentially bloody stools. The 2–3 hour onset and noninflammatory presentation make this unlikely.[3]
- **B. Listeria monocytogenes** — Has a much longer incubation period (days to weeks for invasive disease), and diarrheal illness from Listeria is uncommon. It is primarily a concern in pregnant, elderly, or immunocompromised patients.[4]
- **D. Vibrio cholerae** — Produces profuse "rice water" stools and is associated with exposure to contaminated water or raw shellfish in endemic areas, not a barbecue buffet in a typical setting.[5]

The unrefrigerated buffet setting is a classic scenario for S. aureus contamination, as food handlers colonized with S. aureus can introduce the organism, which then proliferates and produces enterotoxin at room temperature.[6][7][8] Meat and poultry dishes — common at barbecues — are frequently implicated in S. aureus outbreaks.[6]

Would you like to explore the management approach and indications for diagnostic testing in acute foodborne illness?

Relevant images

(CONTENT OMITTED)

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Question 266

A 60-year-old man presents with a 2-day history of increasing difficulty in breathing with a productive cough. He reports having shortness of breath over the last 6 months, but he has felt worse since he contracted a cold that has been traveling around his office. Today, he reports body aches, headache, and fever along with this chronic cough. His past medical history is significant for prediabetes, which he controls with exercise and diet. He has a 30-pack-year smoking history. His blood pressure is 130/85 mmHg, pulse rate is 90/min, temperature is 36.9°C (98.5°F), and respiratory rate is 18/min. Physical examination reveals diminished breath sounds bilateral, a barrel-shaped chest, and measured breathing through pursed lips. A chest X-ray reveals a flattened diaphragm and no signs of consolidation. Pulmonary function testing reveals FEV1/FVC ratio of 60%. Arterial blood gases (ABG) of this patient are most likely to reveal which of the following?

Answer Choices:

(A) Primary respiratory acidosis
(B) Primary respiratory alkalosis
(C) Compensatory respiratory acidosis
(D) Anion gap metabolic acidosis with respiratory alkalosis

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/0b341182-fcc0-45cf-909d-c707edc0cc18

OpenEvidence Explanation

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The answer is **A. Primary respiratory acidosis**.

This patient presents with classic features of **COPD with an acute exacerbation** triggered by a viral upper respiratory infection. Key findings supporting the diagnosis include a 30-pack-year smoking history, 6-month history of progressive dyspnea, barrel-shaped chest, pursed-lip breathing, diminished bilateral breath sounds, flattened diaphragm on chest X-ray, and an FEV1/FVC ratio of 60% (confirming obstructive physiology).

Why primary respiratory acidosis?

In COPD, airflow limitation and V/Q mismatch impair CO_2 elimination, leading to CO_2 retention (hypercapnia). The retained CO_2 is hydrated to form carbonic acid, which dissociates and releases hydrogen ions, lowering pH — the hallmark of **respiratory acidosis**.[1] During acute exacerbations, worsening airflow obstruction and increased V/Q inequality further impair gas exchange, resulting in increased $PaCO_2$ and hypoxemia.[2][3] The GOLD guidelines note that ABGs in COPD exacerbations may show hypercapnia and acidosis ($PaCO_2$ > 45 mmHg and pH < 7.35).[3][4]

Why not the other options?

- **B (Respiratory alkalosis)** would result from hyperventilation and CO_2 blowoff — the opposite of what occurs in obstructive lung disease with air trapping and hypoventilation.
- **C (Compensatory respiratory acidosis)** implies a primary metabolic alkalosis with respiratory compensation. There is no clinical indication of a primary metabolic disorder here; the lung disease is the primary problem.
- **D (Anion gap metabolic acidosis with respiratory alkalosis)** would suggest conditions such as salicylate toxicity or sepsis with lactic acidosis — none of which are supported by this presentation.

The relationship between acute and chronic respiratory acidosis and the degree of renal bicarbonate compensation is illustrated in the following figure:

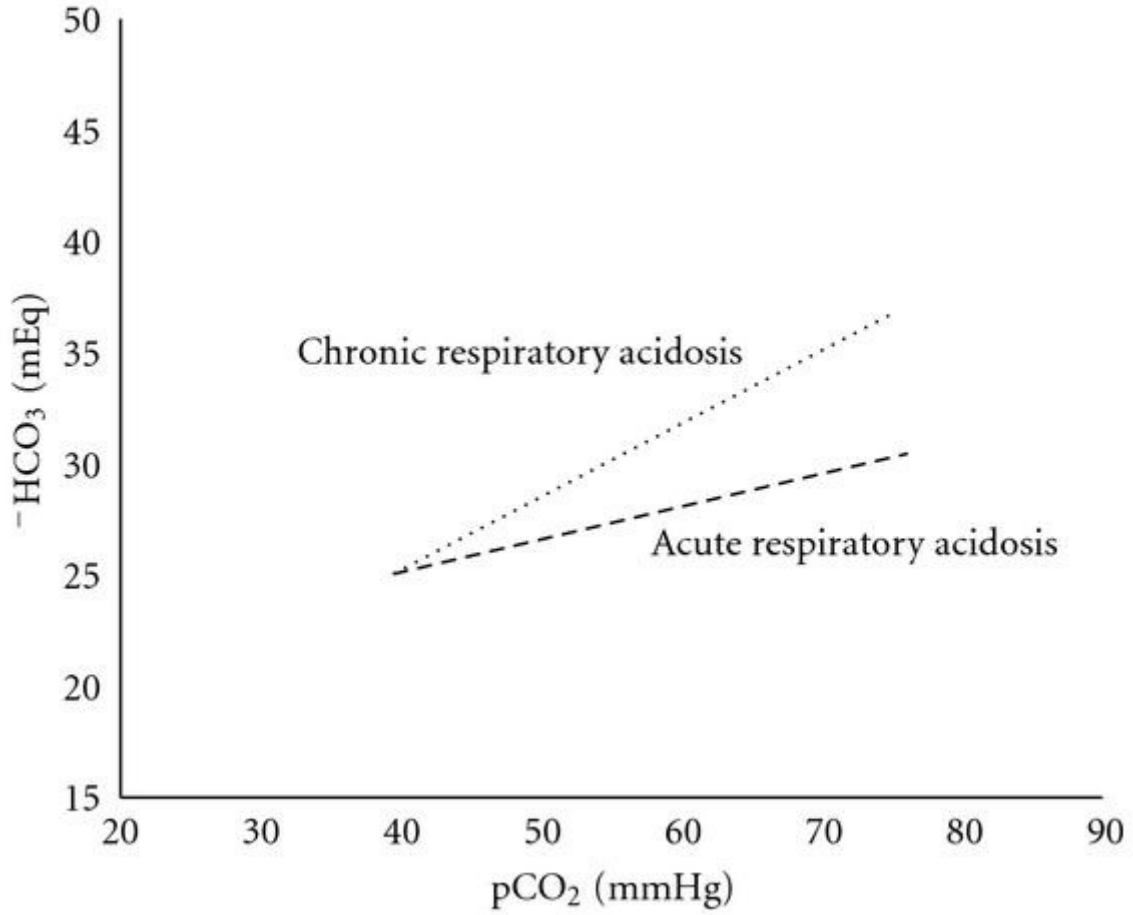


Figure 5. Relationship between pCO 2 and bicarbonate in acute and chronic respiratory acidosis.

In acute respiratory acidosis, bicarbonate rises only modestly (~1 mEq/L per 10 mmHg rise in $PaCO_2$) due to limited intracellular buffering, whereas in chronic respiratory acidosis, renal compensation increases bicarbonate more substantially (~3.5 mEq/L per 10 mmHg rise in $PaCO_2$).[1] This patient likely has a component of both chronic and acute-on-chronic respiratory acidosis given the 6-month symptom history with recent worsening.

Would you like to explore the approach to distinguishing acute from chronic respiratory acidosis using ABG interpretation and expected compensation formulas?

References

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Question 267

A 34-year-old male suffers from inherited hemophilia A. He and his wife have three unaffected daughters. What is the probability that the second daughter is a carrier of the disease?

> **Answer Choices:**
>
> (A) 0%
> (B) 25%
> (C) 50%
> (D) 100%

> **Correct Answer:**
>
> **(D)**
>
> **OpenEvidence Response:**
>
> **(D)** ✓

OpenEvidence Link: https://openevidence.com/ask/33781fb3-4821-48da-83df-f10919fce7d9

OpenEvidence Explanation

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The answer is **D. 100%**.

Hemophilia A is an **X-linked recessive** disorder. The father in this scenario has hemophilia A, meaning his genotype is **X^h Y** (where X^h carries the hemophilia allele). His wife is unaffected and, given that all three daughters are also unaffected, she is almost certainly a non-carrier with genotype **X^H X^H**.

The key genetic reasoning is straightforward:

- The father **must** pass his single X chromosome (X^h) to every daughter (since daughters receive one X from each parent).
- The mother contributes a normal X chromosome (X^H) to each daughter.
- Therefore, **every daughter** of an affected father will have the genotype **X^H X^h** — phenotypically unaffected but an **obligate carrier**.

This applies to all three daughters equally, including the second daughter. The probability is **100%** regardless of birth order, because the inheritance pattern is deterministic for daughters of an affected male.

Would you like to explore the genetic counseling implications for carrier daughters of hemophilia A patients, including the risk to their future offspring?

Question 268

A 76-year-old man is brought to his physician's office by his wife due to progressively worsening hearing loss. The patient reports that he noticed a decrease in his hearing approximately 10 years ago. His wife says that he watches television at an elevated volume and appears to have trouble understanding what is being said to him, especially when there is background noise. He states that he also experiences constant ear ringing and episodes of unsteadiness. On physical examination, the outer ears are normal and otoscopic findings are unremarkable. The patient is unable to repeat the sentence said to him on whisper testing. When a vibrating tuning fork is placed in the middle of the patient's forehead, it is heard equally on both ears. When the vibrating tuning fork is placed by the ear and then on the mastoid process, air conduction is greater than bone conduction. Which of the following structures is most likely impaired in this patient?

Answer Choices:

(A) Tympanic membrane
(B) Malleus
(C) Incus
(D) Cochlea

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/5480926c-7a6a-4ff6-ae48-de20af5574a9

OpenEvidence Explanation

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The answer is **D. Cochlea**.

This patient presents with classic **bilateral sensorineural hearing loss (SNHL)**, most consistent with **presbycusis** (age-related hearing loss). The tuning fork findings confirm this:

- **Weber test (midline):** Sound heard equally in both ears, indicating symmetric hearing loss — consistent with bilateral SNHL (no lateralization). [1]
- **Rinne test (AC > BC):** Air conduction greater than bone conduction bilaterally, which is the expected pattern in sensorineural hearing loss. In conductive hearing loss, bone conduction would be greater than or equal to air conduction (BC ≥ AC).[1]

The clinical features — gradual onset over a decade in a 76-year-old, difficulty with speech discrimination especially in background noise, tinnitus, and episodes of unsteadiness — along with a normal otoscopic exam all point to **inner ear (cochlear) pathology** rather than conductive causes.[2] Presbycusis is the most common cause of SNHL in the elderly and results from loss of neuroepithelial hair cells, neurons, and stria vascularis within the **cochlea**.[2]

The tympanic membrane (A), malleus (B), and incus (C) are components of the outer/middle ear conduction apparatus. Impairment of these structures would produce **conductive** hearing loss, characterized by BC > AC on the Rinne test and lateralization toward the affected ear on the Weber test — neither of which is present here.[3]

Would you like to explore the current evidence on management options for presbycusis, including hearing aids versus cochlear implants in elderly patients?

Relevant images

(CONTENT OMITTED)

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Question 269

A 13-year-old boy is brought to the emergency department by his mother because of a 6-hour history of severe eye pain and blurry vision. He wears soft contact lenses and has not removed them for 2 days. Ophthalmologic examination shows a deep corneal ulcer, severe conjunctival injection, and purulent discharge on the right. Treatment with topical ciprofloxacin is initiated. A culture of the ocular discharge is most likely to show which of the following?

> **Answer Choices:**
>
> (A) Gram-negative, non-maltose fermenting diplococci
> (B) Gram-negative, lactose-fermenting bacilli
> (C) Gram-negative, oxidase-positive bacilli
> (D) Gram-positive, optochin-sensitive diplococci

> **Correct Answer:**
>
> (C)
>
> **OpenEvidence Response:**
>
> (C) ✓

OpenEvidence Link: https://openevidence.com/ask/e4f6d675-681f-435f-b7d2-3323ddaddcb2

OpenEvidence Explanation

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The answer is **C. Gram-negative, oxidase-positive bacilli**, corresponding to **Pseudomonas aeruginosa**.

This clinical scenario — a contact lens wearer with prolonged lens use, severe corneal ulcer, and purulent discharge — is classic for *Pseudomonas aeruginosa* keratitis. *P. aeruginosa* is the most common causative agent of contact lens-related bacterial keratitis, accounting for **>40%** of cases in the United States.[1] [2] It is a **Gram-negative, oxidase-positive bacillus**, which matches answer choice C.

Poor lens care practices such as sleeping in contact lenses (as in this case, where lenses were not removed for 2 days) are a well-established risk factor.[1] *P. aeruginosa* forms biofilms on contact lenses and lens cases, and its virulence factors — including the type III secretion system — contribute to the rapid, aggressive corneal destruction seen in this presentation.[3][4]

Why the other choices are incorrect:

- **A. Gram-negative, non-maltose fermenting diplococci** — describes *Neisseria gonorrhoeae*, which can cause hyperacute conjunctivitis but is not associated with contact lens-related keratitis.
- **B. Gram-negative, lactose-fermenting bacilli** — describes *Escherichia coli* or other Enterobacteriaceae, which are uncommon causes of keratitis.
- **D. Gram-positive, optochin-sensitive diplococci** — describes *Streptococcus pneumoniae*, which can cause keratitis but is not the predominant organism in contact lens-related infections.

Would you like to explore the empiric antibiotic regimens and management guidelines for bacterial keratitis, including when to use fortified antibiotics versus fluoroquinolone monotherapy?

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Question 272

A 9-month-old boy is brought to the physician by his mother because of intermittent watery diarrhea for several months. Pregnancy and delivery were uncomplicated. He was diagnosed with eczematous dermatitis at 3 months old. His height and weight are below the 5th percentile. Immunologic evaluation shows a defect in activated regulatory T cells. A genetic analysis shows a mutation in the FOXP3 gene. This patient is at increased risk for which of the following?

Answer Choices:

(A) Hemorrhagic diathesis
(B) Ocular telangiectasias
(C) Autoimmune endocrinopathy
(D) Retained primary teeth

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/fcd0ad43-25aa-471f-8da2-e94d00bf22f3

OpenEvidence Explanation

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The answer is **C. Autoimmune endocrinopathy**.

This clinical vignette describes **IPEX syndrome** (Immune dysregulation, Polyendocrinopathy, Enteropathy, X-linked), caused by mutations in the **FOXP3** gene, which encodes a master transcription factor essential for the development and function of CD4+ regulatory T (Treg) cells.[1][2] The presentation — a male infant with chronic watery diarrhea, eczematous dermatitis, failure to thrive, and defective regulatory T cells — is classic for IPEX.

The "P" in IPEX stands for **polyendocrinopathy**. Autoimmune endocrine disorders are a hallmark of this syndrome, with **type 1 diabetes mellitus** being the most common endocrinopathy (present in ~50–60% of patients), often with neonatal onset.[1][3][4] Autoimmune thyroid disease (typically hypothyroidism) is the second most common endocrine manifestation.[1][5]

The other answer choices correspond to different conditions:

- **A. Hemorrhagic diathesis** — associated with Wiskott-Aldrich syndrome (WAS gene mutation), which features thrombocytopenia, eczema, and immunodeficiency
- **B. Ocular telangiectasias** — characteristic of ataxia-telangiectasia (ATM gene mutation)
- **D. Retained primary teeth** — associated with hyper-IgE syndrome (STAT3 or DOCK8 mutations)

Would you like to explore the current management strategies for IPEX syndrome, including the role of hematopoietic stem cell transplantation versus immunosuppressive therapy?

Relevant images

(CONTENT OMITTED)

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Question 273

A 57-year-old man comes to the physician because of a 3-week history of abdominal bloating and increased frequency of stools. He describes the stools as bulky, foul-smelling, and difficult to flush. He also has a 4-month history of recurrent dull upper abdominal pain that usually lasts for a few days, worsens after meals, and is not relieved with antacids. He has had a 10-kg (22-lb) weight loss in the past 4 months. He has no personal or family history of serious illness. He has smoked 1 pack of cigarettes daily for 37 years. He has a 12-year history of drinking 6 to 8 beers daily. He is 160 cm (5 ft 3 in) tall and weighs 52 kg (115 lb); BMI is 20 kg/m2. His vital signs are within normal limits. Abdominal examination shows mild epigastric tenderness without rebound or guarding. Bowel sounds are normal. The remainder of the examination shows no abnormalities. Which of the following is the most appropriate next step in diagnosis?

Answer Choices:

(A) Abdominal CT scan
(B) Endoscopic ultrasonography
(C) Abdominal ultrasound
(D) Upper gastrointestinal endoscopy

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/994f6b4e-239c-455a-90e0-99275164cb32

OpenEvidence Explanation

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The correct answer is **A. Abdominal CT scan**.

This patient presents with a classic picture of **chronic pancreatitis** with exocrine pancreatic insufficiency: 4 months of postprandial epigastric pain unrelieved by antacids, steatorrhea (bulky, foul-smelling, difficult-to-flush stools), significant weight loss, and major risk factors (37 pack-year smoking history and heavy alcohol use for 12 years). The most appropriate initial diagnostic step is a **contrast-enhanced abdominal CT scan**.

Why CT is the best initial test:

A contrast-enhanced CT scan is recommended as the **initial diagnostic imaging** for all patients with suspected chronic pancreatitis.[1][2] It is noninvasive, widely available, and can detect hallmark findings such as pancreatic calcifications, ductal dilation, and parenchymal atrophy, which establish the diagnosis.[1][3] CT has a sensitivity of approximately 75% and specificity of 91% for chronic pancreatitis.[3] Importantly, CT can also exclude other causes of chronic abdominal pain, including pancreatic malignancy — a critical consideration given this patient's age, smoking history, and weight loss.[4]

Why not the other options:

- **Endoscopic ultrasonography (B)** — While EUS has high sensitivity (81%), it is invasive, operator-dependent, and prone to false positives. Guidelines recommend EUS only when CT or MRI/MRCP findings are inconclusive, not as a first-line test.[2][5][6]
- **Abdominal ultrasound (C)** — Transabdominal ultrasound has the lowest sensitivity (67%) among imaging modalities for chronic pancreatitis and is limited by bowel gas and body habitus. Many guidelines do not recommend it for initial diagnosis.[3][6]
- **Upper GI endoscopy (D)** — This would evaluate mucosal disease (e.g., peptic ulcer, gastric cancer) but would not assess the pancreatic parenchyma or

ductal system, which is the primary concern here given the steatorrhea and clinical profile.

The recommended stepwise diagnostic approach is **CT first**, followed by MRI/MRCP if CT is normal or equivocal, and then EUS if further evaluation is needed. [2]

Would you like to explore the management of chronic pancreatitis once diagnosed, including pancreatic enzyme replacement therapy and pain management strategies?

Relevant images

(CONTENT OMITTED)

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Question 275

A 56-year-old man presents to his primary care doctor with intermittent chest pain. He reports a 2-month history of exertional chest pain that commonly arises after walking 5 or more blocks. He describes the pain as dull, burning, non-radiating substernal pain. His past medical history is notable for hypercholesterolemia and hypertension. He takes simvastatin and losartan. His temperature is 98.9°F (37.2°C), blood pressure is 150/85 mmHg, pulse is 88/min, and respirations are 18/min. On exam, he is well-appearing and in no acute distress. S1 and S2 are normal. No murmurs are noted. An exercise stress test is performed to further evaluate the patient's pain. Which of the following substances is released locally to increase coronary blood flow during exertion?

Answer Choices:

(A) Adenosine
(B) Inorganic phosphate
(C) Prostaglandin E2
(D) Transforming growth factor beta

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/b3aceb9a-bf4a-444b-81d3-f8d2be7945cd

OpenEvidence Explanation

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The answer is **A. Adenosine**.

Adenosine is the classic locally released substance that increases coronary blood flow during exertion. According to the well-established "adenosine hypothesis" proposed by Berne in 1963, when myocardial oxygen consumption (MVO_2) increases during exercise, the partial pressure of oxygen in cardiac myocytes falls, leading to the breakdown of adenine nucleotides and generation of adenosine. This adenosine then diffuses to and vasodilates the coronary microvessels, increasing blood flow and restoring oxygen delivery.[1][2]

Adenosine exerts its vasodilatory effects primarily through activation of **A2A receptors** on coronary vascular smooth muscle and endothelial cells.[2][3] This mechanism is so well characterized that exogenous adenosine is used clinically as a pharmacological stress agent in patients who cannot exercise, precisely because it mimics the coronary vasodilation that occurs during exertion.[4]

Regarding the other options:

- **Inorganic phosphate** is a byproduct of ATP hydrolysis in skeletal muscle but is not the primary local mediator of coronary vasodilation during exercise.
- **Prostaglandin E2** has vasodilatory properties but has not been shown to play a significant role in steady-state coronary flow regulation during exercise.[5]
- **Transforming growth factor beta (TGF-β)** is involved in chronic vascular remodeling and fibrosis, not acute exercise-induced coronary vasodilation.

It is worth noting that the full picture of exercise-induced coronary vasodilation involves multiple redundant mechanisms, including KATP *channels, nitric oxide, and adrenergic feedforward control, but adenosine remains the most classically recognized local metabolic vasodilator in this context.*[6][7][8]

Would you like to explore how adenosine-based pharmacological stress testing compares to exercise stress testing in diagnostic accuracy for coronary artery disease?

Relevant images

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Question 277

A 60-year-old man with a history of osteoarthritis has been awaiting hip replacement surgery for 3 years. During his annual physical, he reports that he has been taking over the counter pain medications, but that no amount of analgesics can relieve his constant pain. Laboratory results reveal that his renal function has deteriorated when compared to his last office visit 2 years ago. Serum creatinine is 2.0 mg/dL, and urinalysis shows 1+ proteinuria. There are no abnormalities seen on microscopy of the urine. A renal biopsy shows eosinophilic infiltration and diffuse parenchymal inflammation. What is the most likely explanation for this patient's deterioration in renal function?

Answer Choices:

(A) Focal segmental glomerulosclerosis
(B) Ischemic acute tubular necrosis
(C) Nephrotoxic acute tubular necrosis
(D) Toxic tubulointerstitial nephritis

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/66db4f8b-77ef-4bd0-a3a7-3ca9b08f2742

OpenEvidence Explanation

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The correct answer is **D. Toxic tubulointerstitial nephritis**.

This patient's clinical picture — chronic OTC analgesic use (likely NSAIDs) for osteoarthritis over years, progressive renal dysfunction, mild proteinuria, bland urine sediment on microscopy, and a renal biopsy showing **eosinophilic infiltration with diffuse parenchymal inflammation** — is classic for drug-induced tubulointerstitial nephritis caused by chronic analgesic use.[1][2]

Why toxic tubulointerstitial nephritis fits best:

- NSAIDs are among the most common causes of drug-induced acute interstitial nephritis (AIN), and chronic use over months to years is the typical pattern for NSAID-induced AIN (6–18 months or longer).[1]
- The hallmark biopsy findings of drug-induced AIN include interstitial edema, diffuse interstitial inflammation, and tubulitis, with infiltrates composed of lymphocytes, mononuclear cells, and eosinophils. The presence of frequent eosinophils is particularly suggestive of a drug-induced etiology.[1]
- The bland urine sediment (no abnormalities on microscopy) and mild proteinuria are consistent with a tubulointerstitial process rather than a glomerular disease.[2]

Why the other options are less likely:

- **A. Focal segmental glomerulosclerosis (FSGS)** — Would typically present with heavier (nephrotic-range) proteinuria and podocyte foot process effacement on biopsy, not eosinophilic interstitial infiltration.
- **B. Ischemic acute tubular necrosis (ATN)** — Would show muddy brown casts on urinalysis and tubular epithelial cell necrosis on biopsy, not eosinophilic interstitial inflammation. It is also typically associated with hypoperfusion events, not chronic analgesic use.
- **C. Nephrotoxic ATN** — While NSAIDs can cause hemodynamically mediated AKI resembling ATN, the biopsy findings here (eosinophilic infiltration and diffuse parenchymal inflammation) point specifically to an interstitial nephritis pattern rather than isolated tubular necrosis.[1]

Would you like to explore the management approach for NSAID-induced interstitial nephritis, including the role and timing of corticosteroid therapy?

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Question 278

A 62-year-old man presents to the emergency department with shortness of breath. The patient says he feels as if he is unable to take a deep breath. The patient has a past medical history of COPD and a 44-pack-year smoking history. The patient has been admitted before for a similar presentation. His temperature is 98.7°F (37.1°C), blood pressure is 177/118 mmHg, pulse is 123/min, respirations are 33/min, and oxygen saturation is 80% on room air. The patient is started on 100% oxygen, albuterol, ipratropium, magnesium, and prednisone. The patient claims he is still short of breath. Physical exam reveals bilateral wheezes and poor air movement. His oxygen saturation is 80%. Which of the following is the best next step in management?

Answer Choices:

(A) BiPAP
(B) Chest tube placement
(C) Intubation
(D) Needle decompression

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/9300ae46-ed91-4845-9a28-96dc20e51ae6

OpenEvidence Explanation

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The best next step in management is **A. BiPAP** (bilevel positive airway pressure, a form of noninvasive ventilation).

This patient is experiencing a **severe acute exacerbation of COPD** with persistent hypoxemia (SpO_2 80%) despite maximal medical therapy (bronchodilators, corticosteroids, supplemental oxygen). He remains conscious and communicating, which makes him a candidate for noninvasive ventilation (NIV) rather than immediate intubation.

Why BiPAP is correct:

- The 2026 GOLD guidelines recommend NIV as the **first-line ventilatory support** for acute respiratory failure in COPD exacerbations, with an 80–85% success rate in avoiding intubation. NIV improves oxygenation, reduces work of breathing, decreases intubation rates, shortens hospital stays, and improves survival (Evidence A).[1][2]
- An NEJM review similarly confirms that face-mask NIV is strongly recommended as first-line therapy for COPD exacerbations with respiratory failure, as it efficiently offloads respiratory muscles and counteracts dynamic hyperinflation.[3]

Why not the other options:

- **Intubation (C):** Invasive mechanical ventilation is reserved for patients who **fail NIV**, have cardiac/respiratory arrest, severely diminished consciousness, inability to protect the airway, or hemodynamic instability. This patient is alert and has not yet had a trial of NIV.[1]
- **Chest tube (B) and needle decompression (D):** These are indicated for pneumothorax. There is no clinical evidence of pneumothorax in this scenario — bilateral wheezes and poor air movement are consistent with severe bronchospasm, not unilateral absent breath sounds or tension physiology.

The critical teaching point is that in a conscious COPD patient with respiratory failure who has failed initial medical therapy, **NIV should be trialed before proceeding to intubation**.[1][3][4]

Would you like to explore the specific settings and monitoring parameters for BiPAP in acute COPD exacerbations, including criteria for recognizing NIV failure and escalating to intubation?

Relevant images

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Question 279

A 76-year-old man is brought to the physician by his wife because of low back pain and weakness for the past 4 weeks. He says that the pain is sharp, radiates to his left side, and has a burning quality. He has had a cough occasionally productive of blood-streaked sputum for the past 2 months. He has had 3.2-kg (7.0-lb) weight loss in that time. He is now unable to walk without assistance and has had constipation and difficulty urinating for the past 2 weeks. He has hypertension treated with enalapril. He has smoked 1 pack of cigarettes daily for 60 years. His temperature is 37°C (98.6°F), pulse is 75/min, and blood pressure is 150/80 mm Hg. He is oriented to person, place, and time. Neurologic examination shows 3/5 strength of the lower extremities. Deep tendon reflexes are hyperreflexive. Babinski sign is present bilaterally. Sensory examination shows decreased sensation to pinprick below the T4 dermatome. He is unable to lie recumbent due to severe pain. An x-ray of the chest shows multiple round opacities of varying sizes in both lungs. Which of the following is the most appropriate next step in the management of this patient?

Answer Choices:

(A) Radiation therapy
(B) Intravenous dexamethasone therapy
(C) Intravenous acyclovir therapy
(D) Intravenous ceftriaxone and azithromycin therapy

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/983083a8-de55-4c63-bc9c-02ae4bf25558

OpenEvidence Explanation

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The correct answer is **B. Intravenous dexamethasone therapy**.

This patient presents with classic findings of **metastatic spinal cord compression (MSCC)** from a likely lung malignancy: a 60-pack-year smoker with hemoptysis, weight loss, multiple pulmonary opacities on chest x-ray, and progressive neurologic deficits including lower extremity weakness (3/5), hyperreflexia, bilateral Babinski signs, a T4 sensory level, and bowel/bladder dysfunction. The most appropriate **immediate** next step is **intravenous dexamethasone**, which should be initiated as soon as MSCC is clinically suspected, even before confirmatory imaging.[1][2][3]

Why dexamethasone first? MSCC is a medical emergency. Glucocorticoids reduce peritumoral edema, alleviate pain, and preserve neurologic function while definitive treatment (radiation therapy and/or surgery) is being arranged.[3][4] The NCCN CNS Cancers Guidelines specify that for spinal cord compression, **steroids** are the first treatment step, with a recommended minimum dose of dexamethasone 4 mg every 6 hours (doses may range from 10–100 mg).[5] A randomized trial demonstrated that high-dose dexamethasone combined with radiation therapy improved ambulatory rates at 3 months (81% vs. 63%) and 6 months (59% vs. 33%) compared to radiation alone.[4][6]

> "Glucocorticoids reduce neurologic impairment and spinal pain, but the most effective doses have not been established. An initial dose of 100 mg of dexamethasone has been used, but a small trial indicates that lower doses are probably equally effective."
>
> —Alexander E. Ropper, M.D. et al., Baylor College of Medicine. Acute Spinal Cord Compression. N Engl J Med. April 06, 2017.
>
> Used under license from The New England Journal of Medicine.

Why not the other options?

- **A. Radiation therapy** — While radiation is a critical component of definitive MSCC treatment, it is not the immediate first step. Steroids should be

administered first to reduce cord edema and stabilize neurologic function while radiation planning is arranged.[5][7]

- **C. Intravenous acyclovir** — This would treat herpes zoster, which can cause radicular pain with a burning quality. However, the upper motor neuron signs (hyperreflexia, bilateral Babinski), T4 sensory level, and bowel/bladder dysfunction indicate cord compression rather than a dermatomal viral process. Additionally, the pulmonary findings point to malignancy.

- **D. Intravenous ceftriaxone and azithromycin** — This would treat community-acquired pneumonia. While the patient has a cough, the hemoptysis, weight loss, and multiple round opacities are far more consistent with malignancy than infection, and antibiotics would not address the spinal cord compression.

Would you like to explore the evidence comparing surgical decompression versus radiation therapy alone as definitive treatment for MSCC?

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Question 280

A 32-year-old man arrives to his primary care physician to discuss his fear of flying. The patient reports that he has had a fear of flying since being a teenager. He went on a family vacation 15 years ago, and during the flight there was turbulence and a “rough landing”. Since then he has avoided flying. He did not go to his cousin’s wedding because it was out of the country. He also was unable to visit his grandmother for her 80th birthday. The last time his job asked him to meet a client out of state, he drove 18 hours instead of flying. Two years ago he promised his fiancé they could fly to Florida. Upon arrival at the airport, he began to feel dizzy, lightheaded, and refused to go through security. During the clinic visit, the patient appears anxious and distressed. He recognizes that his fear is irrational. He is upset that it is affecting his relationship with his wife. Additionally, his current job may soon require employees in his sales position to fly to meet potential clients. He is embarrassed to have a conversation with his manager about his fear of flying. Which of the following is the best therapy for the patient’s condition?

Answer Choices:

(A) Alprazolam
(B) Cognitive behavioral therapy
(C) Fluoxetine
(D) Psychodynamic psychotherapy

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/03714f33-1373-4666-a9ca-1436c49e8bf1

OpenEvidence Explanation

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The best therapy for this patient's condition is **B. Cognitive behavioral therapy (CBT)**.

This patient presents with a classic **specific phobia** (aviophobia/fear of flying) — characterized by a persistent, irrational fear triggered by a specific stimulus, with marked avoidance behavior causing significant functional impairment in personal and professional life. He recognizes the fear is irrational, which is typical of specific phobia.

Exposure-based CBT is the first-line treatment of choice for specific phobias.[1][2][3] The key therapeutic component is graduated exposure to the feared stimulus (in vivo or imaginal), which breaks the cycle of avoidance behavior and enables new safety learning.[2] A review in The Lancet Psychiatry identified exposure therapy as the "current treatment of choice" for specific phobias, with large effect sizes demonstrated in meta-analyses.[1] A JAMA review similarly confirmed that clinical practice guidelines recommend CBT as first-line psychotherapy for anxiety disorders, with medium to large effect sizes compared to control conditions.[3]

Why the other options are incorrect:

- **Alprazolam (A):** Benzodiazepines may provide short-term anxiolysis but do not address the underlying phobia, carry risk of dependence, and have not been shown to significantly reduce specific phobia symptoms. They do not produce lasting behavioral change.[4]
- **Fluoxetine (C):** SSRIs are first-line pharmacotherapy for generalized anxiety disorder, social anxiety disorder, and panic disorder, but pharmacotherapy alone is not the preferred treatment for specific phobias. CBT with exposure has been shown to reduce anxiety symptoms more than fluoxetine in comparative studies.[4]
- **Psychodynamic psychotherapy (D):** The evidence base for psychodynamic therapy in anxiety disorders is substantially weaker than for CBT. It lacks the structured exposure component critical for treating specific phobias.[2]

Would you like to explore the specific exposure therapy protocols used for fear of flying, including virtual reality exposure therapy approaches?

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Question 281

A 75-year-old man presents to a medical clinic for evaluation of a large, tense, pruritic bulla on his inner thighs, abdomen, and lower abdomen. A skin biopsy is performed, which shows an epidermal basement membrane with immunoglobulin G (IgG) antibodies and linear immunofluorescence. Which of the following is the most likely cell junction to which the antibodies bind?

> **Answer Choices:**
>
> (A) Desmosomes
> (B) Gap junctions
> (C) Hemidesmosomes
> (D) Tight junctions

> **Correct Answer:**
>
> (C)
>
> **OpenEvidence Response:**
>
> (C) ✓

OpenEvidence Link: https://openevidence.com/ask/5e971e2e-0b8e-4267-8d3d-25cfc68cedfc

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OpenEvidence Explanation

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The correct answer is **C. Hemidesmosomes**.

The clinical presentation — a 75-year-old man with large, tense, pruritic bullae on the inner thighs and abdomen, with linear IgG deposition at the epidermal

basement membrane on direct immunofluorescence — is classic for **bullous pemphigoid** (BP).

In BP, IgG autoantibodies target two **hemidesmosomal** proteins: **BP180** (a 180 kDa transmembrane glycoprotein, also known as type XVII collagen) and **BP230** (a 230 kDa intracellular plaque protein).[1][2] These hemidesmosomes are the cell junctions that anchor basal keratinocytes to the underlying basement membrane at the dermal-epidermal junction. Autoantibody binding to these hemidesmosomal components triggers complement activation, inflammatory cell recruitment, and protease release, ultimately causing subepidermal blister formation.[3][4]

Why the other options are incorrect:

- **A. Desmosomes** — Targeted in pemphigus (vulgaris and foliaceus), where autoantibodies bind desmogleins at cell-cell junctions, producing flaccid (not tense) blisters with intraepidermal (not subepidermal) separation.[5]
- **B. Gap junctions** — Involved in intercellular communication; not targeted in autoimmune blistering diseases.
- **D. Tight junctions** — Form paracellular barriers; not the target in pemphigoid diseases.

Would you like to explore the distinguishing features between bullous pemphigoid and other subepidermal autoimmune blistering diseases such as epidermolysis bullosa acquisita or linear IgA bullous dermatosis?

Relevant images

(CONTENT OMITTED)

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Question 283

Twelve hours after admission to the hospital because of a high-grade fever for 3 days, a 15-year-old boy has shortness of breath. During this period, he has had generalized malaise and a cough productive of moderate amounts of green sputum. For the past 10 days, he has had fever, a sore throat, and generalized aches; these symptoms initially improved, but worsened again over the past 5 days. His temperature is 38.7°C (101.7°F), pulse is 109/min, respirations are 27/min, and blood pressure is 100/70 mm Hg. Pulse oximetry on room air shows an oxygen saturation of 93%. There are decreased breath sounds and crackles heard over the upper right lung field. His hemoglobin concentration is 13.3 g/dL, leukocyte count is 15,000/mm3, and platelet count is 289,000/mm3. An x-ray of the chest shows a right upper-lobe infiltrate. Which of the following is the most likely cause of this patient's symptoms?

Answer Choices:

(A) Streptococcus pneumoniae
(B) Mycoplasma pneumoniae
(C) Chlamydophila pneumoniae
(D) Haemophilus influenzae

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/e6bce77c-64bb-40e5-92f2-0eeec66220a9

OpenEvidence Explanation

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The answer is **A. Streptococcus pneumoniae**.

The clinical presentation in this case is classic for ***secondary bacterial pneumonia due to* S. pneumoniae following a preceding viral upper respiratory infection. Several key features point to this diagnosis:**

Biphasic illness pattern: The patient initially had fever, sore throat, and generalized aches for 10 days that initially improved but then worsened over the past 5 days with high-grade fever, productive cough with purulent (green) sputum, and shortness of breath. This "improve-then-worsen" pattern is the hallmark of bacterial superinfection complicating a viral respiratory illness. *S. pneumoniae* is the paradigmatic pathogen in post-viral bacterial pneumonia.[1][2][3]

Typical bacterial pneumonia features: The presentation includes high fever (38.7°C), tachycardia, tachypnea, leukocytosis (15,000/mm³), purulent sputum, focal crackles, and a **lobar infiltrate** (right upper lobe) on chest radiograph — all consistent with a typical bacterial pneumonia rather than an atypical pathogen.[4][5]

Why not the other options:

- ***Mycoplasma pneumoniae*** (B) — While *M. pneumoniae* is common in this age group, it characteristically presents with a slowly progressive course of malaise, sore throat, low-grade fever, and dry cough developing over 3–5 days. It is associated with lower WBC counts, lower procalcitonin, and prolonged prodromal symptoms without the acute biphasic deterioration seen here. The high WBC count, purulent sputum, and lobar consolidation are more consistent with a typical bacterial pathogen.[6][7]
- ***Chlamydophila pneumoniae*** (C) — Also an atypical pathogen that tends to cause a more indolent course with lower inflammatory markers, not the acute lobar consolidation with leukocytosis seen here.[4]

- ***Haemophilus influenzae*** (D) — While it can cause bacterial pneumonia, its prevalence has decreased significantly due to routine childhood vaccination. S. *pneumoniae* remains the most common bacterial cause of CAP across all age groups.[5][8]

The combination of a preceding viral illness with initial improvement, followed by acute worsening with high fever, purulent sputum, leukocytosis, and lobar consolidation is most consistent with secondary pneumococcal pneumonia.[1][3]

Would you like to explore the recommended empiric antibiotic regimens for community-acquired pneumonia in hospitalized adolescents?

Relevant images

(CONTENT OMITTED)

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Question 286

A 27-year-old HIV positive female gave birth to a 7lb 2oz (3.2 kg) baby girl. The obstetrician is worried that the child may have been infected due to the mother's haphazard use of her anti-retroviral medications. Which of the following assays would a hospital use detect the genetic material of HIV if the child had been infected?

Answer Choices:

(A) Enzyme-linked immunosorbent assay (ELISA)
(B) Rapid HIV antibody test
(C) Polymerase chain reaction
(D) Southern blot

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/a810b263-e0c8-4893-807f-062aabbf409d

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OpenEvidence Explanation

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The answer is **C. Polymerase chain reaction (PCR)**.

Practice Guideline

The American Academy of Pediatrics (AAP) recommends that **polymerase chain reaction (PCR) assays** that directly detect HIV DNA or RNA be used as the gold standard for diagnostic testing of infants and young children younger than 18 months.[1] This is because passively transferred maternal HIV antibodies may be detectable in an exposed but uninfected infant's bloodstream until approximately **18 months of age**, making antibody-based tests (ELISA, rapid HIV antibody tests) unreliable — they cannot distinguish between true infant infection and passive transfer of maternal antibodies.[1]

PCR-based nucleic acid tests directly detect the **genetic material** of HIV rather than the host immune response, allowing definitive diagnosis in the neonatal period.[1] For infants at highest risk of infection — including those whose mothers received no antiretroviral drugs during pregnancy or had haphazard medication use — an HIV nucleic acid amplification test (NAAT) should be performed at birth or in the first few days of life, with repeat testing at 14–21 days, 1–2 months, and 4–6 months of age.[1] In the absence of maternal ART, as many as 30–40% of infants with HIV infection can be identified by 48 hours of age using these assays.[1]

Why the other options are incorrect:

- **A. ELISA** and **B. Rapid HIV antibody test** — Both detect HIV antibodies, not genetic material. In neonates, maternal IgG antibodies cross the placenta and persist for up to 18 months, producing false-positive results that do not indicate true infant infection.[1][2]
- **D. Southern blot** — While Southern blot can detect DNA sequences, it is not used clinically for HIV diagnosis in neonates. It is a labor-intensive research technique that lacks the sensitivity and practicality of PCR-based assays.

The question specifically asks which assay detects the "genetic material" of HIV, which directly points to PCR — a nucleic acid amplification technique that detects HIV DNA or RNA.[1][3]

Would you like to explore the recommended antiretroviral prophylaxis regimens for high-risk neonates born to mothers with suboptimal viral suppression?

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Question 287

A 53-year-old man presents to his physician's office with a persistent cough which he has had over the last few months. He was diagnosed with chronic obstructive pulmonary disease (COPD) the previous year and since then has been on a short-acting β-agonist to help alleviate his symptoms. Since his diagnosis, he has quit smoking, a habit which he had developed about 30 years ago. He used to smoke about 2 packs of cigarettes daily. Today, he has come in with an increase in his symptoms. He tells his physician that he has been having a fever for the past 3 days, ranging between 37.8°–39°C (100°F–102.2°F). Along with this, he has a persistent cough with copious amounts of greenish-yellow sputum. He has also been having difficulty breathing. On examination, his temperature is 38.6°C (101.5°F), the respirations are 22/min, the blood pressure is 110/80 mm Hg, and the pulse is 115/min. Slight crackles and respiratory wheezes are prominent in the lower lung fields. His FEV1 is 57% of his normal predicted value. He is started on oxygen and a dose of oral prednisone. At this time, which of the following should also be considered as a treatment option?

Answer Choices:

(A) Doxycycline
(B) Ciprofloxacin
(C) Erythromycin
(D) Antibiotics would not be appropriate at this time

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/83787217-15e3-4ed8-9474-64b6dd2623e5

OpenEvidence Explanation

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The answer is **A. Doxycycline**.

This patient is presenting with an **acute exacerbation of COPD (AECOPD)** characterized by the classic triad of increased dyspnea, increased sputum volume, and **purulent (greenish-yellow) sputum**, along with fever — all strongly suggesting a bacterial etiology. Antibiotics are clearly indicated here (eliminating option D), and the question is which antibiotic is most appropriate.

Why doxycycline? Guidelines from GOLD, the AAFP, and a JAMA review all recommend **first-line oral antibiotics** for AECOPD with purulent sputum, including **doxycycline, trimethoprim-sulfamethoxazole, amoxicillin/clavulanate, or macrolides**.[1][2][3] Doxycycline (a tetracycline) is among the most commonly used first-line agents and covers the typical pathogens — *Haemophilus influenzae*, *Streptococcus pneumoniae*, and *Moraxella catarrhalis*.[4] A network meta-analysis also found doxycycline to be significantly better than placebo for microbiological response (OR 3.84; 95% CI 1.96–7.54).[5]

Why not the other options?

- **Ciprofloxacin (B):** Fluoroquinolones are reserved for patients with repeated exacerbations, suspected bacterial resistance, or treatment failure on first-line agents — not as initial therapy.[1][5]
- **Erythromycin (C):** While macrolides as a class are recommended, erythromycin specifically is poorly tolerated (GI side effects, drug interactions) and is not a preferred choice for AECOPD treatment. Azithromycin is the preferred macrolide when this class is used.
- **No antibiotics (D):** This patient has purulent sputum with increased dyspnea and fever — precisely the clinical scenario where antibiotics are indicated per GOLD guidelines (Evidence A).[3][6]

Would you like to explore the role of prophylactic macrolide therapy in reducing future COPD exacerbation frequency?

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Question 288

An 8-year-old boy is brought to the physician because of headaches for the past 2 weeks. His headaches tend to occur in the morning and are associated with nausea and vomiting. One month ago, the patient was admitted to the hospital because of fever, irritability, and neck rigidity, and he was successfully treated with antibiotics. His temperature today is 37.5°C (98.5°F). An MRI of the brain shows bilateral ventricular enlargement and enlargement of the subarachnoid space. Which of the following is the most likely explanation of the patient's condition?

Answer Choices:

(A) Increased CSF production by the choroid plexus
(B) Impaired CSF flow through the arachnoid granulations
(C) Impaired CSF drainage into the subarachnoid space
(D) Impaired CSF drainage into the fourth ventricle

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/dedc8984-07c4-4311-8284-8de73c1478bb

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OpenEvidence Explanation

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The correct answer is **B. Impaired CSF flow through the arachnoid granulations**.

This child presents with morning headaches, nausea, and vomiting — classic signs of raised intracranial pressure — following a recent episode of **bacterial meningitis** (fever, irritability, neck rigidity treated with antibiotics). The MRI shows **bilateral ventricular enlargement and enlargement of the subarachnoid space**, which is the hallmark of **communicating hydrocephalus**.

Why answer B is correct:

Communicating hydrocephalus is one of the most common complications of bacterial meningitis. The mechanism involves **impaired CSF reabsorption at the arachnoid granulations** due to inflammatory exudate, fibrosis, and scarring from the meningeal infection.[1][2] In experimental pneumococcal meningitis, CSF outflow resistance from the subarachnoid space to the venous system is markedly increased, and this impairment persists even after CSF sterilization with antibiotics.[3] The key imaging finding — enlargement of both the ventricles and the subarachnoid space — confirms that CSF flows freely from the ventricles into the subarachnoid space (ruling out obstruction within the ventricular system) but cannot be absorbed into the venous circulation through the damaged arachnoid granulations.[1][4]

Why the other answers are incorrect:

- **A (Increased CSF production):** CSF overproduction is exceedingly rare and is essentially limited to choroid plexus papillomas. Meningitis does not cause clinically significant CSF hypersecretion.[5]
- **C (Impaired CSF drainage into the subarachnoid space):** This would describe non-communicating (obstructive) hydrocephalus, where CSF is blocked within the ventricular system. In that case, the subarachnoid space would not be enlarged — but here it is dilated, indicating CSF reaches the subarachnoid space freely.[4][6]
- **D (Impaired CSF drainage into the fourth ventricle):** This would also represent obstructive hydrocephalus (e.g., aqueductal stenosis), which would cause dilation of the lateral and third ventricles but not the fourth ventricle or subarachnoid space.[6]

Would you like to explore the management options for post-meningitis communicating hydrocephalus in pediatric patients, including indications for shunting versus endoscopic third ventriculostomy?

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Question 291

A 32-year-old woman presents to the emergency department because she has a cord-like rash on her left calf that is red and painful to touch. She says that she has had multiple such lesions previously. Other medical history reveals that she has had 3 past spontaneous abortions at < 10 weeks of gestational age but has never been diagnosed with any diseases. She drinks socially but has never smoked or used drugs. She has never taken any medications except for over the counter analgesics and antipyretics. Physical exam shows that the cord-like lesion is tender, thick, and hardened on palpation. In addition, she has a lacy mottled violaceous rash on multiple extremities. Which of the following antibodies would most likely be found in this patient's blood?

Answer Choices:

(A) Anti-cardiolipin
(B) Anti-centromere
(C) Anti-histone
(D) Anti-ribonucleoprotein

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/03b569ee-e267-4f23-aa61-978d2f604749

OpenEvidence Explanation

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The answer is **A. Anti-cardiolipin**.

This patient's presentation is classic for **antiphospholipid syndrome (APS)**. The key clinical features pointing to this diagnosis include:

- **Recurrent superficial thrombophlebitis** — the cord-like, tender, thick, hardened lesion on the calf represents superficial venous thrombosis, a well-recognized cutaneous manifestation of APS.[1]
- **Recurrent early pregnancy loss** — three spontaneous abortions before 10 weeks of gestation. The revised Sapporo classification criteria include ≥3 unexplained consecutive spontaneous abortions before the 10th week of gestation as an obstetric criterion for APS.[2]
- **Livedo reticularis** — the lacy, mottled, violaceous rash on multiple extremities is the most frequently observed cutaneous manifestation of APS and is significantly associated with antiphospholipid antibody positivity (OR 2.91 for livedo in aPL-positive vs. aPL-negative patients).[1][3]

APS is defined by thrombotic or obstetrical events in the setting of persistent antiphospholipid antibodies, which include lupus anticoagulant, **anticardiolipin antibodies**, and anti-β2-glycoprotein I antibodies.[4] Anticardiolipin antibodies are positive in approximately 84–90% of APS patients, making them the most likely antibody to be found in this patient's blood.[2]

The other answer choices correspond to different autoimmune conditions:

- **Anti-centromere** (B) — associated with limited cutaneous systemic sclerosis (CREST syndrome)
- **Anti-histone** (C) — associated with drug-induced lupus
- **Anti-ribonucleoprotein** (D) — associated with mixed connective tissue disease

Would you like to explore the recommended workup and management approach for a newly suspected case of antiphospholipid syndrome?

Relevant images

(CONTENT OMITTED)

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Question 292

A 28-year-old female visits her physician for workup of a new onset diastolic murmur found on physical examination. Past medical history is insignificant. Her temperature is 37.0 degrees C, blood pressure is 115/75 mm Hg, pulse is 76/min, and respiratory rate is 16/min. The patient denies dyspnea, fatigue, and syncope. Transthoracic echocardiography reveals a large, pedunculated tumor in the left atrium. This patient is most at risk for:

Answer Choices:

(A) Abrupt hypotension
(B) Sudden cardiac death
(C) Acute arterial occlusion
(D) Septic embolism

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/f016e88d-3871-4bd9-a4a8-e2700488cd25

OpenEvidence Explanation

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The correct answer is **C. Acute arterial occlusion**.

A large, pedunculated left atrial mass in a young woman with a diastolic murmur is the classic presentation of a **cardiac myxoma**, the most common primary cardiac tumor. The greatest risk to this patient is **systemic embolization** leading to acute arterial occlusion. Embolism occurs in **30–50% of patients** with cardiac myxomas, with fragments of the gelatinous tumor or overlying thrombus breaking off and traveling into the systemic arterial circulation.[1][2] The cerebral arteries are most commonly affected, but occlusion of peripheral, visceral, renal, and coronary arteries can also occur.[1][3]

The diastolic murmur in this case is caused by the tumor obstructing the mitral valve orifice during diastole, mimicking mitral stenosis — a characteristic finding sometimes accompanied by a "tumor plop".[1][4][5]

Why the other options are less correct:

- **A. Abrupt hypotension** — While very large myxomas can obstruct the mitral valve and cause hemodynamic compromise (particularly with positional changes), this is less common than embolization and is not the primary risk.
- **B. Sudden cardiac death** — This is rare with atrial myxomas. Sudden death is more associated with primary cardiac arrhythmias or ventricular tumors (e.g., rhabdomyomas).
- **D. Septic embolism** — Septic emboli arise from infective endocarditis, not from cardiac myxomas. Myxoma emboli are composed of tumor fragments or bland thrombus, not infected material.

The following figure illustrates the echocardiographic and pathological features of cardiac myxoma, including a large myxoma prolapsing through the mitral valve during diastole (panels A–B) and the two morphological variants — smooth-surfaced (panel E, associated with obstruction) and villous/friable (panel F, associated with embolization).[4]

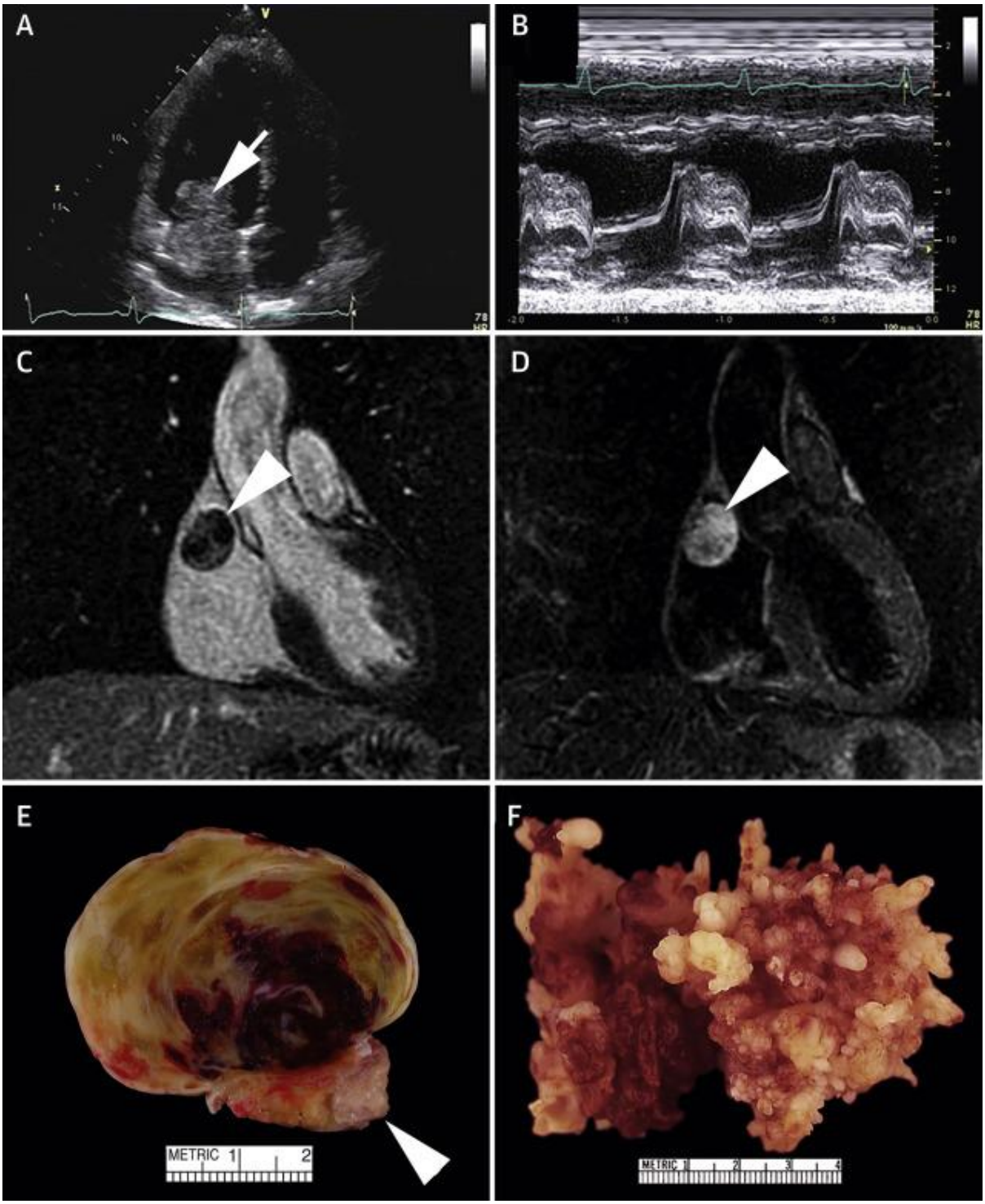


Figure 3. Cardiac Myxoma

Would you like to explore the surgical management and recurrence risk of cardiac myxomas, including the role of wide excision and surveillance echocardiography?

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Question 295

A 32-year-old female complains to her gynecologist that she has had irregular periods for several years. She has severe facial acne and dense black hairs on her upper lip, beneath her hairline anterior to her ears, and the back of her neck. Ultrasound reveals bilateral enlarged ovaries with multiple cysts. Which of the following is the patient most likely increased risk of developing?

> **Answer Choices:**
>
> (A) Endometrial carcinoma
> (B) Addison disease
> (C) Wegener granulomatosus
> (D) Eclampsia

> **Correct Answer:**
>
> **(A)**
>
> **OpenEvidence Response:**
>
> **(A)** ✓

OpenEvidence Link: https://openevidence.com/ask/5d1630fd-3504-4cfa-8f5d-51e2e02f72ba

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OpenEvidence Explanation

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The correct answer is **A. Endometrial carcinoma**.

This patient presents with classic features of **polycystic ovary syndrome (PCOS)**: irregular menstrual periods (oligo/anovulation), severe acne and hirsutism

(hyperandrogenism), and bilateral enlarged polycystic ovaries on ultrasound — fulfilling the Rotterdam diagnostic criteria. Among the listed options, PCOS is most strongly associated with an increased risk of **endometrial carcinoma**.

Pathophysiology of the association: Chronic anovulation in PCOS results in prolonged exposure of the endometrium to unopposed estrogen without the counterbalancing effects of cyclical progesterone. This promotes endometrial hyperplasia, which can progress to endometrial carcinoma.[1][2] Additional contributing factors include hyperandrogenism (androgen receptors are expressed in endometrial tissue), insulin resistance, hyperinsulinemia, and obesity — all common in PCOS.[3][4]

Magnitude of risk: Multiple meta-analyses consistently demonstrate a **~3- to 5-fold increased risk** of endometrial cancer in women with PCOS compared to controls.[5][6][7] A large Danish nationwide cohort study found an overall HR of 3.02 (95% CI 2.03–4.49), with the risk being particularly elevated in premenopausal women (HR 5.82, 95% CI 3.64–9.30).[5] The lifetime risk of endometrial cancer in women with PCOS has been estimated as high as **9%**.[1]

Why the other options are incorrect:

- **B. Addison disease** — an autoimmune adrenal insufficiency condition with no established association with PCOS.
- **C. Wegener granulomatosis (granulomatosis with polyangiitis)** — a systemic vasculitis unrelated to PCOS.
- **D. Eclampsia** — while PCOS is associated with increased pregnancy complications including preeclampsia, eclampsia is not the most characteristic long-term cancer risk associated with PCOS, and endometrial carcinoma is the best-established malignancy risk.[1]

Would you like to explore the recommended strategies for endometrial surveillance and prevention of endometrial hyperplasia in women with PCOS?

Relevant images

(CONTENT OMITTED)

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Question 296

A 52-year-old fisherman presents to the clinic for an evaluation of a pigmented lesion on his neck. He states that he first noticed the lesion last year, but he believes that it has been slowly growing in size. Dermatopathology determines that the lesion contains neoplastic cells of melanocytic origin. Which of the following characteristics of the lesion would likely be found on physical examination?

> **Answer Choices:**
>
> (A) Brown-black color in one area of the lesion to red-white in a different area
> (B) Macule that is 5mm in diameter
> (C) Well-circumscribed papule with smooth borders
> (D) Itching and pain to palpation

> **Correct Answer:**
>
> **(A)**
>
> **OpenEvidence Response:**
>
> **(A)** ✓

OpenEvidence Link: https://openevidence.com/ask/3cfcd135-6466-4bbd-8939-7a35407eeef4

OpenEvidence Explanation

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The correct answer is **A. Brown-black color in one area of the lesion to red-white in a different area**, which reflects the **color variegation** characteristic of melanoma — the "C" in the ABCDE criteria.

This patient has a confirmed neoplasm of melanocytic origin (melanoma) on the neck of a 52-year-old fisherman with chronic sun exposure — a classic presentation for cutaneous melanoma. The ABCDE mnemonic describes the hallmark physical examination features of melanoma:[1][2][3]

- **A**symmetry — one half does not match the other
- **B**order irregularity — ragged, notched, or blurred edges
- **C**olor variegation — nonuniform pigmentation with different shades of tan, brown, black, and sometimes **red, white, or blue** within the same lesion
- **D**iameter — typically **>6 mm**
- **E**volving — changing in size, shape, or color

Answer A describes color variegation, a key melanoma feature where different areas of the lesion display different colors (brown-black in one area, red-white in another).[2]

Why the other options are incorrect:

- **B (5 mm macule):** Melanomas are typically >6 mm in diameter. A 5 mm lesion falls below this threshold. Additionally, melanomas are often raised or have variable topography rather than being a simple flat macule.[2][4]
- **C (Well-circumscribed papule with smooth borders):** This describes a benign nevus. Melanomas characteristically have **irregular, ragged borders** — the opposite of smooth, well-circumscribed margins.[4]
- **D (Itching and pain):** While itching can occasionally occur in melanoma (listed as a minor criterion in the Glasgow 7-point checklist), most patients with melanoma have **no skin discomfort whatsoever**. Itching and pain are not reliable or characteristic findings on physical examination of melanoma.[5]

Would you like to explore the recommended biopsy techniques and workup for a suspicious pigmented lesion concerning for melanoma?

Relevant images

(CONTENT OMITTED)

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Question 298

An 18-month-old girl is brought to the pediatrician by her mother for vaginal bleeding. The mother states that she noticed the bleeding today, which appeared as brown discharge with clots in the patient's diaper. The mother denies frequent nosebleeds or easy bruising. She also denies any known trauma. She does mention that the patient has been limping and complaining of left leg pain since a fall 2 months ago. On physical exam, there are multiple 2-3 cm hyperpigmented patches on the patient's trunk. There is bilateral enlargement of the breasts but no pubic hair. The vaginal orifice is normal and clear with an intact hymen. A plain radiograph of the left lower leg shows patchy areas of lytic bone and sclerosis within the femoral metaphysis. Which of the following is associated with the patient's most likely diagnosis?

Answer Choices:

(A) Bitemporal hemianopsia
(B) Hypertension
(C) Pheochromocytoma
(D) Polyostotic fibrous dysplasia

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/aa4978b5-8be1-4cd1-8fc3-71c38677ae79

OpenEvidence Explanation

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The correct answer is **D. Polyostotic fibrous dysplasia**.

This presentation is classic for **McCune-Albright syndrome (MAS)**, which is characterized by the triad of:

1. **Café-au-lait macules** — the hyperpigmented patches on the trunk
2. **Gonadotropin-independent (peripheral) precocious puberty** — vaginal bleeding at 18 months with breast development but no pubic hair, consistent with estrogen-mediated effects from autonomous ovarian cysts
3. **Polyostotic fibrous dysplasia** — the patchy lytic and sclerotic bone lesions in the femoral metaphysis, explaining the limping and leg pain[1][2][3]

MAS results from postzygotic somatic activating mutations in the **GNAS gene**, which encodes the Gsα subunit, leading to constitutive cAMP pathway activation in a mosaic distribution of affected tissues.[4][5]

Why the other options are incorrect:

- **A. Bitemporal hemianopsia** — This would suggest a pituitary or chiasmal lesion causing central precocious puberty. MAS causes peripheral (gonadotropin-independent) precocious puberty from autonomous ovarian estrogen production, not from a central lesion.[6]
- **B. Hypertension** — Not a characteristic feature of MAS. This might be seen with congenital adrenal hyperplasia or pheochromocytoma-associated syndromes.
- **C. Pheochromocytoma** — Associated with MEN 2, neurofibromatosis type 1, or von Hippel-Lindau syndrome, but not with MAS. While neurofibromatosis type 1 also features café-au-lait spots, those spots have smooth ("coast of California") borders, whereas MAS café-au-lait spots have irregular ("coast of Maine") borders.[2]

Would you like to explore the diagnostic workup and management approach for McCune-Albright syndrome, including the role of imaging and endocrine evaluation?

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Question 299

A 72-year-old woman is admitted to the hospital for treatment of unstable angina. Cardiac catheterization shows occlusion that has caused a 50% reduction in the diameter of the left circumflex artery. Resistance to blood flow in this vessel has increased by what factor relative to a vessel with no occlusion?

Answer Choices:

(A) 64
(B) 16
(C) 8
(D) 4

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/f1949a5c-01c0-4a5f-bc4f-e02f746a267a

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OpenEvidence Explanation

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The answer is **B. 16**.

This question applies **Poiseuille's Law**, which states that resistance to flow through a vessel is inversely proportional to the **fourth power of the radius**:

$$R \propto \frac{1}{r^4}$$

Key reasoning:

- A 50% reduction in **diameter** means a 50% reduction in **radius** (the radius is halved).
- If the new radius is (r/2), the new resistance is proportional to (\frac{1}{(r/2)^4} = \frac{1}{r^4/16} = \frac{16}{r^4}).
- Therefore, resistance increases by a factor of **16** relative to the original vessel.

This principle underscores why even modest degrees of arterial stenosis can produce significant hemodynamic consequences — a 50% reduction in vessel diameter leads to a 16-fold increase in resistance, substantially reducing blood flow and contributing to myocardial ischemia as seen in this patient's unstable angina.

Would you like to explore how percent diameter stenosis correlates with fractional flow reserve (FFR) and clinical decision-making for revascularization?

Question 304

A 35-year-old man presents to the emergency room due to shortness of breath that started an hour ago while playing football with some friends. He has had similar episodes in the past when he also had to be rushed to the hospital. Physical examination shows body temperature is 37.2°C (98.9°F), pulse rate is 100/min, respiratory rate is 28/min and blood pressure is 110/60 mm Hg. Also, it shows decreased breath sounds on both sides, the peak expiratory flow rate is 200 L/min and SpO2 is 89% on room air. The man is given an initial treatment with nebulization using an inhaled short-acting β-agonist. An arterial blood gas analysis shows the following:
pH 7.48
PaO2 59 mm Hg
PaCO2 26 mm Hg
HCO3- 26 mEq/L
After administering oxygen by mask, the man's PaO2 increases to 75 mm Hg. Which of the following is the most likely cause of this patient's condition?

Answer Choices:

(A) Asthma attack
(B) Carbon monoxide (CO) poisoning
(C) Neuromuscular disease
(D) Acute respiratory distress syndrome (ARDS)

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/c170a331-9da1-41a6-ae36-d832e7511141

OpenEvidence Explanation

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The most likely cause of this patient's condition is **A. Asthma attack**.

This presentation is classic for an **acute asthma exacerbation**: a young man with recurrent episodes of exercise-triggered dyspnea requiring emergency visits, bilateral decreased breath sounds (from air trapping), reduced peak expiratory flow (200 L/min), hypoxemia (SpO2 89%), and response to inhaled short-acting β-agonist. The ABG findings further support this diagnosis.

ABG interpretation:

- **pH 7.48** (respiratory alkalosis) with **PaCO2 26 mmHg** (hyperventilation) — this is the expected early compensatory response in an acute asthma exacerbation, where increased respiratory drive leads to hypocapnia.[1][2]
- **PaO2 59 mmHg** — hypoxemia from V/Q mismatch due to bronchoconstriction.
- **PaO2 improves to 75 mmHg with supplemental oxygen** — this response to oxygen is characteristic of V/Q mismatch (as seen in asthma), where supplemental oxygen can overcome the ventilation-perfusion inequality.[3]

Why the other options are incorrect:

- **B. Carbon monoxide poisoning** — CO poisoning causes tissue hypoxia but typically presents with a normal or near-normal PaO2 on ABG (since PaO2 measures dissolved oxygen, not hemoglobin-bound oxygen). It would not cause decreased breath sounds bilaterally, reduced PEF, or respond to β-agonist nebulization.[3]
- **C. Neuromuscular disease** — Neuromuscular respiratory failure characteristically causes **hypoventilation with hypercapnia** (elevated PaCO2), not the respiratory alkalosis seen here. The PaCO2 would be elevated, not 26 mmHg.[2][4]
- **D. ARDS** — ARDS involves intrapulmonary shunting, which causes **refractory hypoxemia** that responds poorly to supplemental oxygen. In this

patient, PaO2 improved from 59 to 75 mmHg with oxygen, arguing against significant shunt physiology. Additionally, ARDS requires bilateral radiographic opacities and an identifiable risk factor (e.g., sepsis, aspiration, trauma), none of which are present here.[3][5][6]

The key distinguishing features are the recurrent exercise-triggered episodes, response to SABA, respiratory alkalosis with hypocapnia, and improvement in PaO2 with supplemental oxygen — all hallmarks of acute asthma.[1][7]

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Question 305

A 48-year-old homeless male is brought to the emergency department, by the police, for altered mental status. Past medical records are unavailable. A physical exam on admission reveals scleral icterus and a flapping tremor of the wrists during extension. The patient is admitted to the hospital and his treatment is started after appropriate investigation. The next morning on rounds, he complains of eleven episodes of diarrhea and near-constant flatulence overnight. His mental status has improved and his hand tremor has resolved. Which of the following medications did this patient most likely receive after admission?

Answer Choices:

(A) Thiamine
(B) Lactulose
(C) Naloxone
(D) Rifaximin

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/fb2d6753-e959-4366-bc4c-b1cdd6476835

OpenEvidence Explanation

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The answer is **B. Lactulose**.

This patient presents with classic findings of **hepatic encephalopathy**: altered mental status, scleral icterus (indicating liver disease), and **asterixis** (the "flapping tremor" of the wrists during extension), which is the hallmark motor finding of this condition. The clinical context of a homeless male with signs of chronic liver disease makes alcohol-related cirrhosis the most likely underlying etiology.

Lactulose is the first-line treatment for hepatic encephalopathy. It works as an osmotic laxative that acidifies colonic contents, converting ammonia (NH_3) to ammonium (NH_4^+), which cannot be absorbed across the intestinal wall, thereby reducing serum ammonia levels. The expected side effects — **profuse diarrhea and flatulence** — are consistent with this patient's overnight complaints and actually indicate therapeutic effect. His improved mental status and resolution of asterixis confirm a clinical response to treatment.

Why not the other options:

- **A. Thiamine** — Important in homeless/alcoholic patients to prevent Wernicke encephalopathy, but it does not cause diarrhea or flatulence and would not explain the asterixis or scleral icterus.
- **C. Naloxone** — Used for opioid overdose reversal; does not cause diarrhea/flatulence as a prominent feature and does not fit the clinical picture of liver disease with asterixis.
- **D. Rifaximin** — A non-absorbable antibiotic used as adjunctive therapy for hepatic encephalopathy (primarily for secondary prophylaxis of recurrent episodes), but it does **not** typically cause profuse diarrhea and flatulence. Lactulose is the more likely initial treatment given the described side-effect profile.

Would you like to explore the evidence comparing lactulose monotherapy versus lactulose plus rifaximin for acute hepatic encephalopathy management?

Question 308

A 50-year-old man with congestive heart failure (CHF) was started on an experimental analog of atrial natriuretic peptide. Which of the following would he expect to experience?

Answer Choices:

(A) Increased water reabsorption by the renal collecting ducts
(B) Vasoconstriction, increased blood pressure, aldosterone release
(C) Increased glomerular filtration rate, restricted aldosterone release, vascular smooth muscle dilation
(D) Increased plasma calcium and decreased renal reabsorption of phosphate

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/66d6b275-0b4d-467e-8dad-4f308f626037

OpenEvidence Explanation

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The correct answer is **C. Increased glomerular filtration rate, restricted aldosterone release, vascular smooth muscle dilation**.

Atrial natriuretic peptide (ANP) is a hormone released by atrial myocytes in response to atrial stretch, and its physiologic effects directly oppose the renin-

angiotensin-aldosterone system. An experimental ANP analog would be expected to produce the following three key effects described in option C:

1. **Increased GFR** — ANP dilates afferent renal arterioles and constricts efferent arterioles, increasing glomerular capillary pressure and thereby raising the glomerular filtration rate.[1][2]

2. **Inhibition of aldosterone release** — ANP suppresses both renin secretion and aldosterone synthesis/secretion, counteracting RAAS activation.[1][2][3]

3. **Vascular smooth muscle relaxation (vasodilation)** — ANP stimulates cGMP production via guanylyl cyclase receptors, leading to systemic vasodilation and reduced peripheral resistance.[3][4]

Why the other options are incorrect:

- **A (Increased water reabsorption)** — ANP does the opposite: it antagonizes vasopressin action in the collecting duct, thereby inhibiting water reabsorption and promoting diuresis.[1]

- **B (Vasoconstriction, increased BP, aldosterone release)** — This describes the effects of the RAAS/sympathetic system, which ANP functionally opposes.[2][3]

- **D (Increased plasma calcium, decreased phosphate reabsorption)** — This describes the action of parathyroid hormone, which is unrelated to natriuretic peptide physiology.

The following figure illustrates the integrated physiologic effects of natriuretic peptides on the cardiovascular, renal, and endocrine systems:

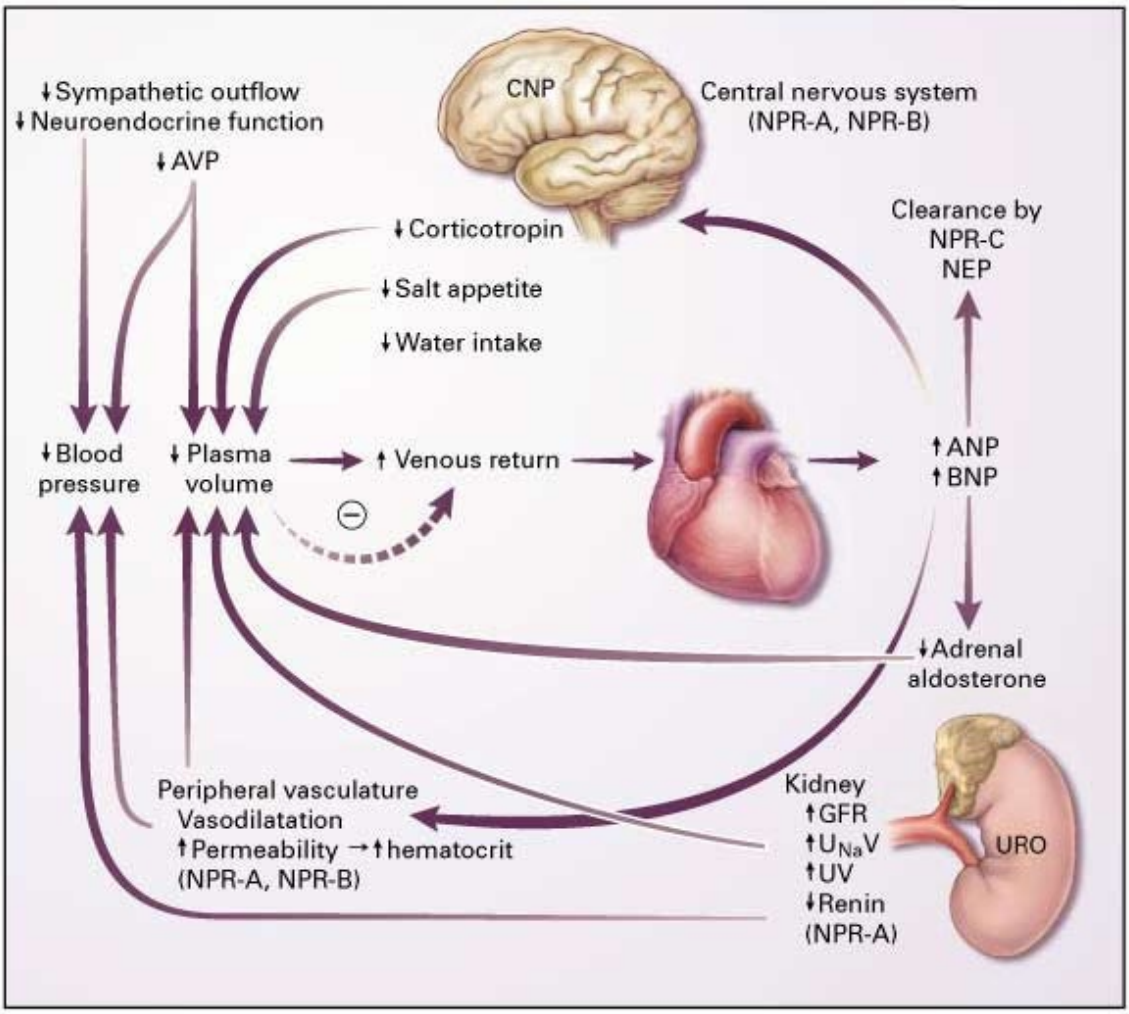


Figure 3. Physiologic Effects of Natriuretic Peptides Released from the Heart When Venous Return Is Increased.

Used under license from The New England Journal of Medicine.

Would you like to explore how natriuretic peptide resistance develops in advanced heart failure and its clinical implications for ANP-based therapies?

References

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Question 309

A 56-year-old man is brought to the emergency room after a motor vehicle accident. The patient's vitals are as follows: blood pressure 80/40 mm Hg, heart rate 111/min, respiratory rate 39/min, and temperature 37.1°C (98.8°F). On physical examination, the patient is unconscious with a GCS of 9/15 and is cyanotic. There are open fractures of the left femur and left tibia, a likely shoulder dislocation, multiple contusions on the limbs and thorax, and a puncture wound on the left side of his chest. There are no breath sounds on the left side and there is hyperresonance to percussion on the left. Preparations are made for an emergency needle thoracostomy to be performed to treat this patient's likely tension pneumothorax. Which one of the following is the best choice to provide informed consent for this procedure?

Answer Choices:

(A) The patient's closest relatives (spouse, child or parent), who must be brought to the hospital as fast as possible
(B) One of the witnesses at the scene of the car accident, who should be brought to the hospital as fast as possible
(C) The hospital ethics committee
(D) Informed consent is not needed in this case

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/9a5f7482-6004-43a4-948d-760d5323fee2

OpenEvidence Explanation

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The correct answer is **D. Informed consent is not needed in this case**.

This scenario represents a classic application of the **emergency exception rule** (also called the "doctrine of implied consent" or "presumed consent"). Three conditions are met here that invoke this exception:

1. **Life-threatening emergency** — The patient has a tension pneumothorax with hemodynamic instability (BP 80/40, HR 111, cyanosis), requiring immediate needle thoracostomy to prevent death.

2. **The patient lacks decisional capacity** — GCS of 9/15 renders the patient unconscious and unable to provide consent.

3. **No surrogate decision-maker is immediately available** — There is no mention of family, advance directive, or authorized surrogate at bedside.

Under these circumstances, consent is **presumed** based on the ethical and legal rationale that a reasonable person would consent to life-saving treatment if able to be asked.[1][2][3] The ACOG Committee on Ethics states that in life-threatening emergencies where the patient cannot consent and no surrogate is available, it is ethically acceptable to provide life-saving treatment using presumed consent.[1] The AAN similarly affirms that consent may be presumed when there is risk of death or unacceptable morbidity.[3]

Waiting for relatives (option A), witnesses (option B), or an ethics committee (option C) would introduce dangerous and potentially fatal delays. The ACEP guidelines on treatment of minors — which apply analogously to incapacitated adults — explicitly state that hospital personnel should **not delay treatment** while waiting for consent.[4] While efforts to contact a surrogate should continue in parallel, they must not delay emergent intervention.[1]

Would you like to explore how the documentation of emergency presumed consent should be handled in the medical record?

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1. Informed Consent and Shared Decision Making in Obstetrics and Gynecology: ACOG Committee Opinion, Number 819. Committee on Ethics. Obstetrics and Gynecology. 2021;137(2):e34-e41. doi:10.1097/AOG.0000000000004247.

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4. Evaluation and Treatment of Minors. Paul Ishimine MD, Ashley Foster MD, Ann Dietrich MD, et al. American College of Emergency Physicians (2021)

Question 315

A 27-year-old woman was referred to a dermatology clinic due to a changing discoloration of her fingers from white to red to blue. Although she has not had any recent changes in her daily routines, she also complains of increasing fatigue, muscle weakness, and weight loss. She has a blood pressure of 126/77 mm Hg, respiratory rate of 14/min, and heart rate of 88/min. Physical examination reveals regular heart and lung sounds. Anti-U1 RNP antibodies and increased creatinine kinase were found in her serum. What is the most likely diagnosis in this patient?

Answer Choices:

(A) Mixed connective tissue disease
(B) Polymyositis
(C) Systemic sclerosis
(D) Rheumatoid arthritis

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/57455e89-4f29-4277-a1ae-b2850ec6cfa3

OpenEvidence Explanation

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The most likely diagnosis is **A. Mixed connective tissue disease (MCTD)**.

This patient presents with a classic triad that defines MCTD:

1. **Raynaud's phenomenon** — the triphasic color change of the fingers (white → red → blue) is present in virtually all MCTD patients (up to 100% in case series).[1]

2. **Inflammatory myopathy** — muscle weakness with elevated creatine kinase indicates myositis, a hallmark feature of MCTD.[1]

3. **Anti-U1 RNP antibodies** — these are a **sine qua non** for the diagnosis of MCTD; high titers are found in nearly all MCTD patients and are required by all classification criteria sets.[2][3]

The constitutional symptoms (fatigue, weight loss) are also consistent with an active systemic connective tissue disease.

Why not the other options?

- **Polymyositis (B):** While the elevated CK and muscle weakness could suggest polymyositis, isolated polymyositis does not explain Raynaud's phenomenon, and anti-U1 RNP is not a myositis-specific antibody — it is a myositis-associated antibody that points toward an overlap/connective tissue disease rather than primary inflammatory myopathy.[4][5]

- **Systemic sclerosis (C):** Raynaud's phenomenon is common in systemic sclerosis, but the characteristic antibodies are anti-centromere or anti-topoisomerase I (anti-Scl-70), not anti-U1 RNP. Additionally, systemic sclerosis typically presents with skin thickening (sclerodactyly, diffuse skin fibrosis), which is not described here.[6]

- **Rheumatoid arthritis (D):** There is no mention of joint symptoms (synovitis, morning stiffness), and anti-U1 RNP is not characteristic of RA. Elevated CK and Raynaud's phenomenon are not typical RA features.

MCTD is defined by the combination of features overlapping SLE, systemic sclerosis, and inflammatory myopathy in the presence of high-titer anti-U1 RNP antibodies.[3][7] This patient's presentation — Raynaud's phenomenon, myositis (elevated CK + weakness), constitutional symptoms, and positive anti-U1 RNP — fits this diagnosis most precisely.

References

1. Clinicopathological Features of Mixed Connective Tissue Disease-Related Myositis: A Case Series. Sakamoto N, Izumi R, Suzuki N, Tateyama M, Aoki M.. Muscle & Nerve. 2025;71(4):583-592. doi:10.1002/mus.28360.

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Question 319

A 22-year-old man presents to a psychiatrist complaining of mood fluctuations. He is accompanied by his mother who reports that the patient recently experienced a 5-day episode of minimal sleep and unusual levels of energy. The patient admits to spending $2,000 of his parent's money, without asking, on a down payment for a motorcycle. The episode resolved after 5 days, at which point the patient felt guilty and upset. The patient's medical history is notable for multiple month-long episodes in the past 2 years of feeling sad, sleeping more than usual, being uninterested in his hobbies, and feeling constantly tired and guilty. The patient has a history of severe meningoencephalitis at the age of 17 requiring four days in the intensive care unit. During that episode, he reported seeing monkeys in his hospital room. On exam, he is a well-appearing, cooperative male in no acute distress. He is alert and oriented with a normal affect. He states that he feels sad and guilty about what happens. He denies suicidal ideation. Which of the following is the most likely diagnosis in this patient?

Answer Choices:

(A) Bipolar II disorder
(B) Cyclothymic disorder
(C) Persistent depressive disorder
(D) Schizoaffective disorder

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/1527c973-1d90-4e0b-86f4-58034baf4855

OpenEvidence Explanation

(CONTENT OMITTED)

The most likely diagnosis is **A. Bipolar II disorder**.

This patient meets DSM-5-TR criteria for bipolar II disorder based on two key features:

Hypomanic episode: The 5-day episode of decreased sleep, increased energy, and impulsive spending ($2,000 on a motorcycle without permission) meets criteria for hypomania — a distinct period of elevated mood and increased energy lasting **at least 4 consecutive days**, with symptoms including decreased need for sleep, increased goal-directed activity, and excessive involvement in activities with painful consequences.[1][2] Critically, the episode lasted only 5 days (not ≥1 week) and did not require hospitalization, which distinguishes it from a manic episode and thus rules out bipolar I disorder.[1]

Major depressive episodes: The patient has experienced multiple month-long episodes over 2 years characterized by sadness, hypersomnia, anhedonia, fatigue, and guilt — meeting criteria for recurrent major depressive episodes.[2]

Why the other options are incorrect:

- **B. Cyclothymic disorder** — Requires that criteria for a full hypomanic episode and a major depressive episode have **never** been met; this patient meets criteria for both. The presence of a major depressive episode alone precludes cyclothymic disorder.[2]
- **C. Persistent depressive disorder** — Does not account for the hypomanic episode. Persistent depressive disorder involves chronic depressive symptoms without episodes of hypomania or mania.[2]
- **D. Schizoaffective disorder** — Requires psychotic symptoms (delusions or hallucinations) occurring for at least 2 weeks in the absence of a mood episode. This patient's only hallucinations (seeing monkeys) occurred during meningoencephalitis at age 17, which is attributable to a medical condition (ICU delirium/encephalitis), not a primary psychotic disorder.[2]

Would you like to explore the first-line pharmacotherapy options for bipolar II disorder, particularly for managing the depressive episodes that dominate the clinical course?

References

1. Diagnosis and Treatment of Bipolar Disorder: A Review. Nierenberg AA, Agustini B, Köhler-Forsberg O, et al.. JAMA. 2023;330(14):1370-1380. doi:10.1001/jama.2023.18588.

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Question 322

A 62-year-old man is brought to his primary care physician by his wife who is concerned about the patient's frequent falls. Approximately 6 months ago, she started noticing that he was walking more slowly than usual. He has fallen more than 6 times in the past month, and she is worried that he will sustain a serious injury if he does not stop falling. The patient is a retired banking executive and was active as a triathlete until the age of 60. He does not smoke and drinks 2-3 alcoholic beverages per day. His family history is notable for normal pressure hydrocephalus in his mother and Alzheimer dementia in his father. His temperature is 97.8°F (36.6°C), blood pressure is 131/81 mmHg, pulse is 68/min, and respirations are 19/min. On exam, his movements appear slowed and forced. He shuffles his feet when he walks. Tone is increased in his upper and lower extremities bilaterally. This patient's condition is most strongly associated with which of the following histologic findings on brain autopsy?

Answer Choices:

(A) Accumulations of beta-pleated sheets
(B) Atrophy of the caudate nucleus
(C) Intracellular inclusions of alpha-synuclein
(D) Intracellular inclusions of hyperphosphorylated tau

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/b03c4dac-cd2f-4264-80b4-dc7ccbc17690

OpenEvidence Explanation

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Wait — let me reconsider this carefully. The clinical presentation describes bradykinesia, shuffling gait, increased tone (rigidity), and frequent falls in a 62-year-old man. These are cardinal features of parkinsonism. Let me search to confirm the histologic findings.

(CONTENT OMITTED)

The correct answer is **C. Intracellular inclusions of alpha-synuclein**.

This patient presents with classic features of **Parkinson disease**: bradykinesia (slowed, forced movements), shuffling gait, frequent falls, and bilateral rigidity (increased tone in upper and lower extremities). The onset at age 62 is consistent with the peak age of onset between 60–70 years.[1]

The pathologic hallmark of Parkinson disease is the **Lewy body**, an intraneuronal inclusion composed primarily of aggregated **α-synuclein** protein.[2][3][4] As described in a JAMA review:

> "Parkinson disease is characterized by death of dopaminergic neurons in the substantia nigra. The pathologic hallmark of Parkinson disease is the Lewy body, a neuronal inclusion consisting largely of α-synuclein protein aggregations."
>
> —Melissa J. Armstrong, MD, MSc1,2 et al., Department of Neurology, University of Florida College of Medicine, Gainesville and other institutions. Diagnosis and Treatment of Parkinson Disease: A Review. JAMA. February 11, 2020.
>
> Used under license from JAMA Network.

The following figure demonstrates the immunohistochemical composition of Lewy bodies, showing α-synuclein (red) and ubiquitin (green) within these intraneuronal inclusions.

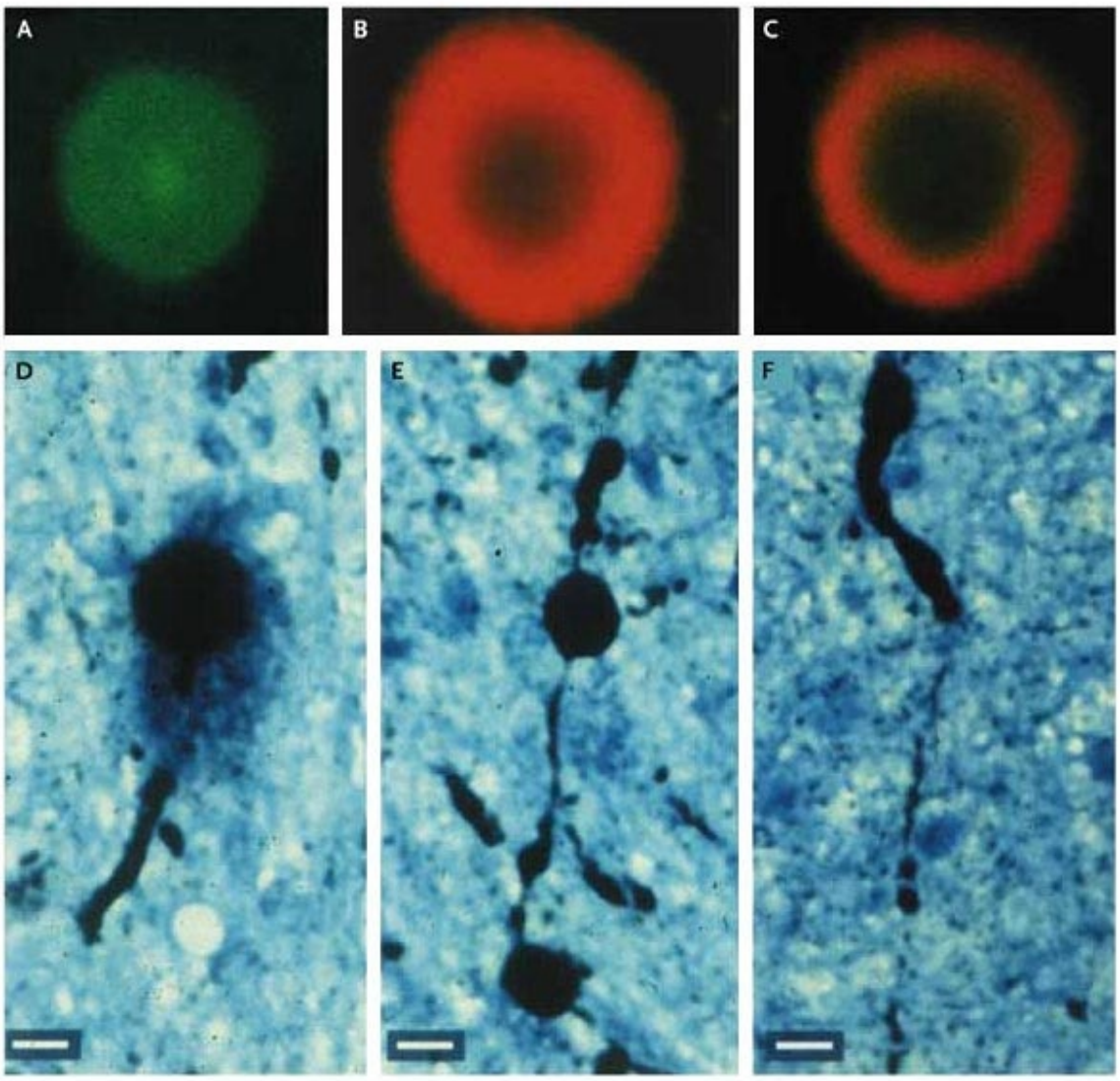


Figure 4. Immunohistochemical Analysis of Sections from the Substantia Nigra of a Patient with Sporadic Parkinson's Disease, Indicating the Involvement of α-Synuclein in the Formation of Lewy Bodies and Lewy Neurites.

Used under license from The New England Journal of Medicine.

Why the other options are incorrect:

- **A. Accumulations of beta-pleated sheets** — characteristic of Alzheimer disease (amyloid-beta plaques) and prion diseases, not Parkinson disease.
- **B. Atrophy of the caudate nucleus** — the hallmark of Huntington disease, which presents with chorea, psychiatric symptoms, and cognitive decline.
- **D. Intracellular inclusions of hyperphosphorylated tau** — characteristic of progressive supranuclear palsy (PSP), corticobasal degeneration, and Alzheimer disease (neurofibrillary tangles). While PSP can present with

parkinsonism and falls, it is distinguished by early postural instability, vertical supranuclear gaze palsy, and axial rigidity greater than limb rigidity. The classic presentation described here — with shuffling gait, bilateral limb rigidity, and bradykinesia — is most consistent with idiopathic Parkinson disease and its associated α-synuclein pathology.[6][7]

Note that the expert opinion tool initially suggested answer D, but the clinical presentation and histopathologic evidence strongly support **answer C** as the correct choice.

Would you like to explore how progressive supranuclear palsy is clinically distinguished from idiopathic Parkinson disease, particularly given the overlap in early presentations?

References

1. ACR Appropriateness Criteria® Movement Disorders and Neurodegenerative Diseases. Expert Panel on Neurological Imaging, Harvey HB, Watson LC, et al.. Journal of the American College of Radiology : JACR. 2020;17(5S):S175-S187. doi:10.1016/j.jacr.2020.01.042.

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Question 324

A 55-year-old man is brought to the emergency department with altered mental status. The patient is in acute distress and cannot provide history due to disorientation. Temperature is 38.7°C (101.6°F), blood pressure is 80/50 mm Hg, pulse is 103/min, respiratory rate is 22/min, and BMI is 20 kg/m2. On examination, his sclera and skin are icteric. On abdominal examination, the patient moans with deep palpation to his right upper quadrant.
Laboratory test
Complete blood count
Hemoglobin 14.5 g/dL
MCV 88 fl
Leukocytes 16,500/mm3
Platelets 170,000/mm3
Basic metabolic panel
Serum Na+ 147 mEq/L
Serum K+ 3.8 mEq/L
Serum Cl- 106 mEq/L
Serum HCO3- 25 mEq/L
BUN 30 mg/dL
Serum creatinine 1.2 mg/dL
Liver function test
Total bilirubin 2.8 mg/dL
AST 50 U/L
ALT 65 U/L
ALP 180 U/L
The patient is treated urgently with intravenous fluid, dopamine, and broad spectrum antibiotics. The patient's blood pressure improves to 101/70 mm Hg. On ultrasound of the abdomen, the common bile duct is dilated. What is the best next step in the management of this patient?

> **Answer Choices:**
>
> (A) ERCP
> (B) MRCP
> (C) Percutaneous transhepatic cholangiogram

(D) CT abdomen

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/7d046323-742e-4e82-8570-ba7c0a011af4

OpenEvidence Explanation

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The best next step is **A. ERCP (endoscopic retrograde cholangiopancreatography)**.

This patient presents with **Reynolds' pentad** — fever, jaundice, right upper quadrant pain (Charcot's triad), plus hypotension and altered mental status — consistent with **severe (Grade III) acute cholangitis** with organ dysfunction. The ultrasound confirms a dilated common bile duct, indicating biliary obstruction. After initial hemodynamic stabilization with IV fluids, vasopressors, and antibiotics (which has been accomplished here), the next step is urgent biliary decompression.

ERCP is the treatment of choice for biliary decompression in moderate-to-severe acute cholangitis, as recommended by the ASGE, Tokyo Guidelines 2018, and WSES guidelines.[1][2][3] ERCP is both diagnostic and therapeutic — it allows visualization of the obstruction and simultaneous drainage via sphincterotomy, stone extraction, or stent placement. The ASGE favors ERCP over percutaneous transhepatic biliary drainage (PTBD) given reduced length of stay and fewer adverse events.[3] A meta-analysis of over 7,500 patients demonstrated that ERCP within 48 hours significantly reduces in-hospital mortality (OR 0.52) and

length of stay.[4] For patients with neurological dysfunction (altered mental status, as in this case), biliary drainage within 12 hours has been shown to dramatically reduce mortality.[5]

Why not the other options:

- **MRCP** (B) is a diagnostic-only modality and would delay therapeutic intervention in a patient who already has a confirmed dilated CBD and a clinical picture clearly indicating obstructive cholangitis.
- **Percutaneous transhepatic cholangiogram** (C) is a second-line option reserved for cases where ERCP fails or is not feasible (e.g., surgically altered anatomy).[3]
- **CT abdomen** (D) would add diagnostic information but would not provide the therapeutic drainage this patient urgently needs.

Would you like to explore the specific Tokyo Guidelines severity grading criteria and how they guide the timing and approach to biliary drainage?

Relevant images

(CONTENT OMITTED)

References

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Question 325

A 31-year-old woman comes to the physician because of a 5-month history of intermittent flank pain. Over the past 2 years, she has had five urinary tract infections. Her blood pressure is 150/88 mm Hg. Physical examination shows bilateral, nontender upper abdominal masses. Serum studies show a urea nitrogen concentration of 29 mg/dL and a creatinine concentration of 1.4 mg/dL. Renal ultrasonography shows bilaterally enlarged kidneys with multiple parenchymal anechoic masses. Which of the following is the most likely diagnosis?

Answer Choices:

(A) Medullary sponge kidney
(B) Autosomal dominant polycystic kidney disease
(C) Autosomal recessive polycystic kidney disease
(D) Obstructive cystic dysplasia

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/663c27cb-824d-4ee3-b6a1-aacbbe72c561

OpenEvidence Explanation

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The answer is **B. Autosomal dominant polycystic kidney disease (ADPKD)**.

This presentation is classic for ADPKD. The key features that point to this diagnosis include:

- **Age of presentation**: ADPKD is typically diagnosed in individuals aged **27 to 42 years**, consistent with this 31-year-old patient. By contrast, autosomal recessive polycystic kidney disease (ARPKD) primarily presents perinatally or in early childhood.[1][2][3]
- **Bilateral enlarged kidneys with multiple parenchymal anechoic masses**: ADPKD is characterized by bilateral, symmetrical cyst distribution and enlarged cystic kidneys, typically detectable by ultrasound in the third to fourth decade of life. The anechoic masses on ultrasound represent fluid-filled cysts.[4]
- **Hypertension (150/88 mmHg)**: Hypertension affects **70–80%** of patients with ADPKD and may occur in young adults, often preceding decline in kidney function.[1][4]
- **Recurrent urinary tract infections**: UTIs are a recognized complication of ADPKD, as cysts can become infected and structural distortion of the kidneys predisposes to infection.[4]
- **Elevated BUN and creatinine**: The mildly elevated serum creatinine (1.4 mg/dL) and BUN (29 mg/dL) reflect early kidney function decline, consistent with progressive cystic disease.

Why not the other options?

- **Medullary sponge kidney** (A): Characterized by cystic dilation of collecting ducts in the renal medulla, not bilateral kidney enlargement with large parenchymal cysts. It does not cause palpable abdominal masses.
- **Autosomal recessive polycystic kidney disease** (C): Presents in infancy or early childhood with bilateral kidney enlargement and is associated with congenital hepatic fibrosis. Presentation at age 31 would be exceedingly rare.[2][3]
- **Obstructive cystic dysplasia** (D): Results from urinary tract obstruction during fetal development, typically diagnosed in utero or in neonates, and is usually unilateral.

Would you like to explore the current evidence on tolvaptan therapy and risk stratification using the Mayo Imaging Classification for patients with ADPKD at high risk of progression?

Relevant images

(CONTENT OMITTED)

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Question 328

A 27-year-old woman, gravida 2, para 1, at 40 weeks' gestation is admitted to the hospital in active labor. The patient reports severe pelvic pain. Pregnancy has been complicated by gestational diabetes. Pregnancy and delivery of her first child were uncomplicated. Current medications include insulin, folic acid, and a multivitamin. Vital signs are within normal limits. The cervix is 100% effaced and 10 cm dilated; the vertex is at -1 station. The fetal heart rate is reactive with no decelerations. Epidural anesthesia is performed and the patient's symptoms improve. Ten minutes later, the patient has dizziness. Her pulse is 68/min, respirations are 16/min, and blood pressure is 90/60 mm Hg. Intravenous fluid resuscitation is begun. Which of the following is the most likely underlying cause of the patient's hypotension?

Answer Choices:

(A) Sympathetic block
(B) Hypovolemia
(C) Acute pulmonary hypertension
(D) Aortocaval compression

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/469176ea-cde2-491a-96cd-db900b27f296

OpenEvidence Explanation

(CONTENT OMITTED)

The correct answer is **A. Sympathetic block**.

The hypotension occurring **10 minutes after epidural anesthesia** in this laboring patient is most consistent with **sympathetic blockade**, a well-recognized minor adverse effect of neuraxial analgesia. The ACOG Practice Bulletin on Obstetric Analgesia and Anesthesia identifies maternal hypotension from sympathetic blockade as a common complication of neuraxial blocks, with approximately **10% of women** developing hypotension with low-dose neuraxial labor analgesia.[1] The mechanism involves blockade of sympathetic nerve fibers, leading to vasodilation, venous pooling, decreased systemic vascular resistance, and reduced venous return.[2][3]

Why the other options are less likely:

- **B. Hypovolemia** — There is no indication of hemorrhage or fluid loss. Vital signs were normal prior to the epidural, and the temporal relationship directly implicates the epidural as the cause.
- **C. Acute pulmonary hypertension** — This would be exceedingly rare in a healthy 27-year-old and would not be expected to develop acutely following epidural placement. It would also typically present with tachycardia and respiratory distress.
- **D. Aortocaval compression** — While aortocaval compression by the gravid uterus can contribute to hypotension in late pregnancy (and can exacerbate neuraxial-induced hypotension), it is a positional phenomenon that would have been present before the epidural. The key clinical clue is the **temporal relationship** — the hypotension developed specifically after epidural placement, pointing to the sympathetic block as the primary underlying cause. Aortocaval compression is a contributing factor but not the new precipitant.[4][5]

The ASA recommends prophylactic vasopressor infusion (phenylephrine or norepinephrine) and IV crystalloid co-loading to address the primary mechanism of neuraxial hypotension — reduction in systemic vascular resistance from sympathetic blockade.[4]

Would you like to explore the management algorithm for neuraxial-induced hypotension during labor, including vasopressor selection and dosing?

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Question 334

A 51-year-old woman was recently diagnosed with type II diabetes. Due to the cumulative effects of diabetes, various health screenings and vaccinations are routinely recommended. Which of the following vaccinations or screening measures are recommended in patients with diabetes?

> **Answer Choices:**
>
> (A) Urinalysis every 6 months
> (B) Comprehensive foot exam every year
> (C) Weekly foot inspections by patient or family member
> (D) Meningococcal vaccine

> **Correct Answer:**
>
> **(B)**
>
> **OpenEvidence Response:**
>
> **(B)** ✓

OpenEvidence Link: https://openevidence.com/ask/43128054-6bcf-4183-a7b2-944550627af2

OpenEvidence Explanation

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The correct answer is **B. Comprehensive foot exam every year**.

The ADA Standards of Care recommends performing a **comprehensive foot evaluation at least annually** in all patients with diabetes to identify risk factors for ulcers and amputations.[1] This examination should include inspection of the

skin, assessment of foot deformities, neurological assessment (10-g monofilament testing or Ipswich touch test with at least one additional assessment), and vascular assessment including pulses in the legs and feet.[1][2]

Why the other options are incorrect:

- **A. Urinalysis every 6 months** — While screening for diabetic kidney disease is recommended, the standard is an annual urine albumin-to-creatinine ratio (UACR), not a urinalysis every 6 months.
- **C. Weekly foot inspections by patient or family member** — The ADA recommends **daily** foot surveillance (not weekly) for patients with loss of protective sensation, including self-inspection using palpation or a visual inspection with an unbreakable mirror. The IWGDF guidelines similarly recommend daily foot washing and care.[1][3]
- **D. Meningococcal vaccine** — Meningococcal vaccination is not specifically recommended for patients with diabetes. The vaccines recommended for adults with diabetes include influenza (annually), pneumococcal (PCV15 or PCV20), hepatitis B (for those ≤59 years), Tdap boosters, COVID-19, and recombinant zoster vaccine (for those ≥50 years). Meningococcal vaccine is not part of this list.[4]

Patients at higher risk (e.g., those with sensory loss, prior ulceration, or amputation) should have their feet inspected at every clinical visit, and follow-up frequency should be adjusted based on risk stratification.[1][2][3]

Would you like to explore the complete set of recommended annual screenings for patients with newly diagnosed type 2 diabetes, including retinopathy, nephropathy, and cardiovascular risk assessments?

Relevant images

(CONTENT OMITTED)

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Question 335

A 23-year-old man presents with sudden loss of consciousness while pitching in a baseball game. There is no history of injury. Consciousness is regained after cardiopulmonary resuscitation. Past medical history is negative for any neurological and cardiovascular problems. Physical examination reveals a prominent A wave on the jugular venous pulse and a double apical impulse. There are no audible murmurs. An S4 is present. What is the most likely diagnosis?

> **Answer Choices:**
>
> (A) Hypertrophic cardiomyopathy
> (B) Aortic stenosis
> (C) Takotsubo cardiomyopathy
> (D) Restrictive cardiomyopathy

> **Correct Answer:**
>
> **(A)**
>
> **OpenEvidence Response:**
>
> **(A)** ✓

OpenEvidence Link: https://openevidence.com/ask/de89b7ff-e71c-4140-b417-e22af461bfec

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OpenEvidence Explanation

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The correct answer is **A. Hypertrophic cardiomyopathy (HCM)**.

This presentation is classic for HCM: a young athlete experiencing **sudden loss of consciousness during exertion**, with physical examination findings of a **prominent jugular A wave** (from reduced ventricular compliance), a **double apical impulse** (bifid or trifid point of maximal impulse from forceful atrial contraction against a stiff ventricle), and an **S4 gallop** (reflecting diastolic dysfunction) — all in the absence of a prior cardiac history.

Why HCM fits best:

- HCM is the **most common cause of sudden cardiac death in young competitive athletes** in the United States, accounting for approximately one-third of cardiovascular deaths in autopsy-based studies. The scenario of syncope or cardiac arrest during vigorous exertion (pitching) in a previously healthy young man is the hallmark presentation.[1][2]
- The 2024 AHA/ACC HCM guidelines describe the classic physical findings: a prominent apical point of maximal impulse (often bifid or trifid), an S4 from a noncompliant left ventricle, and a prominent jugular A wave from reduced ventricular compliance. Notably, patients **without left ventricular outflow tract obstruction (LVOTO) may have no audible murmur**, which is consistent with this case.[3][4][5]

Why the other options are less likely:

- **Aortic stenosis (B):** Would typically produce a harsh crescendo-decrescendo systolic murmur radiating to the carotids, and a double apical impulse is not characteristic. It accounts for ≤5% of sudden deaths in young athletes.[1]
- **Takotsubo cardiomyopathy (C):** Occurs predominantly in postmenopausal women triggered by emotional or physical stress, not in young male athletes. It does not produce a double apical impulse or prominent A wave.
- **Restrictive cardiomyopathy (D):** While it can cause prominent jugular venous distension and elevated filling pressures, the hallmark findings are bilateral atrial enlargement and Kussmaul sign rather than a double apical impulse. It is an exceedingly rare cause of sudden death in young athletes.[6]

Would you like to explore the current recommendations for sudden cardiac death risk stratification and ICD implantation in young patients diagnosed with HCM?

Relevant images

(CONTENT OMITTED)

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Question 339

A 45-year-old woman presents to the clinic with her husband to discuss her most recent problem. She and her husband recently bought a new house in the area. While cleaning the house, they discovered a nest of spiders. She reports blacking out and waking up outside the house with a bandage on her arm. Her husband says that she began screaming and ran out of the house, breaking a window, and cutting her arm. The patient says she has tried to enter the house several times over the last several months but can not bring herself to cross the threshold for fear of more spiders. She wants to overcome her extreme and irrational fear. Which of the following is the most effective treatment to overcome this patient's arachnophobia?

Answer Choices:

(A) Desensitization
(B) Metoprolol
(C) Alprazolam
(D) Psychotherapy

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/807c3d45-582b-4feb-acd9-fe9624fb47b3

OpenEvidence Explanation

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The answer is **A. Desensitization**.

Systematic desensitization (also called exposure-based therapy) is the most effective treatment for specific phobias such as arachnophobia. This technique involves gradual, controlled exposure to the feared stimulus — in this case, spiders — allowing the patient to progressively overcome avoidance behavior and extinguish the fear response.

Exposure therapy is the **current treatment of choice** for specific phobias.[1] A meta-analysis of 33 randomized trials demonstrated that exposure-based treatments produced large effect sizes relative to no treatment and outperformed both placebo conditions and alternative psychotherapeutic approaches.[2] In vivo exposure (direct contact with the phobic stimulus) was particularly effective, outperforming imaginal exposure and virtual reality at post-treatment.[2]

Why the other options are incorrect:

- **B. Metoprolol** — Beta-blockers may be used for performance anxiety (e.g., stage fright) to manage physiological symptoms like tachycardia and tremor, but they do not address the underlying phobic fear or avoidance behavior.

- **C. Alprazolam** — Benzodiazepines can provide short-term anxiolysis but do not produce lasting resolution of phobias. Pharmacotherapy data for specific phobias have generally not been promising. Additionally, benzodiazepines may interfere with the extinction learning that is central to successful exposure therapy.[3][4]

- **D. Psychotherapy** — While this is a broad and technically correct category (desensitization is a form of psychotherapy), the question distinguishes "psychotherapy" as a separate answer choice. In this context, "desensitization" refers specifically to the exposure-based behavioral technique that has the strongest evidence for specific phobias, whereas generic "psychotherapy" (e.g., psychodynamic or interpersonal therapy) has a weaker evidence base for this condition.[5]

The key distinction in this question is that desensitization/exposure therapy is the specific, most effective intervention, whereas "psychotherapy" as listed is a broader, less targeted option.

Would you like to explore the specific protocols for conducting systematic desensitization, including the differences between single-session and multi-session exposure approaches for specific phobias?

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Question 341

A 28-year-old primigravid woman at 39 weeks gestation is admitted to the hospital in active labor. On examination, the cervix is 100% effaced and 10 cm dilated. After 5 minutes of pushing, there is a prolonged deceleration of the fetal heart rate to 90/min. A decision to perform an episiotomy is made to expedite vaginal delivery. The anesthesiologist locates the ischial spines by palpating the posterolateral vaginal sidewall and administers an anesthetic. Three minutes later, pinching the posterior vulva does not provoke pain. The anesthetized nerve most likely also supplies which of the following structures?

Answer Choices:

(A) Skin of the lateral thigh
(B) External anal sphincter
(C) Skin of the mons pubis
(D) Detrusor muscle

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/136c2078-2e3f-496b-abca-72d8a1720efb

OpenEvidence Explanation

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The correct answer is **B. External anal sphincter**.

The nerve anesthetized in this scenario is the **pudendal nerve** (S2–S4), which is blocked by injecting local anesthetic near the ischial spines via the posterolateral vaginal sidewall — the classic pudendal nerve block used to facilitate episiotomy and perineal repair.[1][2]

The pudendal nerve has three terminal branches:[3][4][5]

1. **Inferior rectal (anal) nerve** — innervates the **external anal sphincter**, perianal skin, and mucous membrane of the lower anal canal
2. **Perineal nerve** — innervates the posterior labial skin, superficial perineal muscles (bulbospongiosus, ischiocavernosus, superficial transverse perineal), and the external urethral sphincter
3. **Dorsal nerve of the clitoris/penis** — provides cutaneous supply to the clitoris/penis

The loss of pain sensation on pinching the posterior vulva confirms successful blockade of the perineal branch. Because the block is performed at the main trunk near the ischial spine, all three branches are anesthetized, including the inferior rectal nerve supplying the **external anal sphincter**.[5][6]

Why the other options are incorrect:

- **A. Skin of the lateral thigh** — supplied by the lateral femoral cutaneous nerve (L2–L3), not the pudendal nerve.
- **C. Skin of the mons pubis** — supplied by the ilioinguinal nerve (L1) and genitofemoral nerve (L1–L2).
- **D. Detrusor muscle** — innervated by parasympathetic fibers from the pelvic splanchnic nerves (S2–S4) via the pelvic nerve, not the pudendal nerve. The pudendal nerve supplies the voluntary external urethral sphincter, but the detrusor is a smooth muscle under autonomic control.[7]

Would you like to explore the clinical complications and failure rates of pudendal nerve blocks in obstetric practice?

Relevant images

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Question 342

A 55-year-old woman with a history of HIV presents to the emergency department with progressive dyspnea, fever, and dry cough for the past 4 days. She has not been compliant with antiretroviral or prophylactic medication. On evaluation, the patient is in moderate respiratory distress. The temperature is 38.8°C (102.0°F), the blood pressure is 124/82 mm Hg, the pulse is 96/min, and the respiratory rate is 20/min. Pulse oximetry is 92% on 4 L oxygen by nasal cannula. Her CD4 count is 180 cells/μL. IV antibiotics and glucocorticoids are administered. After 30 minutes, the patient develops severe respiratory distress. Repeat vital signs show: temperature 38.3°C (101.0°F), blood pressure 80/50 mm Hg, pulse 104/min, respiration rate 32/min and pulse oximetry 85% on nasal cannula. The trachea deviates to the left. Breath sounds are absent on the right side and the neck veins are distended. Telemetry shows sinus tachycardia. Which of the following is the best next step in the management of this patient?

Answer Choices:

(A) Discontinue antibiotics
(B) Perform an arterial blood gas
(C) Needle thoracostomy
(D) Stat chest X-ray

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/2159f454-a536-4f98-a589-edc6ce1852d1

OpenEvidence Explanation

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The best next step is **C. Needle thoracostomy**.

This patient presents with the classic clinical triad of **tension pneumothorax**: tracheal deviation (to the contralateral side), absent breath sounds on the affected side, and jugular venous distension, accompanied by hemodynamic instability (hypotension, tachycardia) and worsening hypoxia. In the context of HIV with a low CD4 count and noncompliance with prophylaxis, the likely underlying etiology is Pneumocystis jirovecii pneumonia (PJP), which is a well-known cause of secondary spontaneous pneumothorax.

Tension pneumothorax is a clinical diagnosis that requires immediate decompression — imaging should not delay treatment. Per ATLS principles and the WSES-AAST Thoracic Trauma Guidelines, when tension pneumothorax is suspected based on clinical findings, emergent needle decompression at the 2nd intercostal space in the midclavicular line (or the 5th intercostal space in the midaxillary line) should be performed immediately, followed by definitive tube thoracostomy.[1] A JAMA Surgery review similarly states that tension pneumothorax "is a medical emergency and should initially be managed with immediate needle thoracentesis to decompress trapped and expanding pleural air before the placement of a formal chest tube".[2]

Why the other options are incorrect:

- **A. Discontinue antibiotics** — While anaphylaxis can cause hypotension and respiratory distress, it does not explain tracheal deviation, unilateral absent breath sounds, or JVD. This presentation is not consistent with an allergic reaction.
- **B. Perform an arterial blood gas** — An ABG would not change immediate management and would delay life-saving intervention.
- **D. Stat chest X-ray** — Obtaining imaging before decompression in a hemodynamically unstable patient with clinical signs of tension pneumothorax is inappropriate and potentially fatal. Tension pneumothorax is diagnosed clinically, not radiographically.[3][4]

Would you like to explore the association between Pneumocystis jirovecii pneumonia and spontaneous pneumothorax, including risk factors and management considerations?

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Question 343

A 22-year-old woman with polycystic ovarian syndrome comes to the emergency department because of a 1-day history of left lower abdominal pain that began suddenly while she was running. Her last menstrual period was 2 weeks ago. Physical examination shows tenderness to palpation over the left adnexa and rebound tenderness in the left lower quadrant. There is no tenderness in the right lower quadrant. Urine pregnancy test is negative. An ultrasound is ordered to confirm the diagnosis of ruptured ovarian cyst. Visualization of fluid in which of the following locations would be most consistent with this diagnosis?

Answer Choices:

(A) Rectouterine pouch
(B) Hepatorenal space
(C) Splenorenal angle
(D) Rectovesical pouch

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/34289a84-ca02-4e78-bb13-be499fa8e4da

OpenEvidence Explanation

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The answer is **A. Rectouterine pouch** (pouch of Douglas).

In females, the **rectouterine pouch** (also called the pouch of Douglas or cul-de-sac) is the most dependent portion of the peritoneal cavity when a patient is upright or supine. Free fluid from a ruptured ovarian cyst gravitates to this space first, making it the earliest and most sensitive location to detect free pelvic fluid on ultrasound.[1][2] Transvaginal ultrasonography routinely evaluates the cul-de-sac for accumulated fluid, and its presence in this location is a classic finding associated with ruptured ovarian cysts and hemoperitoneum.[3][4][5]

Key distinctions among the answer choices:

- **Rectouterine pouch (A)** — the most dependent peritoneal space in females, located between the uterus and rectum. This is where fluid from a ruptured ovarian cyst would first collect.
- **Hepatorenal space (B)** (Morison's pouch) — the most dependent space in the upper abdomen; fluid accumulates here with large-volume hemoperitoneum but would not be the first or most consistent finding with a pelvic source.
- **Splenorenal angle (C)** — a left upper quadrant space; not the expected location for fluid from a pelvic source.
- **Rectovesical pouch (D)** — this space exists only in **males** (between the rectum and bladder). In females, the uterus intervenes between the bladder and rectum, creating the vesicouterine and rectouterine pouches instead.

The negative pregnancy test and clinical presentation (sudden onset left lower quadrant pain during exercise in a young woman with PCOS) are classic for a ruptured ovarian cyst, and cul-de-sac fluid on ultrasound supports this diagnosis.[3][6]

Would you like to explore the ultrasound criteria that help differentiate ruptured hemorrhagic ovarian cysts from other causes of acute pelvic pain and free fluid?

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Question 347

A 66-year-old woman presents to her primary care provider with several days of left flank pain radiating to the abdomen and groin. The patient states that she has noticed a pink tinge to her urine as well. Of note, she has not had any fevers, but endorses several months of fatigue and constipation. The patient was previously healthy except for mild untreated hypertension. On exam, her temperature is 98.6°F (37.0°C), blood pressure is 130/84 mmHg, pulse is 76/min, and respirations are 12/min. On further workup, the patient is found to have calcium oxalate nephrolithiasis with hypercalciuria. Blood studies demonstrate increased parathyroid hormone (PTH) and hypercalcemia. Which of the following is the most likely cause?

Answer Choices:

(A) Primary hyperparathyroidism
(B) Pseudopseudohypoparathyroidism
(C) Secondary hyperparathyroidism
(D) Tertiary hyperparathyroidism

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/2291a1b1-9496-4e4c-8221-b77cf0cf6d3f

OpenEvidence Explanation

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The answer is **A. Primary hyperparathyroidism**.

This patient presents with the classic features of **primary hyperparathyroidism (PHPT)**: **hypercalcemia with an elevated (non-suppressed) PTH**, calcium oxalate nephrolithiasis with hypercalciuria, and systemic symptoms of hypercalcemia including fatigue, constipation, and hypertension. The combination of elevated PTH driving hypercalcemia — rather than responding to it — is the hallmark of primary hyperparathyroidism.[1][2]

Why the other options are incorrect:

- **Secondary hyperparathyroidism (C)** is a physiologic response to **hypocalcemia** (not hypercalcemia), most commonly from chronic kidney disease or vitamin D deficiency. PTH is elevated, but serum calcium is low or low-normal.[2][3]
- **Tertiary hyperparathyroidism (D)** occurs after **long-standing secondary hyperparathyroidism** (typically in end-stage renal disease or post-renal transplant), when parathyroid glands become autonomous and cause hypercalcemia. This patient has no history of chronic kidney disease.[2][4]
- **Pseudopseudohypoparathyroidism (B)** is a rare genetic condition (Albright hereditary osteodystrophy phenotype without biochemical abnormalities) — patients have **normal calcium and normal PTH levels**, making it inconsistent with this presentation.[5]

PHPT is the most common cause of hypercalcemia in otherwise healthy outpatients, most frequently caused by a single parathyroid adenoma (~80% of cases), with peak prevalence in postmenopausal women.[1][6] The classic mnemonic "stones, bones, groans, and psychic moans" captures the symptomatic presentation: nephrolithiasis, skeletal disease, gastrointestinal complaints (constipation), and neurocognitive symptoms (fatigue).[1]

Would you like to explore the current surgical indications for parathyroidectomy in primary hyperparathyroidism based on the most recent consensus guidelines?

Relevant images

(CONTENT OMITTED)

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Question 349

A 16-year-old patient presents to the physician's office with an absence of menstruations. Her last period was 6 months ago. Since almost a year and a half ago, she intentionally restricted her diet at the expense of carbohydrates, exercised intensively, and lost 18.0 kg (39.7 lb). She had her menarche at the age of 12 and menstruated normally until last year. She is not sexually active. On physical examination, the vital signs include blood pressure 100/60 mm Hg, heart rate 55/min, respiratory rate 12/min, and temperature 35.9°C (96.6°F). Her weight is 55.0 kg (121.3 lb), and her height is 166 cm (5 ft 5 in). Physical examination reveals the good development of muscles and decreased adiposity. A bone scan shows decreased calcium mineral deposits. Which statement about this patient's condition is correct?

Answer Choices:

(A) This patient has insulin resistance
(B) Decreased adiposity contributes to hypoestrogenemia in this patient
(C) The patient is likely to have decreased blood estrogen concentration due to increased liver metabolism
(D) The patient should be checked for hyperthyroidism because such extensive lipolysis is likely to result from thyroid hyperfunction

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/bbbc4408-4363-40f7-a2bc-18969b818e75

OpenEvidence Explanation

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The correct answer is **B. Decreased adiposity contributes to hypoestrogenemia in this patient**.

This patient presents with classic **functional hypothalamic amenorrhea (FHA)** in the setting of intentional caloric restriction, excessive exercise, significant weight loss (18 kg), bradycardia, hypothermia, decreased adiposity, and decreased bone mineral density — all consistent with an eating disorder (likely anorexia nervosa, restricting subtype).

The following figure illustrates the neuroendocrine pathways underlying FHA, showing how decreased adiposity leads to reduced leptin, which in turn suppresses GnRH pulsatility and results in hypoestrogenemia.

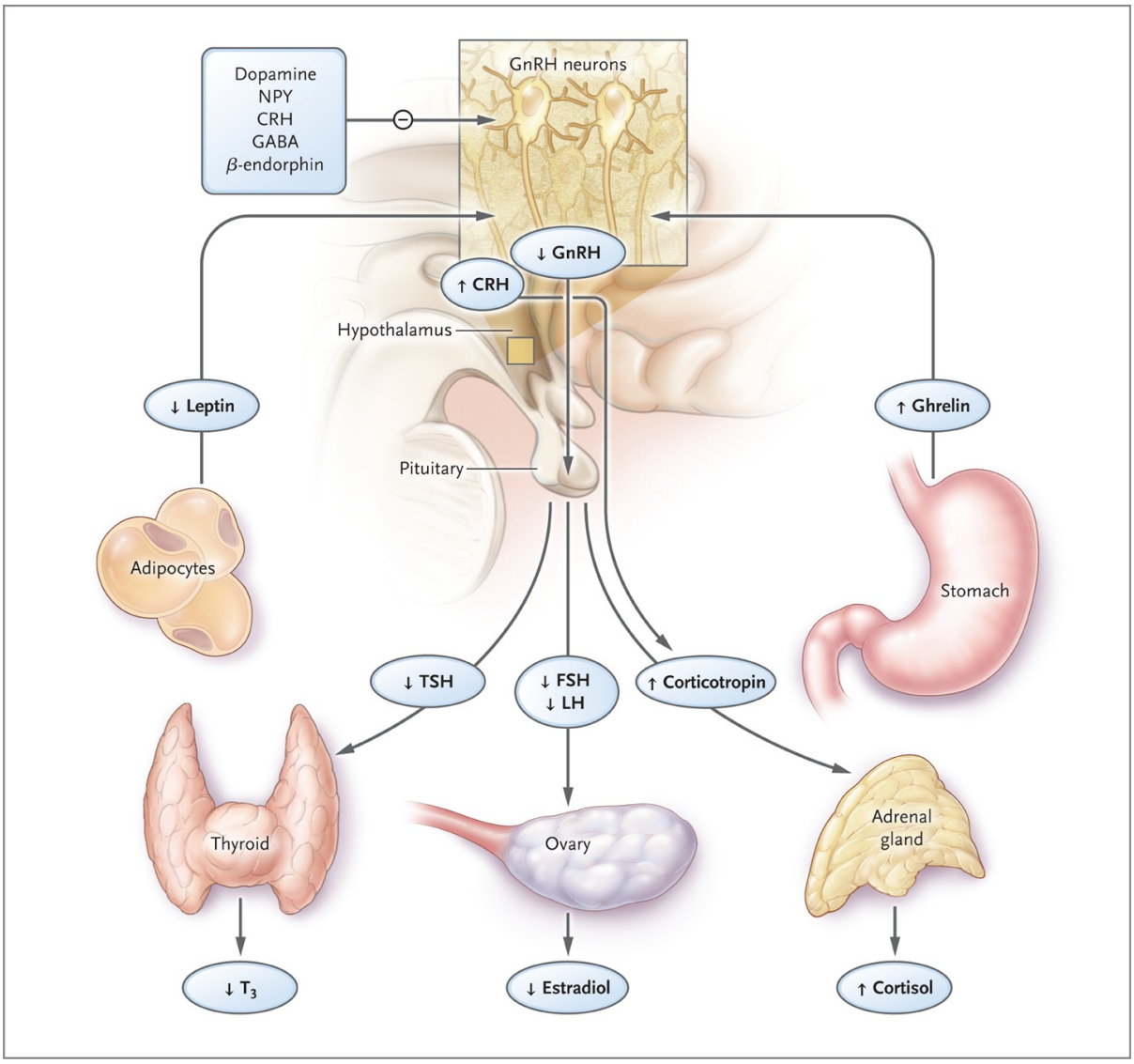


Figure 1. Hormonal and Other Changes in Patients with Hypothalamic Amenorrhea.

Used under license from The New England Journal of Medicine.

Why B is correct: Decreased fat mass directly contributes to hypoestrogenemia through multiple mechanisms. Adipose tissue produces **leptin**, a key permissive signal for normal GnRH pulsatility and gonadotropin secretion. When fat stores are depleted, leptin levels fall, leading to suppression of GnRH pulsatility and reduced LH secretion — resulting in hypogonadotropic hypogonadism and low estradiol levels.[2][3] Additionally, adipose tissue itself is a site of peripheral estrogen production via aromatase activity. Studies have shown that an increase in fat mass is the most important factor in resumption of menstrual cycles, with all girls achieving body fat >24% resuming menses compared to none with body fat <18%.[2]

Why the other options are incorrect:

- **A (Insulin resistance):** This patient has low energy availability and is underweight relative to her prior weight. FHA is associated with **low insulin levels** (not insulin resistance), as the body adapts to a state of energy deficit.[3][4]
- **C (Increased liver metabolism of estrogen):** The hypoestrogenemia in FHA results from **decreased ovarian production** due to suppressed GnRH/LH pulsatility — not from increased hepatic clearance of estrogen.[3][4]
- **D (Hyperthyroidism):** This patient's weight loss is clearly attributable to intentional caloric restriction and excessive exercise. FHA is actually associated with **low T3** (nonthyroidal illness syndrome / sick euthyroid), not hyperthyroidism. Her bradycardia and hypothermia are consistent with a hypometabolic state, the opposite of thyroid hyperfunction.[5][6]

Would you like to explore the recommended management approach for bone density loss in adolescents with functional hypothalamic amenorrhea?

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Question 351

A 26-year-old nurse comes to the physician because of a 2-month history of fatigue. She has had a lot of stress at work and has been on sick leave for 2 weeks, but states that she would like to return to work. She has had several episodes of lower abdominal pain. She says, I know I have cancer. She requests a diagnostic laparoscopy. She was diagnosed with peptic ulcer disease 6 months ago. Her only medication is omeprazole. The patient appears pale. Her temperature is 36.5° C (97.7° F), pulse is 120/min, and blood pressure is 90/65 mm Hg. On mental status examination she is tired and has a depressed mood. Physical examination shows pale conjunctivae and dry mucous membranes. There are numerous crusts along the course of her left arm veins. A grade 2/6 systolic ejection murmur is heard along the right-upper sternal border. Abdominal examination shows no abnormalities. There is generalized weakness of the proximal muscles.
Laboratory studies show:
Hemoglobin 7.5 g/dL
Mean corpuscular volume 89 µm3
Reticulocyte count 13.3%
Serum
Sodium 139 mEq/L
Potassium 3.9 mEq/L
Calcium 8.5 mg/dL
Test of the stool for occult blood is negative. Abdominal ultrasonography show no abnormalities. Which of the following is the most likely diagnosis?

Answer Choices:

(A) Factitious disorder
(B) Somatic symptom disorder
(C) Conversion disorder
(D) Acute small bowel hemorrhage

Correct Answer:

(A)

> **OpenEvidence Response:**
>
> **(A)** ✓

OpenEvidence Link: https://openevidence.com/ask/8de6cf00-cc05-4bf7-a70f-656cc9cbf4c3

OpenEvidence Explanation

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The most likely diagnosis is **A. Factitious disorder**.

This case presents a constellation of findings that are classic for **factitious disorder imposed on self** (formerly Munchausen syndrome):

Key clinical clues pointing to factitious disorder:

- **Healthcare worker** (nurse) — approximately 50–67% of patients with factitious disorder work in health-related occupations, giving them the knowledge and access to induce illness[1][2]
- **Numerous crusts along the course of left arm veins** — this is the most critical physical finding, strongly suggesting repeated self-phlebotomy (covert blood withdrawal) as the mechanism of self-induced illness
- **Severe normocytic anemia (Hb 7.5 g/dL, MCV 89) with elevated reticulocyte count (13.3%)** — consistent with blood loss anemia with appropriate marrow response, but the **negative fecal occult blood test and normal abdominal ultrasound** exclude common GI sources
- **Hemodynamic instability** (tachycardia 120/min, hypotension 90/65) with signs of volume depletion (pale conjunctivae, dry mucous membranes) — consistent with significant ongoing blood loss
- **Eagerly requesting invasive procedures** (diagnostic laparoscopy) — a hallmark behavioral feature of factitious disorder[1]

- **Conviction of having cancer** ("I know I have cancer") despite no supporting evidence — reflects the dramatic illness narrative typical of factitious disorder

Why not the other options:

- **Somatic symptom disorder (B)** — involves excessive thoughts, feelings, or behaviors related to somatic symptoms, but there is no evidence of deceptive falsification of symptoms. The crusted veins and objective anemia indicate self-induced pathology, not merely disproportionate concern about symptoms.[3]
- **Conversion disorder (C)** — presents with neurological symptoms (e.g., weakness, paralysis, sensory loss) incompatible with recognized neurological pathophysiology. The proximal muscle weakness here is explained by severe anemia, not a functional neurological symptom.[3]
- **Acute small bowel hemorrhage (D)** — while the anemia and hemodynamic instability could suggest GI bleeding, the negative fecal occult blood, normal abdominal ultrasound, and venous crusting pattern make this far less likely than self-phlebotomy as the source of blood loss.

The systolic ejection murmur (grade 2/6) and proximal muscle weakness are both explained by the severe anemia itself (flow murmur and anemia-related myopathy), rather than representing separate pathology.[4]

Is there additional information about the patient's prior hospitalizations, IV access history, or whether the venous crusting was addressed during the encounter?

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Question 353

A 56-year-old woman comes to the physician because of a 2-week history of fatigue and painless bruising over her arms and trunk. She has also had several episodes of nosebleeds that resolved with compression after a few minutes. She recently completed treatment for a urinary tract infection. She has had no changes in her weight. She has type 2 diabetes mellitus and hypertension. Her last menstrual cycle was 5 years ago. She does not smoke or drink alcohol. Home medications include metformin, amlodipine, and enalapril. Her vital signs are within normal limits. Physical examination shows pale conjunctivae. There are ecchymoses and petechiae over the upper extremities, chest, and back. There is no lymphadenopathy. The remainder of the physical examination is unremarkable. Laboratory studies show:
Hemoglobin 8.7 mg/dL
Leukocyte count 1100/mm3
Platelet count 54,000/mm3
Reticulocyte count 0.1%
Mean corpuscular volume 93 µm3
Serum
Total bilirubin 1.1 mg/dL
LDH 80 U/L
Which of the following is most likely to confirm the diagnosis?

Answer Choices:

(A) Serum transferrin level
(B) Bone marrow biopsy
(C) Peripheral blood smear
(D) Serum porphobilinogen level

Correct Answer:

(B)

OpenEvidence Response:

> **(B)** ✓

OpenEvidence Link: https://openevidence.com/ask/2a02b414-74a2-422f-8ede-bb704ff1532e

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OpenEvidence Explanation

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The answer is **B. Bone marrow biopsy**.

This patient presents with **pancytopenia** (anemia, leukopenia, and thrombocytopenia), a **very low reticulocyte count (0.1%)**, normocytic anemia (MCV 93), and clinical features of fatigue, bruising, petechiae, and epistaxis — a presentation consistent with **aplastic anemia** or another bone marrow failure syndrome such as myelodysplastic syndrome (MDS). The normal LDH and bilirubin argue against a hemolytic process, and the low reticulocyte count indicates inadequate marrow production rather than peripheral destruction.

Bone marrow biopsy is the confirmatory test for aplastic anemia. A hypocellular bone marrow with replacement of hematopoietic elements by fat is required for diagnosis.[1] A 1–2 cm core biopsy is essential for accurate assessment of cellularity, as aspirate spicules can be misleadingly cellular due to residual pockets of hematopoiesis.[1] The biopsy also helps distinguish aplastic anemia from hypoplastic MDS, which can present similarly but carries different prognostic and therapeutic implications.[2][3]

Why the other options are incorrect:

- **A. Serum transferrin level** — useful for evaluating iron deficiency anemia, which typically presents with microcytic anemia and does not cause pancytopenia.
- **C. Peripheral blood smear** — while part of the initial workup and helpful for identifying morphologic clues (e.g., blasts, dysplasia), it cannot confirm aplastic anemia. The blood film in aplastic anemia characteristically "lacks

major pathological features", and the definitive finding of marrow hypocellularity requires biopsy.[4]

- **D. Serum porphobilinogen level** — used to diagnose acute intermittent porphyria, which presents with abdominal pain and neuropsychiatric symptoms, not pancytopenia.

Would you like to explore how aplastic anemia is distinguished from hypoplastic MDS on bone marrow biopsy, including the role of cytogenetics and molecular testing?

Relevant images

(CONTENT OMITTED)

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Question 354

A 35-year-old man returns to the clinic to follow up for his chronic stomach pain. At the last visit a few months ago, he explained that he had been experiencing discomfort in his upper abdomen for awhile. He had never vomited up any blood and had not had any substantial weight loss. He did not take any medications, did not smoke, and had no family history of gastric cancer. At that time, the doctor empirically started him on a proton pump inhibitor (PPI). Today, despite the PPI, the patient says he is still experiencing discomfort. Hearing this, the doctor decides to order a urease breath test. What is the most likely cause of this patient's chronic stomach pain?

Answer Choices:

(A) Gastroesophgeal sphincter dysfunction
(B) Nonsteroidal anti-inflammatory drugs
(C) Heliobacter pylori infection
(D) Excessive gastrin

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/6688eb41-7d06-4abc-a2f2-eabf25602eab

OpenEvidence Explanation

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The answer is **C. Helicobacter pylori infection**.

The key clinical clue is the physician's decision to order a **urea breath test**, which is a noninvasive test specifically used to detect active *H. pylori* infection.[1][2] This test works by having the patient ingest ^{13}C-labeled urea; if *H. pylori* is present in the stomach, its urease enzyme breaks down the urea, producing ^{13}C-labeled CO_2 that is detected in the breath.[2]

The clinical scenario follows the standard **"test-and-treat" approach** recommended by the ACG for uninvestigated dyspepsia in patients under 60 without alarm features.[3] This patient is 35, has no alarm symptoms (no hematemesis, no weight loss), takes no NSAIDs, and has no family history of gastric cancer. After an empiric PPI trial failed to resolve symptoms, the next appropriate step is testing for *H. pylori* — the most common infectious cause of peptic ulcer disease and chronic gastritis.[1][4]

Why the other options are incorrect:

- **A. Gastroesophageal sphincter dysfunction** — GERD typically presents with heartburn and regurgitation, and would be expected to improve with PPI therapy. A urea breath test would not be the next diagnostic step.[5][6]
- **B. NSAIDs** — The stem explicitly states the patient takes no medications, ruling out NSAID-induced gastropathy.[5]
- **D. Excessive gastrin** — Zollinger-Ellison syndrome (gastrinoma) presents with refractory, multiple ulcers and often diarrhea; it is rare and would not be the initial suspicion in a young patient with uncomplicated dyspepsia. A serum gastrin level, not a urea breath test, would be the appropriate test.[4]

Would you like to explore the recommended first-line eradication regimens for *H. pylori* and how to confirm successful treatment?

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Question 355

A 32-year-old G1P1 patient presents to her obstetrician after having a positive pregnancy test at home. She reports that she and her husband had been trying to have a child for the past three months. She has no history of sexually transmitted disease, intravenous drug use, or blood transfusions, and she has never traveled outside of the United States. She was up-to-date on all immunizations before her pregnancy. Ultrasound is consistent with an 8-week gestational sac. The patient requests as few tests as possible, although she does not want to compromise the health of her fetus. Which of the following screening tests should be performed on all pregnant women?

Answer Choices:

(A) HIV, syphilis, and hepatitis B
(B) HIV, syphilis, and N. gonorrhea
(C) HIV, hepatitis B, and hepatitis C
(D) HIV, syphilis, hepatitis B, N. gonorrhea, and C. trachomatis

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/21adf39e-aaf6-402e-843e-57438ad42fcc

OpenEvidence Explanation

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The correct answer is **A. HIV, syphilis, and hepatitis B**.

These three infections represent the screening tests that should be performed on **all** pregnant women regardless of risk factors, as universally recommended by the USPSTF, CDC, and ACOG.[1][2][3] The key distinction in this question is between universal screening (recommended for every pregnant woman) and risk-based screening:

Universal screening in pregnancy includes HIV, syphilis, and hepatitis B. These are recommended at the first prenatal visit for all pregnant women because of the severe consequences of vertical transmission and the availability of effective interventions (antiretroviral therapy for HIV, penicillin for syphilis, and neonatal immunoprophylaxis for hepatitis B).[2][4]

Risk-based vs. universal screening for the other infections:

- **Chlamydia** — The CDC recommends universal screening only for pregnant women **younger than 25 years**; for women ≥25, screening is based on risk factors (new or multiple sex partners, etc.). This 32-year-old patient in a monogamous relationship would not meet criteria.[4]
- **Gonorrhea** — Similarly, the CDC recommends screening for pregnant women <25 years or those with risk factors, not universally for all pregnant women.[4][5]
- **Hepatitis C** — While some recent guidelines (e.g., AAFP 2023) have moved toward universal screening, hepatitis C screening has traditionally been risk-based rather than universal in pregnancy. The CDC's 2020 recommendation for universal hepatitis C screening applies to all adults but was not historically part of the standard prenatal panel for all pregnant women.[2]

Given this patient's age (32), monogamous relationship, and lack of risk factors, option A — **HIV, syphilis, and hepatitis B** — represents the minimum set of screening tests that should be performed on all pregnant women.[1][2][3]

Would you like to explore the evolving recommendations around universal hepatitis C screening in pregnancy and how recent guideline updates may be changing standard prenatal panels?

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Question 356

A 29-year-old man is referred by his marriage counselor to the outpatient psychiatry clinic. The patient's wife is with him and states that her husband is always complaining and critical of others. He was recently fired from his job to which he claims that his boss was jealous of his hard work. He also does not trust his neighbors and thinks they are out to get all the nice things he has. His wife also says that he has begun to doubt her fidelity and believes that even the marriage counselor is on her side. Which of the following psychiatric disorders also belongs to the same cluster of symptoms?

Answer Choices:

(A) Schizotypal personality disorder
(B) Obsessive-compulsive personality disorder
(C) Antisocial personality disorder
(D) Personality disorder not otherwise specified

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/359cd0d6-de27-4f75-8aa2-b6d872a2360e

OpenEvidence Explanation

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The answer is **A. Schizotypal personality disorder**.

The clinical vignette describes **paranoid personality disorder (PPD)**, characterized by pervasive distrust and suspiciousness — this patient suspects his boss of jealousy, believes neighbors are "out to get" his possessions, doubts his wife's fidelity, and perceives the marriage counselor as biased against him. These features align with DSM-5 diagnostic criteria for PPD, including unjustified suspicions of exploitation, doubts about loyalty, and recurrent suspicions regarding spousal fidelity.[1]

PPD belongs to **Cluster A** personality disorders, which also includes **schizoid** and **schizotypal** personality disorders. Individuals with Cluster A disorders often appear odd or eccentric.[1] Among the answer choices, only schizotypal personality disorder is a Cluster A disorder.

The other options fall into different clusters:

- **Antisocial personality disorder** → Cluster B (dramatic, emotional, erratic) [1][2]
- **Obsessive-compulsive personality disorder** → Cluster C (anxious, fearful) [1][2]
- **Personality disorder not otherwise specified** → not assigned to any cluster[1]

Notably, paranoid and schizotypal personality disorders share traits of suspiciousness, interpersonal aloofness, and paranoid ideation, though schizotypal personality disorder additionally features magical thinking, unusual perceptual experiences, and odd thinking and speech.[1]

Would you like to explore the distinguishing clinical features between paranoid personality disorder and delusional disorder (persecutory type), which can be a challenging differential?

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Question 357

A 24-year-old man is brought to the emergency department by the police. He was found unconscious and covered in bruises outside of a local bar. The patient has a past medical history of polysubstance abuse, depression, multiple suicide attempts, neuropathic pain, and schizophrenia. As part of the patient's initial workup, a head CT is performed which is unremarkable, and an arterial blood gas is performed as seen below:

pH: 7.29
PaCO2: 95 mm Hg
PaO2: 70 mm Hg
Bicarbonate: 24 mEq/L

Which of the following is the most likely etiology of this patient's current presentation?

> **Answer Choices:**
>
> (A) Amitriptyline
> (B) Cocaine
> (C) Ethylene glycol
> (D) Heroin

> **Correct Answer:**
>
> **(D)**
>
> **OpenEvidence Response:**
>
> **(D)** ✓

OpenEvidence Link: https://openevidence.com/ask/7434a118-ba1a-448f-8c7d-e6a20796b235

OpenEvidence Explanation

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The answer is **D. Heroin**.

The ABG reveals a **pure acute respiratory acidosis**: pH 7.29, $PaCO_2$ 95 mmHg, with a normal bicarbonate of 24 mEq/L. The markedly elevated $PaCO_2$ with normal bicarbonate (no renal compensation yet) indicates acute hypoventilation, and the normal bicarbonate rules out a metabolic component. In an unconscious patient with polysubstance abuse found outside a bar, this pattern is classic for **opioid-induced respiratory depression**.[1][2]

Why heroin fits:

- The **sine qua non of opioid intoxication is respiratory depression**, manifesting as decreased respiratory rate, hypoventilation, and CO_2 retention. Heroin suppresses the medullary respiratory center, leading to acute hypercapnia with uncompensated respiratory acidosis — exactly the ABG pattern shown.[1][2][3]
- The clinical picture — unconsciousness, polysubstance abuse history, and being found down — is consistent with heroin overdose.[4]

Why the other options are less likely:

- **Amitriptyline (A):** While tricyclic antidepressants can cause sedation, the primary toxicity involves anticholinergic effects, QRS prolongation, and seizures. Severe respiratory depression to this degree is not the hallmark finding.[5]
- **Cocaine (B):** Cocaine is a stimulant that causes tachycardia, hypertension, and agitation — not respiratory depression. It would not produce this ABG pattern.
- **Ethylene glycol (C):** This causes a high **anion gap metabolic acidosis** (not respiratory acidosis), with low bicarbonate and compensatory hyperventilation (low $PaCO_2$). The normal bicarbonate of 24 mEq/L effectively rules this out.[6]

Would you like to explore the approach to naloxone dosing and monitoring in suspected opioid overdose, including considerations for polysubstance ingestion?

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Question 359

A 40-year-old male presents to your office complaining that he is too weak to climb stairs or brush his hair. He denies any headaches or change in vision. A muscle biopsy reveals CD8+ lymphocyte infiltration in the endomysium. Which of the following is the most likely diagnosis?

Answer Choices:

(A) Systemic lupus erythematosus
(B) Polymyalgia rheumatica
(C) Polymyositis
(D) Dermatomyositis

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/e9123e98-4df2-4155-9d69-0fe249742ac8

OpenEvidence Explanation

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The answer is **C. Polymyositis**.

The combination of **proximal muscle weakness** (difficulty climbing stairs and brushing hair) and a muscle biopsy showing **CD8+ lymphocyte infiltration in the endomysium** is the hallmark histopathologic finding of polymyositis. In polymyositis, CD8+ cytotoxic T cells surround and invade healthy-appearing,

nonnecrotic muscle fibers that aberrantly express MHC class I antigen — a finding termed the "CD8/MHC-I complex".[1][2] This endomysial CD8+ T-cell–mediated cytotoxicity is the primary immunopathologic mechanism, with perforin granules directed toward the muscle fiber surface causing myonecrosis.[1]

Why not the other choices:

- **Dermatomyositis (D):** Biopsy shows **perivascular and perimysial** inflammation with predominantly **CD4+ T cells, B cells, and plasmacytoid dendritic cells** — not endomysial CD8+ infiltration. The pathogenesis is complement-mediated (C5b-9) microangiopathy with perifascicular atrophy. Additionally, characteristic skin findings (heliotrope rash, Gottron papules) are absent here.[1][2]
- **Polymyalgia rheumatica (B):** Causes proximal pain and stiffness (not true weakness) in patients typically >50 years old, with no primary muscle inflammation on biopsy.
- **Systemic lupus erythematosus (A):** Can cause myalgias but does not typically produce endomysial CD8+ T-cell infiltration on muscle biopsy.

The following figure illustrates the characteristic endomysial inflammatory infiltrate seen in polymyositis, with CD8+ T cells invading nonnecrotic muscle fibers.

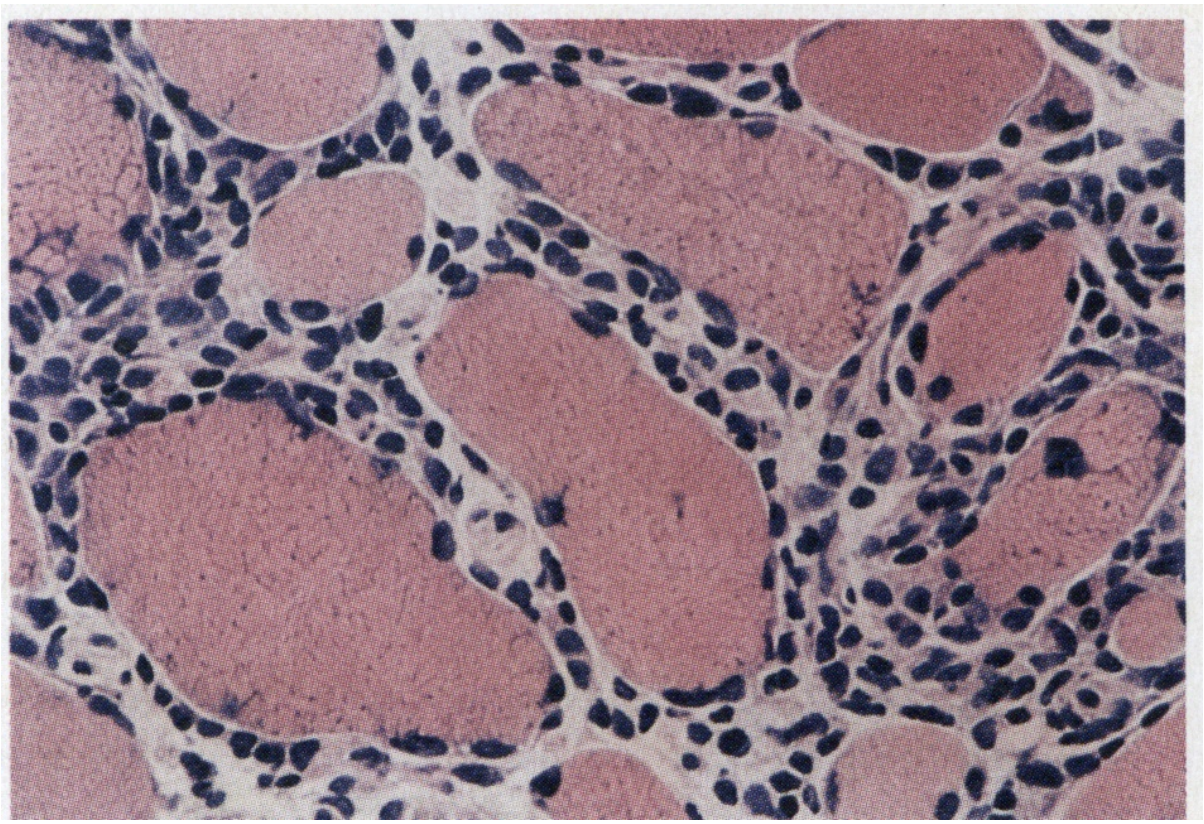


Figure 2. Transverse Section of a Fresh-Frozen Muscle-Biopsy Specimen from a Patient with Polymyositis (Hematoxylin and Eosin, ×430).

Used under license from The New England Journal of Medicine.

Would you like to explore how inclusion body myositis is distinguished from polymyositis, given that both share the CD8/MHC-I complex on biopsy?

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Question 360

A 6-month-old boy presents to his pediatrician for a wellness examination. The mother reports that her child has difficulty rolling from his back to his front and sitting unsupported. The patient is able to smile and furrow his brow normally, but she has noticed that he has a weak cry and suck. He was born at 38 weeks gestation via a spontaneous vaginal delivery without any complications. The mother said that the patient appeared normal until the past few weeks. On physical exam, his extraocular muscle movements are intact, and a symmetric smile is seen. He has symmetric flaccid weakness of both his upper and lower extremities. He also has a bell-shaped chest. Deep tendon reflexes are diminished. Which of the following is the most likely cause of this patient's symptoms?

Answer Choices:

(A) Anterior horn cell degeneration
(B) Axonal demyelination
(C) Decreased acetylcholine receptor density
(D) Myonecrosis

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/ff66bbdf-c82b-40ad-8af7-b6984e1f8655

OpenEvidence Explanation

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The correct answer is **A. Anterior horn cell degeneration**.

This presentation is classic for **spinal muscular atrophy (SMA) type I** (Werdnig-Hoffmann disease), which is caused by degeneration of alpha motor neurons in the **anterior horn cells** of the spinal cord due to homozygous loss of function of the SMN1 gene.[1][2]

The key clinical features pointing to this diagnosis include:

- **Onset before 6 months** with initially normal appearance followed by progressive weakness[2][3]
- **Symmetric flaccid weakness** of proximal limbs with inability to roll over or sit unsupported[2][4]
- **Bell-shaped chest** — a hallmark finding resulting from weakened intercostal muscles with relative sparing of the diaphragm, producing paradoxical breathing[2][5]
- **Weak cry and suck** — reflecting bulbar denervation[2][6]
- **Diminished deep tendon reflexes** — consistent with a lower motor neuron/peripheral process[7]
- **Preserved extraocular movements and facial expression** (smile, brow furrowing) — extraocular and upper facial muscles are characteristically spared in SMA[2]

Why the other answers are incorrect:

- **B. Axonal demyelination** — This would suggest Guillain-Barré syndrome or a peripheral neuropathy. GBS typically presents with ascending weakness and areflexia but would not produce a bell-shaped chest or the chronic progressive pattern seen here.[8]
- **C. Decreased acetylcholine receptor density** — This describes myasthenia gravis, which presents with fatigable weakness, ptosis, and ophthalmoplegia. Notably, deep tendon reflexes are typically preserved in neuromuscular junction disorders.[7][9]

- **D. Myonecrosis** — This would suggest a primary muscle disorder (e.g., muscular dystrophy), which typically presents with elevated creatine kinase levels and would not produce the pattern of spared facial/extraocular muscles with bell-shaped chest characteristic of SMA.[10][11]

SMA type I is the most common form, accounting for approximately 50–80% of SMA cases, and is the leading genetic cause of infant mortality.[3][4] FDA-approved disease-modifying therapies including nusinersen are now available.[12]

Would you like to explore the current treatment landscape for SMA type I, including the comparative efficacy of nusinersen, onasemnogene abeparvovec, and risdiplam?

Relevant images

(CONTENT OMITTED)

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Question 361

A 6-day-old male newborn is brought to the physician because he has become increasingly irritable and restless over the past 2 days. During this period, he has had 12 bowel movements. He feeds 10 to 12 times a day. He was born at 38 weeks' gestation and weighed 1800 g (3 lb 15 oz); he currently weighs 1700 g (3 lb 12 oz). His mother has Graves' disease and received propylthiouracil during the last trimester of pregnancy. She has a history of intravenous heroin use. His temperature is 36.9°C (98.4°F), pulse is 180/min, and respirations are 50/min. Examination shows mild diaphoresis and a firm 2-cm midline neck swelling. The lungs are clear to auscultation. Which of the following is the most appropriate next step in management?

Answer Choices:

(A) Methimazole and propranolol therapy
(B) Potassium iodide therapy
(C) Naloxone therapy
(D) Calcium gluconate therapy

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/a5afe19b-c05b-4464-8abd-57ad45ef54cf

OpenEvidence Explanation

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The answer is **A. Methimazole and propranolol therapy**. This neonate is presenting with **neonatal Graves' disease (neonatal thyrotoxicosis)** caused by transplacental passage of maternal TSH receptor antibodies (TRAb).

Clinical reasoning: The key features pointing to neonatal hyperthyroidism include:

- Mother with **Graves' disease** treated with propylthiouracil (PTU) during pregnancy
- Onset of symptoms at **day 4–6 of life** — classic timing, as maternal PTU clears from the neonatal circulation faster than TRAb, unmasking hyperthyroidism toward the end of the first week[1][2]
- **Irritability, tachycardia** (180/min), **frequent feeding**, **diarrhea** (12 bowel movements/day), **diaphoresis**, and **weight loss** — all classic sympathetic hyperactivity signs of thyrotoxicosis
- **Midline neck swelling** (goiter) — consistent with thyroid stimulation by maternal TRAb
- **Low birth weight** for gestational age (1800 g at 38 weeks) — associated with poorly controlled maternal Graves' disease[2]

Why methimazole + propranolol: The American Thyroid Association guidelines recommend **methimazole (MMI)** as the antithyroid drug of choice for neonatal hyperthyroidism, with **propranolol** added for severe sympathetic symptoms such as significant tachycardia.[1][3] PTU is no longer preferred in neonates due to the risk of hepatotoxicity.[1][4] A literature-based management algorithm similarly recommends MMI as first-line, with β-blockers for sympathetic hyperactivity.[3][5]

Why not the other options:

- **B. Potassium iodide** — Reserved for refractory cases in conjunction with MMI, not first-line therapy[3]
- **C. Naloxone** — Would address neonatal opioid withdrawal (NAS), which can present similarly with irritability and diarrhea. However, the goiter, tachycardia to 180/min, diaphoresis, and maternal Graves' disease make

thyrotoxicosis the primary diagnosis. Additionally, naloxone is not the standard treatment for NAS (supportive care and morphine/methadone are preferred)

- **D. Calcium gluconate** — Used for neonatal hypocalcemia, which does not fit this presentation

This condition is self-limited, typically resolving in **1–3 months** as maternal TRAb levels decline.[1][3]

Would you like to explore how to differentiate neonatal thyrotoxicosis from neonatal abstinence syndrome when both risk factors are present?

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Question 362

A previously healthy 29-year-old man comes to the emergency department because of burning with urination for several days. He has also had pain in the right ankle for 3 days and pain and swelling in the left knee for 1 day. Two weeks ago, he had several days of fever and bloody diarrhea, for which he was treated with antibiotics. Examination shows a small left knee effusion and bilateral conjunctival injection. Which of the following is the most likely additional finding in this patient?

Answer Choices:

(A) Circular erythematous rash with central clearing
(B) Pain on passive extension of the fingers
(C) Palpable mass in the right lower quadrant
(D) Tenderness at the insertion of the Achilles tendon

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/f5c86551-a335-44ab-8ef6-49df53229ad6

OpenEvidence Explanation

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The answer is **D. Tenderness at the insertion of the Achilles tendon**.

This clinical vignette describes **reactive arthritis** (formerly Reiter's syndrome), presenting with the classic triad of **arthritis** (right ankle pain, left knee effusion), **urethritis** (burning with urination), and **conjunctivitis** (bilateral conjunctival injection), occurring approximately two weeks after an episode of infectious dysentery (fever and bloody diarrhea).[1][2][3]

Enthesitis — inflammation at tendon or ligament insertion sites — is considered a **hallmark feature** of reactive arthritis and the broader spondyloarthritis family.[4][5][6] The Achilles tendon insertion on the calcaneus is one of the most commonly affected entheseal sites. A population-based study of reactive arthritis following enteric infections found that enthesitis was actually the most frequent musculoskeletal finding, even more common than frank arthritis.[7] Heel pain and other sites of enthesopathy, along with dactylitis ("sausage digits"), are described as important clinical clues to reactive arthritis.[1]

Why the other options are incorrect:

- **A (Circular erythematous rash with central clearing)** — This describes erythema migrans, the hallmark of Lyme disease, not reactive arthritis.
- **B (Pain on passive extension of the fingers)** — This suggests flexor tenosynovitis (Kanavel sign), associated with septic flexor sheath infection, not reactive arthritis.
- **C (Palpable mass in the right lower quadrant)** — This could suggest an appendiceal abscess or Crohn's disease, neither of which fits this presentation.

Would you like to explore the management approach for reactive arthritis, including the role of NSAIDs, intra-articular corticosteroids, and disease-modifying agents for chronic cases?

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Question 364

A 34-year-old man currently staying at an addiction center presents to the staff psychiatrist with diarrhea and painful muscle cramps. He has been discontinuing heroin over the last month as part of his treatment plan. He is HIV positive, hepatitis B (HBV) positive, and was recently treated for an infection with Streptococcus pneumoniae. He reports pain over his abdomen, knees, and shoulder. To comprehensively treat these symptoms, which of the following would be the best therapy?

Answer Choices:

(A) Methadone
(B) Naloxone
(C) Alvimopan
(D) Loperamide

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/1fc2b286-0b8b-4d3f-8929-11b04810c6b0

OpenEvidence Explanation

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The best answer is **A. Methadone**.

This patient is experiencing **opioid withdrawal symptoms** (diarrhea, painful muscle cramps, diffuse pain) during heroin discontinuation. The question asks for the therapy that would **comprehensively** treat these symptoms — this is the key distinction among the answer choices.

Why Methadone (A) is correct:

Methadone is a full μ-opioid receptor agonist that comprehensively addresses opioid withdrawal by acting at the same receptors as heroin. It treats the full spectrum of withdrawal symptoms — diarrhea, muscle cramps, pain, autonomic hyperactivity, and cravings — through a single mechanism.[1][2] Controlled trials demonstrate that methadone tapers are superior to α2-adrenergic agonist-based regimens and placebo for managing withdrawal symptoms and retaining patients in treatment.[2][3] Methadone also reduces HIV and HCV transmission risk in patients with opioid use disorder, which is particularly relevant given this patient's HIV and HBV status.[1][4]

Why the other options are incorrect:

- **B. Naloxone** — An opioid antagonist used to reverse opioid overdose. Administering naloxone to a patient in withdrawal would worsen symptoms by further blocking opioid receptors.
- **C. Alvimopan** — A peripherally acting μ-opioid receptor antagonist used to accelerate GI recovery after bowel surgery. It would not treat withdrawal symptoms and could worsen GI complaints.
- **D. Loperamide** — A peripherally acting opioid agonist that treats diarrhea but does not cross the blood-brain barrier in therapeutic doses. While useful as an adjunct for withdrawal-associated diarrhea, it would not address muscle cramps, pain, or other systemic withdrawal symptoms. It is not a comprehensive therapy.[1][5]

The distinction between loperamide and methadone is clinically important: loperamide is an appropriate adjunct medication for a single symptom (diarrhea), whereas methadone is the primary treatment that comprehensively manages the entire withdrawal syndrome.[1][2]

Would you like to explore the comparative effectiveness of methadone versus buprenorphine for managing opioid withdrawal in patients with HIV/HBV coinfection?

Relevant images

(CONTENT OMITTED)

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Question 368

A 20-year-old woman presents with vaginal discharge, pruritus, and painful micturition for the past 5 days. She is sexually active with multiple partners and admits to using barrier protection inconsistently. Her last menstrual period was 2 weeks ago. The patient denies any fever, chills, abdominal pain, menorrhagia, or flank pain. She is afebrile and the vital signs are within normal limits. Speculum examination reveals vaginal erythema with a profuse, greenish-yellow, purulent, malodorous discharge. The vaginal pH is 5.5. Vaginal swab and urine samples are obtained for microscopy and culture, and results are pending. Which of the following is the most likely diagnosis in this patient based on her presentation?

Answer Choices:

(A) Urinary tract infection
(B) Bacterial vaginosis
(C) Trichomonal vaginitis
(D) Chlamydia infection

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/3bb8b71a-4e97-4b15-b8f4-e4c76be3e2e0

OpenEvidence Explanation

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The correct answer is **C. Trichomonal vaginitis**.

This presentation is classic for **Trichomonas vaginalis** infection. The key features pointing to this diagnosis include:

- **Profuse, greenish-yellow, purulent, malodorous discharge** — trichomoniasis is classically associated with a copious yellow-green discharge that may be frothy and foul-smelling[1][2]
- **Elevated vaginal pH (5.5)** — trichomoniasis typically produces a pH >4.5, often >5.4[3][4]
- **Vaginal erythema with pruritus and dysuria** — common symptoms of trichomoniasis include vulvovaginal irritation, itching, and dysuria[5]
- **Risk factors** — sexually active with multiple partners and inconsistent barrier protection, consistent with this STI[1]

Why not the other options:

- **A. Urinary tract infection** — UTI can cause dysuria but does not produce vaginal discharge, vaginal erythema, or elevated vaginal pH. The absence of fever, flank pain, and abdominal pain further argues against complicated UTI, and the predominant vaginal findings localize the pathology to the vagina.
- **B. Bacterial vaginosis** — BV classically presents with a thin, homogeneous, whitish-gray discharge with a fishy odor, not a purulent greenish-yellow inflammatory discharge. BV is also not a true inflammatory condition and typically lacks vaginal erythema, pruritus, and dysuria.[1][2][6]
- **D. Chlamydia infection** — Chlamydia primarily causes cervicitis rather than vaginitis and is often asymptomatic. When symptomatic, it produces mucopurulent cervical discharge rather than the profuse, greenish-yellow vaginal discharge with elevated pH seen here.

The ACOG Practice Bulletin notes that trichomoniasis is associated with an elevated pH level and an inflammatory discharge that may be green-yellow in color.[1] NAAT is the preferred confirmatory test given the limited sensitivity (50–65%) of wet mount microscopy.[5]

Would you like to explore the recommended treatment regimens for trichomoniasis, including the updated CDC guidelines on metronidazole dosing for women versus men?

Relevant images

(CONTENT OMITTED)

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Question 369

A 47-year-old female undergoes a thyroidectomy for treatment of Graves' disease. Post-operatively, she reports a hoarse voice and difficulty speaking. You suspect that this is likely a complication of her recent surgery. What is the embryologic origin of the damaged nerve that is most likely causing this patient's hoarseness?

Answer Choices:

(A) 1st pharyngeal arch
(B) 2nd pharyngeal arch
(C) 3rd pharyngeal arch
(D) 6th pharyngeal arch

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/f639823b-14ad-4189-a7bb-0352cbfb344e

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OpenEvidence Explanation

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The answer is **D. 6th pharyngeal arch**.

Hoarseness following thyroidectomy is most commonly caused by injury to the **recurrent laryngeal nerve (RLN)**, which runs in close proximity to the thyroid gland within the tracheoesophageal groove. The RLN provides motor innervation

to all intrinsic laryngeal muscles except the cricothyroid, and its injury results in vocal fold paralysis with hoarseness and difficulty speaking.[1][2]

The RLN is embryologically derived from the **6th pharyngeal (branchial) arch**.[3][4] During embryonic development, both the right and left inferior laryngeal nerves supply the 6th branchial arch. As the heart descends and the neck elongates, the nerves are dragged inferiorly by their respective aortic arch derivatives — the left RLN loops around the ligamentum arteriosum (6th arch derivative), while the right RLN ultimately recurs around the right subclavian artery (4th arch derivative) after the distal 6th arch regresses on the right.[1][4]

Key pharyngeal arch nerve associations for reference:

- **1st arch** → Trigeminal nerve (CN V)
- **2nd arch** → Facial nerve (CN VII)
- **3rd arch** → Glossopharyngeal nerve (CN IX)
- **4th arch** → Superior laryngeal nerve (branch of CN X)
- **6th arch** → Recurrent laryngeal nerve (branch of CN X)

Would you like to explore the management strategies for recurrent laryngeal nerve injury after thyroidectomy, including the role of laryngeal electromyography in prognosis?

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Question 375

A 22-year-old man with sickle cell disease is brought to the emergency room for acute onset facial asymmetry and severe pain. He was in school when his teacher noted a drooping of his left face. His temperature is 99.9°F (37.7°C), blood pressure is 122/89 mmHg, pulse is 110/min, respirations are 19/min, and oxygen saturation is 98% on room air. Physical exam is notable for facial asymmetry and 4/5 strength in the patient's upper and lower extremity. A CT scan of the head does not demonstrate an intracranial bleed. Which of the following is the most appropriate treatment for this patient?

Answer Choices:

(A) Alteplase
(B) Exchange transfusion
(C) Heparin
(D) Warfarin

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/9082313c-cb3f-43c8-8833-250730a1a8ed

OpenEvidence Explanation

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The correct answer is **B. Exchange transfusion**.

This patient with sickle cell disease is presenting with acute neurological deficits — left facial droop and bilateral 4/5 extremity weakness — consistent with an **acute ischemic stroke**. The CT head has ruled out hemorrhagic stroke. In patients with SCD and acute stroke, **emergency exchange transfusion** is the cornerstone of treatment, with the goal of reducing HbS to less than 30%.[1][2]

Why exchange transfusion over the other options:

- **Alteplase (A):** While alteplase is standard thrombolytic therapy for acute ischemic stroke in the general population, stroke in SCD is typically caused by sickle cell–related vasculopathy (stenosis/occlusion of major cerebral arteries from chronic endothelial injury and sickling) rather than an acute thromboembolic event amenable to thrombolysis. The ASH 2020 guidelines recommend exchange transfusion as the primary intervention for SCD-related stroke. In adults, thrombolytic therapy may be considered if indicated, but exchange transfusion remains the definitive treatment.[1][3]

- **Heparin (C) and Warfarin (D):** There is a lack of experience with antithrombotics for secondary stroke prevention in SCD, and specific recommendations for anticoagulation cannot be stated outside of general treatment guidelines. Neither heparin nor warfarin addresses the underlying pathophysiology of sickle cell vasculopathy.[4]

The ASH 2020 guidelines specifically recommend exchange transfusion over simple transfusion for children and adults with SCD and acute neurological deficits, with prompt transfusion ideally within 2 hours of presentation.[3] The AAP clinical report similarly recommends exchange transfusion or erythrocytapheresis to reduce HbS to <30% and raise hemoglobin to 10 g/dL.[5]

Would you like to explore the long-term secondary stroke prevention strategies in sickle cell disease, including the role of chronic transfusion programs versus hydroxyurea?

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Question 376

A 3-month-old girl is brought to the physician because of a productive cough for 5 days. Over the past month, she has had several episodes of watery stools. She is exclusively breastfed every 3–4 hours for 15–20 minutes. She was delivered vaginally at 38 weeks' gestation at home and has not yet been evaluated by a physician. The mother reports that her child is not gaining weight. The mother had no prenatal care. The infant is at the 5th percentile for height and weight. The infant has not received any immunizations. Her temperature is 38.5°C (101.3°F), pulse is 155/min, respirations are 45/min, and blood pressure is 88/50 mm Hg. Oral examination shows white plaques covering the tongue and the palate. Rales are heard bilaterally on cardiopulmonary examination. Cervical and inguinal lymphadenopathy is present. Which of the following is most likely to confirm the diagnosis?

Answer Choices:

(A) Karyotyping of infant's chromosomes
(B) DNA test for CFTR mutation
(C) Fluorescent treponemal antibody absorption test
(D) Polymerase chain reaction for viral genes

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/9a3bbcfc-c9b9-468b-85b1-c5d6cc1faab9

OpenEvidence Explanation

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The answer is **D. Polymerase chain reaction for viral genes**.

This clinical presentation — a 3-month-old with **failure to thrive** (5th percentile for height and weight), **oral thrush** (white plaques on tongue and palate), **productive cough with bilateral rales** (likely Pneumocystis jirovecii pneumonia), **chronic watery diarrhea**, **generalized lymphadenopathy**, and **no prenatal care** — is classic for **perinatal HIV infection** with rapid disease progression.[1] Rapid progressors with vertically transmitted HIV typically present in the first months of life with this constellation of failure to thrive, chronic diarrhea, oral candidiasis, hepatosplenomegaly, lymphadenopathy, and opportunistic pneumonia.[1][2]

Why PCR for viral genes is the correct confirmatory test:

In infants younger than 18 months, HIV antibody tests cannot be used for diagnosis because transplacentally transferred maternal IgG antibodies may persist, leading to false-positive results.[3][4] **HIV DNA or RNA PCR (nucleic acid tests)** represent the gold standard for diagnosing HIV in this age group, directly detecting viral genetic material rather than relying on the infant's antibody response.[4] These assays can definitively diagnose HIV in most infants by 1–2 months of age.[3]

Why the other options are incorrect:

- **A. Karyotyping** — While Down syndrome (trisomy 21) can cause failure to thrive and immunodeficiency, it does not explain this specific constellation of oral thrush, bilateral pneumonia, chronic diarrhea, and lymphadenopathy in the setting of absent prenatal care.
- **B. CFTR mutation testing** — Cystic fibrosis causes failure to thrive and pulmonary disease, but it does not cause oral thrush, lymphadenopathy, or fever in this pattern.
- **C. FTA-ABS** — Congenital syphilis can cause failure to thrive and lymphadenopathy, but the classic features include mucocutaneous rash,

rhinitis ("snuffles"), hepatosplenomegaly, and bony lesions rather than persistent oral thrush and Pneumocystis-type pneumonia. Additionally, FTA-ABS is not recommended for evaluating congenital syphilis in neonates because treponemal IgG reflects passively transferred maternal antibodies. [5][6][7]

Would you like to explore the recommended timing and schedule for HIV diagnostic testing in perinatally exposed infants, including when to initiate antiretroviral prophylaxis?

Relevant images

(CONTENT OMITTED)

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Question 377

A 30-year-old primigravid woman at 22 weeks' gestation is brought to the emergency department by her husband for lethargy, nausea, and vomiting for 4 days. This morning she became drowsy. She returned from a business trip to Sudan 3 weeks ago. She denies eating any seafood while traveling. Medications include iron supplements and a multivitamin. Her immunizations are up-to-date and she has never received blood products. Her temperature is 38.9°C (102°F), pulse is 92/min, and blood pressure is 122/76 mm Hg. She is oriented to person and place. Examination shows jaundice and mild asterixis. Pelvic examination shows a uterus consistent in size with a 22-week gestation. Laboratory studies show:
Hemoglobin 11.2 g/dL
Prothrombin time 18 sec (INR=2.0)
Serum
Total bilirubin 4.4 mg/dL
Alkaline phosphatase 398 U/L
AST 4,702 U/L
ALT 3,551 U/L
Lactate dehydrogenase 3,412 U/L
Anti-nuclear antibody negative
Anti-smooth muscle antibody negative
Anti-CMV antibody negative
Anti-EBV nuclear antigen antibody negative
An ELISA for HIV is negative. Which of the following is most likely to confirm the diagnosis?

Answer Choices:

(A) HBsAg
(B) Anti-HAV IgG
(C) Anti-HCV IgG
(D) Anti-HEV IgM

Correct Answer:

(D)

> **OpenEvidence Response:**
>
> **(D)** ✓

OpenEvidence Link: https://openevidence.com/ask/803c5952-720a-427b-974f-fdd27044f45c

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OpenEvidence Explanation

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The correct answer is **D. Anti-HEV IgM**.

This presentation is classic for **acute hepatitis E virus (HEV) infection** in a pregnant woman. Several key features point to this diagnosis:

- **Travel to Sudan** (an HEV-endemic region) 3 weeks ago, consistent with the HEV incubation period of 3–8 weeks[1]
- **Second trimester pregnancy** — HEV is uniquely severe in pregnant women, particularly in the second and third trimesters, with incidence of hepatic encephalopathy or acute liver failure reaching ~70% and mortality up to 20–30% in developing countries[2][3]
- **Markedly elevated aminotransferases** (AST 4,702, ALT 3,551) with jaundice, coagulopathy (INR 2.0), and **asterixis** (indicating hepatic encephalopathy) — all consistent with fulminant hepatitis
- **Fecal-oral transmission** — HEV is primarily waterborne, and the patient denied seafood (ruling out a common HAV/HEV source but not water exposure)[1][4]
- **Negative autoimmune markers** (ANA, anti-smooth muscle antibody) and **negative CMV/EBV** exclude other causes

Why the other options are incorrect:

- **A. HBsAg** — Hepatitis B is transmitted via blood/body fluids. The patient has never received blood products, and HBV rarely presents with fulminant hepatitis during pregnancy.[3]
- **B. Anti-HAV IgG** — IgG indicates past infection or vaccination, not acute infection. HAV IgM would be needed for acute diagnosis. Furthermore, HAV typically follows a self-limited course in pregnancy without the severity seen here, and her immunizations are up-to-date (likely including HAV).[1][4]
- **C. Anti-HCV IgG** — HCV is blood-borne and rarely causes acute fulminant hepatitis. IgG also does not distinguish acute from chronic infection.[5]

The ACG and AASLD guidelines recommend testing pregnant women presenting with acute hepatitis for HEV using **HEV IgM antibody**, which appears by 4–6 weeks after exposure.[4][6] This is the most appropriate confirmatory test in this clinical scenario.

Would you like to explore the management approach and maternal-fetal outcomes for fulminant hepatitis E in pregnancy?

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Question 384

Six days after undergoing an aortic valve replacement surgery, a 68-year-old woman has bluish discolorations around the peripheral intravenous catheters and severe right leg pain. She has a history of hypertension and major depressive disorder. She drinks 3 beers daily. Current medications include hydrochlorothiazide, aspirin, prophylactic unfractionated heparin, and fluoxetine. Her temperature is 37.3°C (99.1°F), pulse is 90/min, and blood pressure is 118/92 mm Hg. Examination shows multiple hematomas on the upper extremities around the peripheral intravenous access sites. There is a healing sternal incision. The lungs are clear to auscultation. Cardiac examination shows an aortic click. The right calf is tender, erythematous and swollen. Laboratory studies show:
Hemoglobin 13.1 g/dL
Leukocyte count 9,900/mm3
Platelet count 48,000/mm3
Prothrombin time 15 seconds
Activated partial thromboplastin time 40 seconds
Serum
Urea nitrogen 19 mg/dL
Creatinine 1.1 mg/dL
Alkaline phosphatase 33 U/L
AST 26 U/L
ALT 33 U/L
γ-Glutamyl transferase 45 U/L (N=5–50 U/L)
Which of the following is the most likely underlying mechanism of this patient's symptoms?

Answer Choices:

(A) Deficiency of vitamin K-dependent clotting factors
(B) Phagocytosis of autoantibody-opsonized platelets
(C) Excess circulating thrombin
(D) Autoantibody-mediated platelet activation

Correct Answer:

> **(D)**
>
> **OpenEvidence Response:**
>
> **(D)** ✓

OpenEvidence Link: https://openevidence.com/ask/9dd15993-9768-4487-9413-056cef5c35b6

OpenEvidence Explanation

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The answer is **D. Autoantibody-mediated platelet activation**.

This clinical scenario is classic for **heparin-induced thrombocytopenia (HIT)** with thrombosis (HITT). The key features include:

- **Thrombocytopenia** (platelet count 48,000/mm^3) developing on **postoperative day 6** after aortic valve replacement — fitting the typical 5–10 day onset window[1]
- **Thrombotic complication**: right calf tenderness, erythema, and swelling consistent with deep vein thrombosis (DVT), the most common thrombotic complication of HIT[1]
- **Skin findings**: bluish discolorations and hematomas around IV catheter sites, consistent with skin necrosis at heparin exposure sites[1]
- **Prophylactic unfractionated heparin** exposure — the causative agent

Why answer D and not the others:

HIT is caused by **IgG antibodies directed against complexes of platelet factor 4 (PF4) and heparin**. These antibodies bind to PF4-heparin complexes on the platelet surface and then cross-link **FcγRIIa receptors on platelets**, directly **activating** them.[2][3] This platelet activation generates procoagulant microparticles and thrombin, producing a paradoxically **prothrombotic** state

despite thrombocytopenia.[3][4] The mechanism is specifically autoantibody-mediated platelet activation — not simple destruction or consumption.

- **A (Vitamin K-dependent clotting factor deficiency):** Would cause elevated PT/INR disproportionately; this patient's coagulation studies are only mildly prolonged, and the clinical picture does not fit warfarin effect or liver failure.
- **B (Phagocytosis of autoantibody-opsonized platelets):** This describes immune thrombocytopenic purpura (ITP), which causes bleeding, not thrombosis.
- **C (Excess circulating thrombin):** While thrombin generation is increased in HIT, it is a downstream consequence of antibody-mediated platelet activation, not the primary underlying mechanism. Disseminated intravascular coagulation (DIC) would typically show more deranged coagulation parameters and fibrinogen consumption.

The following figure from Greinacher (NEJM, 2015) illustrates the pathogenesis of HIT, showing how anti-PF4/heparin IgG antibodies activate platelets via FcγRIIa receptors, leading to thrombin generation and thrombosis.

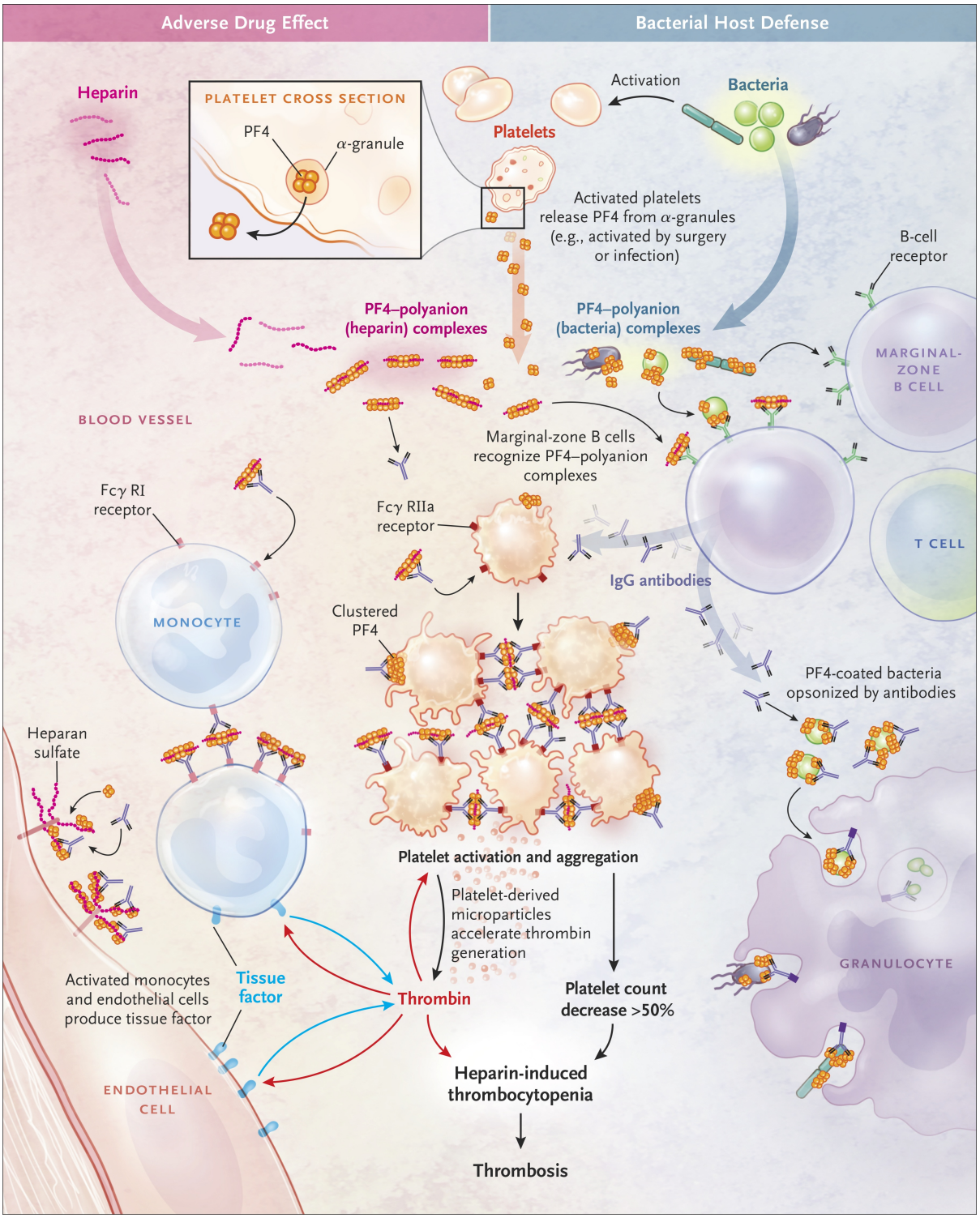


Figure 1. Pathogenesis of Heparin-Induced Thrombocytopenia.

Used under license from The New England Journal of Medicine.

Would you like to explore the diagnostic workup for HIT, including the 4Ts scoring system and the role of PF4/heparin immunoassays versus functional (serotonin release) assays?

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Question 385

A 55-year-old man with chronic hepatitis B virus infection comes to the physician because of generalized fatigue and a 5.4 kg (12 lb) weight loss over the past 4 months. Physical examination shows hepatomegaly. Laboratory studies show an α-fetoprotein concentration of 380 ng/ml (N < 10 ng/mL). A CT scan of the abdomen with contrast shows a solitary mass in the left lobe of the liver that enhances in the arterial phase. Which of the following is the most likely underlying pathogenesis of this patient's current condition?

Answer Choices:

(A) Overexpression of secretory hepatitis antigen
(B) Intracellular accumulation of misfolded protein
(C) Gain of function mutation of a proto-oncogene
(D) Integration of foreign DNA into host genome

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/7bd87bc6-94b5-4772-b679-d7dce0882108

OpenEvidence Explanation

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The correct answer is **D. Integration of foreign DNA into host genome**.

This patient presents with classic features of **hepatocellular carcinoma (HCC)** — chronic hepatitis B, weight loss, hepatomegaly, markedly elevated α-fetoprotein (380 ng/mL), and a liver mass with arterial-phase enhancement on CT. The most likely underlying pathogenesis in HBV-associated HCC is **integration of viral (foreign) DNA into the host hepatocyte genome**.

Why HBV DNA integration is the key mechanism:

HBV is a DNA virus that integrates its genome into host hepatocyte chromosomal DNA early in chronic infection.[1][2] This integration drives hepatocarcinogenesis through several mechanisms:

- **Insertional mutagenesis** — HBV DNA preferentially integrates near cancer-related genes such as the TERT promoter, CCNE1, and MLL4, leading to their aberrant overexpression and promoting cellular immortalization and proliferation.[3][4]
- **Genomic instability** — Integration induces chromosomal rearrangements, translocations, and structural variations that disrupt tumor suppressor genes and activate oncogenes.[5][6]
- **Cis-regulatory effects** — Integrated HBV enhancer elements can drive ectopic expression of nearby host genes, further promoting malignant transformation.[4][5]

HBV DNA integration is considered an early, permanent, and irreversible genetic change that is a hallmark of HBV-associated HCC, even before overt malignancy develops.[3]

Why the other options are incorrect:

- **A (Overexpression of secretory hepatitis antigen)** — While HBsAg is produced in chronic HBV infection, its overexpression is not the primary oncogenic mechanism driving HCC.
- **B (Intracellular accumulation of misfolded protein)** — This describes the mechanism seen with alpha-1 antitrypsin deficiency (where misfolded Z-protein accumulates in hepatocytes), not HBV-related HCC. Although mutant preS/S envelope proteins can activate the unfolded protein response, this is a secondary mechanism, not the primary pathogenesis.[1]

- **C (Gain of function mutation of a proto-oncogene)** — This describes a general oncogenic mechanism (e.g., RAS mutations in other cancers) but is not the characteristic pathogenesis of HBV-related HCC. The oncogenic transformation in HBV-HCC is driven by viral DNA integration rather than a spontaneous gain-of-function point mutation.

Would you like to explore the specific molecular pathways through which HBV's HBx protein contributes to epigenetic dysregulation and hepatocarcinogenesis?

Relevant images

(CONTENT OMITTED)

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Question 388

An 8-week-old male presents with his mother to the pediatrician for a well visit. The patient has been breastfed since birth, and usually feeds for 30 minutes every 2-3 hours. The patient's mother is concerned that her milk production is not keeping up with the patient's nutritional requirements. She reports that about two weeks ago the patient began regurgitating breastmilk through his nose and mouth after some feeds. She reports that he seems mildly upset during the episodes of regurgitation but usually settles down quickly and is hungry again soon afterwards. The patient's mother has already tried limiting the volume of each feed, which seems to have reduced the frequency of the regurgitation. She denies any diarrhea, hematochezia, or family history of food allergies. Her older son had a similar problem with vomiting that resolved around 12 months of age. Four weeks ago, the patient's height and weight were in the 40th and 34th percentiles, respectively. His height and weight are now respectively in the 37th and 36th percentiles. On physical exam, the patient is cooing in his mother's lap and smiles reciprocally with her. He lifts his head and shoulders off the examination table when placed in the supine position. His abdomen is soft, non-tender and non-distended. Bowel sounds are normoactive.

Which of the following is the best next step in management?

Answer Choices:

(A) Initiate proton pump inhibitor
(B) Obtain abdominal ultrasound
(C) Reassurance and counseling on positioning
(D) Recommend modification of mother's diet

Correct Answer:

(C)

OpenEvidence Response:

> (C) ✓

OpenEvidence Link: https://openevidence.com/ask/e1d4c408-cc6e-4172-be91-8f49377dd59e

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OpenEvidence Explanation

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The correct answer is **C. Reassurance and counseling on positioning**.

This infant presents with classic **uncomplicated physiologic gastroesophageal reflux (GER)** — a "happy spitter." Key features supporting this diagnosis include: onset before 8 weeks, non-bilious and non-projectile regurgitation, the infant is thriving (appropriate growth with stable percentiles), no alarm symptoms (no hematemesis, bilious vomiting, or diarrhea), a benign abdominal exam, and normal developmental milestones. The family history of a sibling with similar symptoms resolving by 12 months further supports this.

Gastroesophageal reflux occurs daily in approximately **40% of infants**, typically begins before 8 weeks, peaks around 4 months, and resolves by 12 months of age.[1] The NASPGHAN-ESPGHAN guidelines and the AAFP recommend that clinicians **reassure parents that GER is self-limited and not pathologic**, and does not warrant routine testing or pharmacologic treatment.[1][2] Approximately 80% of infants with uncomplicated GER improve with conservative measures alone, including small frequent feeds and holding the infant upright for 20–30 minutes after feeding.[3]

Why the other options are incorrect:

- **A. Proton pump inhibitor** — The NASPGHAN-ESPGHAN guidelines explicitly recommend against using PPIs or H2RAs for the treatment of crying/distress or visible regurgitation in otherwise healthy infants. Lansoprazole was not found to be effective in infants under 12 months with

symptomatic GER. Acid suppression is reserved for infants who fail conservative measures and have evidence of GERD complications.[2][4]

- **B. Abdominal ultrasound** — An ultrasound would be indicated if pyloric stenosis were suspected (classically presenting with **projectile**, non-bilious vomiting, typically at 3–6 weeks of age, with progressive worsening and possible palpable "olive" mass). This infant's regurgitation is not projectile, growth is maintained, and the presentation is inconsistent with pyloric stenosis.

- **D. Modification of mother's diet** — Maternal dairy elimination may be considered in breastfed infants with suspected cow's milk protein allergy, but this infant has no diarrhea, hematochezia, or family history of food allergies, making this diagnosis unlikely. Dietary modification is a second-line intervention if conservative measures fail.[1][2]

Would you like to explore the distinguishing features between physiologic GER and GERD in infants, including alarm symptoms that warrant further workup?

Relevant images

(CONTENT OMITTED)

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Question 389

A 27-year-old gentleman is brought into the ED after being stabbed in the back by a knife. In addition to the pain from the wound, he complains of weakness in his left leg. Upon physical examination you find that he has no other visible injuries; however, he has 2/5 strength in the left lower extremity. Complete neurologic exam also finds a deficit in vibration sense and light touch on the left lower extremity as well as a loss of pain and temperature sensation in the right lower extremity. Which of the following lesions would result in the syndrome described?

> **Answer Choices:**
>
> (A) Anterior cord lesion
> (B) Posterior cord lesion
> (C) Right cord hemisection
> (D) Left cord hemisection

> **Correct Answer:**
>
> **(D)**
>
> **OpenEvidence Response:**
>
> **(D)** ✓

OpenEvidence Link: https://openevidence.com/ask/c26e1430-29db-4e15-b0e7-6671866a9f33

OpenEvidence Explanation

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The answer is **D. Left cord hemisection** — this presentation is classic for **Brown-Séquard syndrome**, caused by hemisection of the spinal cord on the left side.

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The answer is **D. Left cord hemisection**. This presentation is the classic **Brown-Séquard syndrome**, historically associated with penetrating knife wounds to the spinal cord.[1][2]

Why left hemisection?

Brown-Séquard syndrome results from hemisection of the spinal cord and produces a characteristic triad of findings based on the anatomy of the three major spinal tracts:[2][3]

- **Ipsilateral motor weakness** — The corticospinal tract has already decussated at the medullary pyramids, so a left-sided lesion causes left-sided weakness (2/5 strength in the left lower extremity in this case).
- **Ipsilateral loss of vibration and light touch** — The dorsal columns (carrying proprioception, vibration, and fine touch) ascend ipsilaterally before decussating in the medulla, so a left lesion causes left-sided dorsal column deficits.
- **Contralateral loss of pain and temperature** — The spinothalamic tract crosses within 1–2 levels of entering the cord, so fibers from the right side are traveling in the left lateral spinothalamic tract by the time they reach the lesion level. A left hemisection therefore disrupts pain/temperature from the right side.[4]

Why not the other options?

- **Anterior cord syndrome (A)** would produce bilateral motor loss and bilateral loss of pain/temperature with preserved dorsal column function (proprioception, vibration) — a symmetric deficit, not a hemisection pattern.[1][2]
- **Posterior cord syndrome (B)** causes isolated bilateral proprioceptive loss with preserved motor function and other sensory modalities — does not match this presentation.[2]
- **Right cord hemisection (C)** would produce the mirror image: right-sided weakness and dorsal column loss with left-sided pain/temperature loss — opposite to what is described here.

The following figure from a case report in NEJM illustrates a classic Brown-Séquard syndrome from a penetrating stab wound, with MRI demonstrating the hemisection pattern:

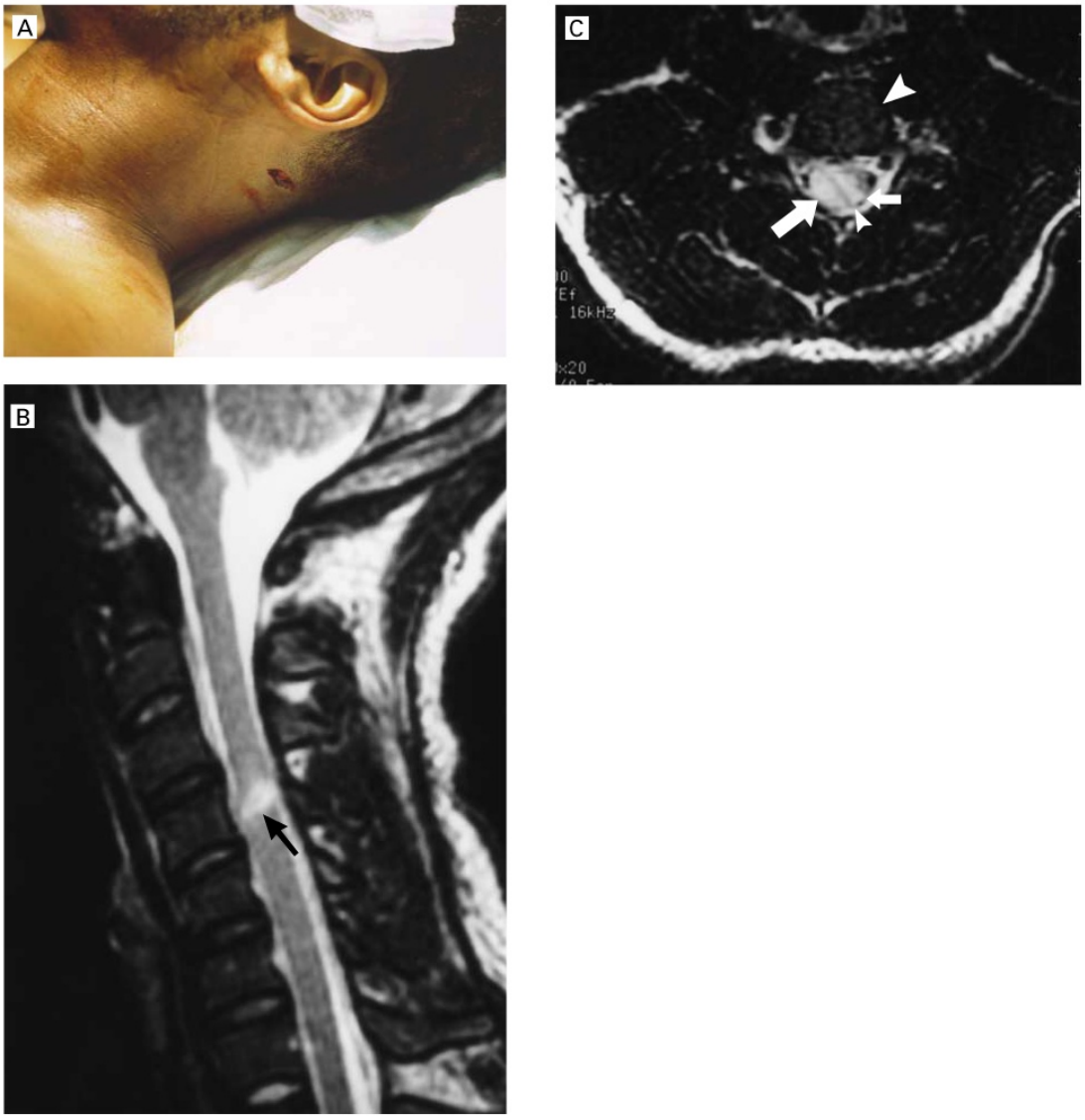


Figure 1.

Used under license from The New England Journal of Medicine.

Would you like to explore the prognosis and management of Brown-Séquard syndrome compared to other incomplete spinal cord injury patterns?

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Question 390

A 58-year-old African American man presents for his yearly wellness visit. He says he has been unsuccessful at losing weight and would like help. His last colonoscopy was 8 years previously, which was normal. Past medical history is significant for obstructive sleep apnea (OSA) and hypertension. Current medications are isosorbide dinitrate/hydralazine and aspirin 81 mg orally daily. He is also on CPAP to manage his OSA. The patient denies any history of smoking or recreational drug use and drinks 1 or 2 beers on weekends. Family history is significant for prostate cancer in his father and hypertension and diabetes mellitus type 2 in his mother. His vital signs include: temperature 36.8°C (98.2°F), pulse 97/min, respiratory rate 16/min, blood pressure 120/75 mm Hg. BMI is 30 kg/m2. Physical examination is unremarkable. Fasting blood glucose is 90 mg/dL. Which of the following preventative screening tests would be most appropriate for this patient at this time?

Answer Choices:

(A) PSA
(B) Digital rectal exam
(C) Abdominal ultrasound
(D) Flexible sigmoidoscopy

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/89f96c8d-b607-48a6-b76e-fac0771bc3fa

OpenEvidence Explanation

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The correct answer is **A. PSA**.

PSA screening is the most appropriate preventive screening test for this patient — a 58-year-old African American man with a family history of prostate cancer in his father. Both of these factors (Black race and first-degree relative with prostate cancer) place him in a high-risk category for prostate cancer, making PSA-based screening clearly indicated.

Why PSA is correct:

- The USPSTF recommends shared decision-making about PSA-based screening for men aged 55–69 years, and specifically acknowledges that African American men may benefit from screening at younger ages given their significantly higher incidence (203.5 vs 121.9 per 100,000) and mortality (44.1 vs 19.1 per 100,000) compared to white men.[1]
- NCCN guidelines recommend that Black/African American individuals and those with a concerning family history begin shared decision-making about PSA screening at **age 40**, with screening at 1- to 2-year intervals. At age 58, this patient is well within the recommended screening window.[2]
- The American Cancer Society similarly recommends that African American males and those with a first-degree relative diagnosed with prostate cancer before age 65 begin screening discussions at age 45.[3]

Why the other options are incorrect:

- **B. Digital rectal exam (DRE):** NCCN guidelines state that DRE should not be used as a stand-alone test for prostate cancer screening. It may be considered as a supplement to PSA but is not the primary screening modality.[2]
- **C. Abdominal ultrasound:** AAA screening with ultrasound is recommended for men aged 65–75 who have ever smoked (USPSTF Grade B). This patient is only 58 years old, has never smoked, and has no family history of AAA — he does not meet screening criteria.[4]

- **D. Flexible sigmoidoscopy:** His last colonoscopy was 8 years ago and was normal. After a normal, high-quality colonoscopy, repeat screening is recommended in **10 years**. He is not yet due for colorectal cancer rescreening by any modality.[5][6]

Would you like to explore the optimal PSA screening interval and follow-up algorithm for high-risk patients based on baseline PSA levels?

Relevant images

(CONTENT OMITTED)

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Question 391

A 34-year-old patient is brought to the emergency room after a motor vehicle accident. An EKG shows sinus tachycardia and chest radiograph reveals an enlarged cardiac silhouette. While observing sinus tachycardia on the patient's telemetry, you note that the radial pulse cannot be palpated during inspiration. What should be the next step in management of this patient?

> **Answer Choices:**
>
> (A) Pericardiocentesis
> (B) Chest CT scan
> (C) Pericardial window
> (D) Insert chest tube

> **Correct Answer:**
>
> **(A)**
>
> **OpenEvidence Response:**
>
> **(A)** ✓

OpenEvidence Link: https://openevidence.com/ask/fa3801e3-10f9-45a5-8881-430a74063f1e

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OpenEvidence Explanation

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The answer is **A. Pericardiocentesis**.

This clinical scenario describes **cardiac tamponade** following blunt chest trauma. The key findings are:

- **Sinus tachycardia** — a compensatory mechanism to maintain cardiac output as pericardial pressure rises[1]
- **Enlarged cardiac silhouette** on chest radiograph — indicating pericardial effusion[2]
- **Loss of radial pulse during inspiration** — this is **pulsus paradoxus**, a hallmark of cardiac tamponade, reflecting exaggerated interventricular interdependence with respiration[1][2]

Pericardiocentesis is the definitive next step for established or impending cardiac tamponade. The 2025 ACC Expert Consensus Statement recommends pericardiocentesis as the therapeutic intervention for cardiac tamponade, especially in urgent or emergency settings, preferably with echocardiographic guidance using a subxiphoid or apical approach.[1] As Spodick described in the NEJM, the treatment of cardiac tamponade is drainage of the pericardial contents, and sudden circulatory collapse warrants pericardiocentesis even without imaging guidance.[3]

Why not the other options?

- **Chest CT scan (B)** — delays definitive treatment in a hemodynamically significant tamponade; CT is not recommended for routine assessment of cardiac tamponade.[1]
- **Pericardial window (C)** — a surgical option reserved for recurrent effusions after prior pericardiocentesis, or when needle drainage is ineffective (e.g., clotted hemopericardium). It is not the initial intervention.[1][4]
- **Chest tube (D)** — addresses pleural pathology (pneumothorax, hemothorax), not pericardial tamponade.

Would you like to explore the nuances of when surgical drainage (pericardial window or thoracotomy) is preferred over pericardiocentesis in traumatic hemopericardium?

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Question 392

A previously healthy 60-year-old man comes to his physician because of progressively worsening shortness of breath for the past 2 months. He does not experience shortness of breath at rest. He also occasionally has a dry cough. He has not had fever, chills, or night sweats. He has smoked a pack of cigarettes daily for the past 40 years. He drinks a beer daily and occasionally more on weekends. He does not use illicit drugs. He is 183 cm (6 ft 0 in) tall and weighs 66 kg (145 lbs); BMI is 19.7 kg/m2. His temperature is 37°C (98.6°F), pulse is 94/min, respirations are 21/min, and blood pressure is 136/88 mm Hg. Lung auscultation reveals a prolonged expiratory phase and end-expiratory wheezing. Spirometry shows an FEV1:FVC ratio of 62%, an FEV1 of 60% of predicted, and a total lung capacity of 125% of predicted. The diffusion capacity of the lung (DLCO) is decreased. Which of the following is the most likely diagnosis?

Answer Choices:

(A) Interstitial lung disease
(B) Hypersensitivity pneumonitis
(C) Chronic obstructive pulmonary disease
(D) Bronchiectasis

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/75d48610-5bbf-4287-b6f1-805a29d49e03

OpenEvidence Explanation

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The answer is **C. Chronic obstructive pulmonary disease (COPD)**.

This presentation is classic for COPD:

- **Risk factor**: 40-pack-year smoking history is the most significant risk factor for COPD.
- **Symptoms**: Progressive exertional dyspnea and dry cough over months, without systemic symptoms (no fever, chills, or night sweats).
- **Physical exam**: Prolonged expiratory phase and end-expiratory wheezing are hallmark findings of obstructive airway disease. Low BMI (19.7) is common in COPD patients with an emphysematous phenotype.
- **Spirometry**: **FEV1:FVC ratio of 62%** (below 70%) confirms airflow obstruction. FEV1 of 60% predicted classifies this as **GOLD Stage II (moderate)** COPD.
- **TLC of 125% predicted** indicates hyperinflation due to air trapping, characteristic of emphysema.
- **Decreased DLCO** reflects destruction of the alveolar-capillary membrane, consistent with the emphysematous component of COPD.

Why not the other options?

- **A. Interstitial lung disease** — Would show a restrictive pattern (reduced TLC, normal or elevated FEV1:FVC ratio) rather than obstruction with hyperinflation. DLCO is decreased in ILD, but the spirometric pattern here is obstructive.
- **B. Hypersensitivity pneumonitis** — Also typically restrictive, and would be expected to present with fever, chills, and an identifiable antigen exposure (e.g., mold, bird droppings). No such history is provided.
- **D. Bronchiectasis** — Can cause obstruction, but typically presents with chronic productive cough with copious purulent sputum, recurrent

infections, and would not explain the hyperinflation or decreased DLCO seen here.

Question 395

A six-year-old boy with a history of asthma currently uses an albuterol inhaler as needed to manage his asthma symptoms. His mother brings him into your office because she feels she has had to increase the patient's use of his inhaler to four times per week for the past month. She also reports that he has woken up three times during the night from his symptoms this month. The boy reports that he is upset because he can't always keep up with his friends in the playground. His past medical history is significant for allergic rhinitis. The patient's temperature is 98°F (36.6°C), blood pressure is 110/70 mmHg, pulse is 88/min, and respirations are 18/min with an oxygen saturation of 98% O2 on room air. Auscultation of his lungs reveals bilateral late expiratory wheezes.

What changes should be made to his current asthma treatment regimen?

> **Answer Choices:**
>
> (A) Maintain current therapy
> (B) Add fluticasone daily
> (C) Add salmeterol twice daily
> (D) Add zileuton twice daily

> **Correct Answer:**
>
> **(B)**
>
> **OpenEvidence Response:**
>
> **(B)** ✓

OpenEvidence Link: https://openevidence.com/ask/93bd6c9a-490d-4cb6-bc4d-025ecb64f772

OpenEvidence Explanation

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The answer is **B. Add fluticasone daily** (a low-dose inhaled corticosteroid).

Classifying this patient's asthma severity: This 6-year-old is currently on SABA monotherapy (Step 1) but now has symptoms >2 days/week (albuterol use 4 times/week), nighttime awakenings 3 times/month, and activity limitation — all consistent with **mild persistent asthma**, which warrants stepping up to Step 2 therapy.[1][2]

Why low-dose ICS is the correct step-up:

Per the NHLBI/NAEPP guidelines for children aged 5–11 years, the preferred Step 2 therapy is a **daily low-dose inhaled corticosteroid** (such as fluticasone) with a SABA as needed for symptom relief.[1] Low-dose ICS minimizes symptoms, reduces SABA use, halves the risk of asthma-related death, and reduces hospitalizations and severe exacerbations.[3] The GINA guidelines similarly recommend daily low-dose ICS as the preferred Step 2 controller for children 6–11 years.[4] Regular ICS ranked best for preventing exacerbations and improving FEV_1 in children with mild asthma.[5]

Why the other options are incorrect:

- **A (Maintain current therapy):** The patient's symptom frequency and nighttime awakenings exceed the thresholds for intermittent asthma, indicating inadequate control on SABA alone.[1]
- **C (Salmeterol):** A LABA should not be used as monotherapy without an ICS — it is only appropriate as add-on therapy at Step 3 or higher. LABAs without concurrent ICS carry a risk of severe exacerbations.[1][3]
- **D (Zileuton):** Zileuton (a 5-lipoxygenase inhibitor) is not approved for children under 12 years of age and is not a preferred Step 2 option. Even leukotriene receptor antagonists (e.g., montelukast) are considered less effective than ICS as first-line controller therapy in children.[6][7]

Would you like to explore the specific ICS dosing recommendations and monitoring parameters for this age group?

Relevant images

(CONTENT OMITTED)

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Question 398

A 65-year-old male presents to the emergency department from his home complaining of dyspnea. He is alert and oriented. The following arterial blood gas readings are drawn: pH: 7.33 (Normal: 7.35-7.45), pCO2: 70 mmHg (Normal: 35-45 mmHg), HCO3 33 (Normal: 21-26 mEq/L) Which of the following is most likely to have produced this patient's condition?

Answer Choices:

(A) Panic attack
(B) Mechanical ventilation
(C) Pulmonary embolus
(D) Chronic obstructive bronchitis

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/7c5e05aa-5646-4cf9-b562-25bc9461a80b

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OpenEvidence Explanation

(CONTENT OMITTED)

The answer is **D. Chronic obstructive bronchitis**.

This ABG demonstrates a **chronic respiratory acidosis with appropriate renal compensation**, which is the hallmark acid-base pattern of COPD/chronic obstructive bronchitis. The key findings are:

- **pH 7.33** (mildly acidotic)
- **pCO2 70 mmHg** (markedly elevated → primary respiratory acidosis)
- **HCO3 33 mEq/L** (elevated → metabolic compensation)

Why chronic, not acute? In chronic respiratory acidosis, the expected compensatory rise in HCO3 is **4–5 mEq/L for each 10 mmHg increase in pCO2** above 40 mmHg.[1] With a pCO2 of 70 (30 mmHg above normal), the expected HCO3 would be approximately 24 + (3 × 4.5) = **~37.5 mEq/L**, which is close to the observed 33. In contrast, acute respiratory acidosis produces only a ~1 mEq/L rise in HCO3 per 10 mmHg increase in pCO2, which would yield an HCO3 of only ~27 — far below what is seen here.[1] This degree of metabolic compensation takes **2–5 days** to develop via renal retention of bicarbonate and excretion of chloride.[1][2]

Stable COPD patients with chronic hypercapnia characteristically maintain pCO2 levels of 45–77 mmHg with only mildly reduced pH values (often ≥7.37), and a pCO2 of 55 mmHg predicts a bicarbonate of ~33 mEq/L.[3] This patient's values fit squarely within this pattern, with a slightly lower pH suggesting a possible acute-on-chronic exacerbation.

Why not the other choices?

- **A. Panic attack** — would cause hyperventilation → respiratory alkalosis (low pCO2, high pH), the opposite of what is seen.
- **B. Mechanical ventilation** — typically used to correct, not cause, hypercapnia; and the patient is at home, alert, and oriented.
- **C. Pulmonary embolus** — classically causes hyperventilation and respiratory alkalosis (low pCO2), not hypercapnia. PE with this degree of CO2 retention would be unusual without pre-existing severe lung disease.

The following figure illustrates the differential bicarbonate response in acute versus chronic respiratory acidosis:

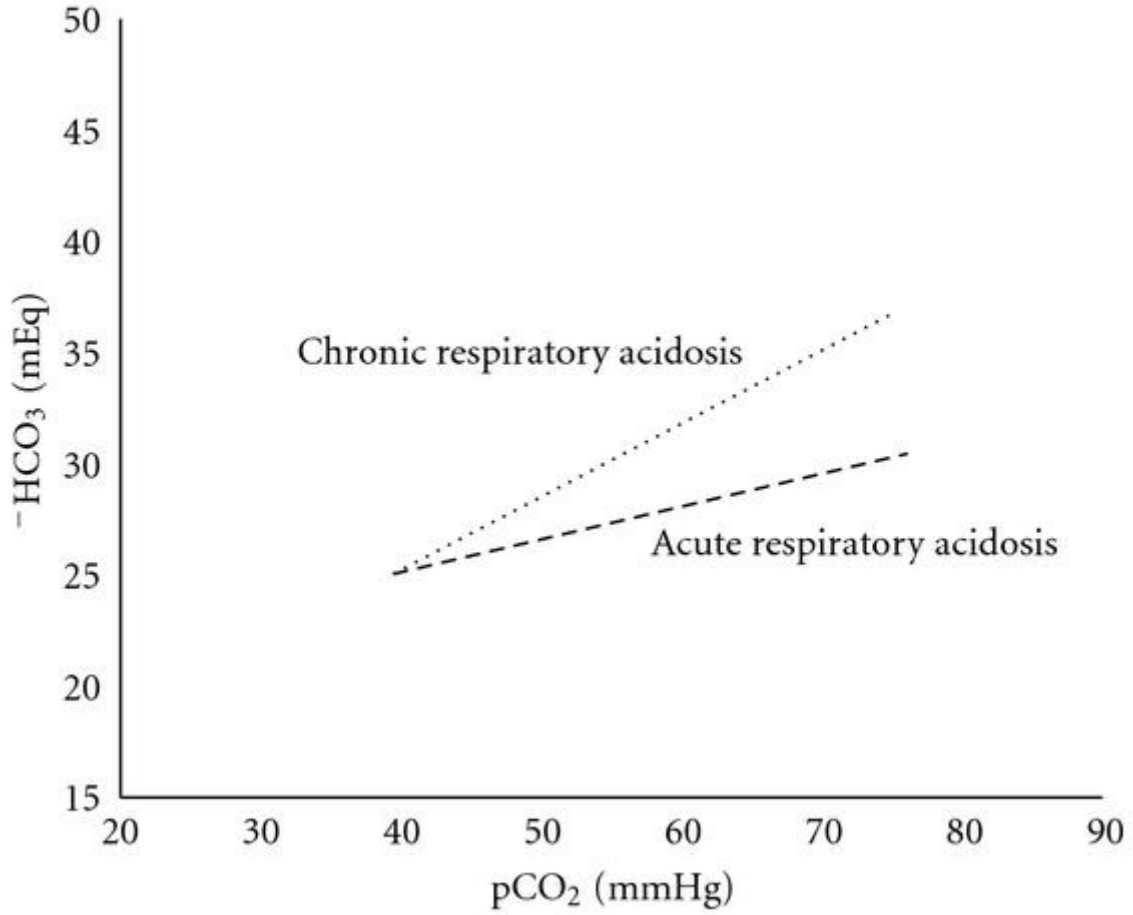


Figure 5. Relationship between pCO 2 and bicarbonate in acute and chronic respiratory acidosis.

Would you like to explore the management approach for acute-on-chronic hypercapnic respiratory failure in COPD, including the role of noninvasive ventilation and target oxygen saturations?

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Question 403

A 6-year-old boy is brought to the physician by his mother because of a 6-month history of mild episodic abdominal pain. The episodes occur every 1–2 months and last for a few hours. The pain is located in the epigastrium, radiates to his back, and is occasionally associated with mild nausea. His mother is concerned that his condition might be hereditary because his older sister was diagnosed with congenital heart disease. He is otherwise healthy and has met all developmental milestones. He is at the 75th percentile for height and the 65th percentile for weight. Physical examination shows no abdominal distention, guarding, or rebound tenderness. Which of the following congenital conditions would best explain this patient's symptoms?

Answer Choices:

(A) Hypertrophic pyloric stenosis
(B) Biliary cyst
(C) Intestinal malrotation
(D) Pancreas divisum

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/db06eb2f-e900-4314-921b-575706c6c6fd

OpenEvidence Explanation

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The answer is **D. Pancreas divisum**.

Pancreas divisum is the most common congenital pancreatic anomaly, resulting from failure of fusion of the dorsal and ventral pancreatic ductal systems during embryogenesis.[1][2] This leads to dominant pancreatic drainage through the minor papilla, which in a subset of patients causes impaired outflow and increased intraductal pressures, precipitating episodes of **recurrent epigastric pain radiating to the back** — a classic pancreatitis-type presentation.[1][3]

Several features of this case point to pancreas divisum:

- **Episodic epigastric pain radiating to the back with nausea** is characteristic of recurrent pancreatitis, the hallmark presentation of symptomatic pancreas divisum. A pediatric surgical series found that children with pancreas divisum and recurrent pancreatitis presented at a **mean age of 6 years** with recurrent episodic epigastric pain and vomiting.[4]
- **Congenital nature**: Pancreas divisum is present from birth, consistent with the question asking for a congenital condition.
- **Family history of congenital heart disease**: Pancreatic developmental anomalies and congenital heart defects share embryologic pathways. Mutations in genes such as **GATA6**, a transcription factor involved in both pancreatic and cardiac development, are associated with pancreatic malformations alongside congenital heart defects. This provides a plausible hereditary link between the sibling's congenital heart disease and this patient's pancreatic anomaly.[5][6]

Why not the other options:

- **A. Hypertrophic pyloric stenosis** — Presents in early infancy (2–4 weeks) with nonbilious projectile vomiting, not episodic epigastric pain in a 6-year-old.[7]
- **B. Biliary cyst (choledochal cyst)** — Typically presents with the classic triad of jaundice, right upper quadrant mass, and abdominal pain; pain does not characteristically radiate to the back in a pancreatitis pattern.

- **C. Intestinal malrotation** — Usually presents in infancy with bilious vomiting; while older children may have chronic abdominal pain, the epigastric-to-back radiation pattern and association with a sibling's congenital heart disease are not characteristic.[7]

Would you like to explore the diagnostic workup for suspected pancreas divisum in pediatric patients, including the role of secretin-enhanced MRCP?

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Question 404

A healthy, full-term 1-day-old female is being evaluated after birth and is noted to have a cleft palate and a systolic ejection murmur at the second left intercostal space. A chest radiograph is obtained which reveals a boot-shaped heart and absence of a thymus. An echocardiogram is done which shows pulmonary stenosis with a hypertrophic right ventricular wall, ventricular septal defect, and overriding of the aorta. Which of the following additional features is expected to be seen in this patient?

Answer Choices:

(A) Seizures due to hypocalcemia
(B) Catlike cry
(C) Hyperthyroidism from transplacental antibodies
(D) Increased phenylalanine in the blood

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/ffbc2ce4-faf6-4217-a4e4-4b8d24236e4a

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OpenEvidence Explanation

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The answer is **A. Seizures due to hypocalcemia**.

This clinical presentation — cleft palate, absent thymus, boot-shaped heart, and echocardiographic findings of **tetralogy of Fallot** (pulmonary stenosis, right ventricular hypertrophy, VSD, and overriding aorta) — is classic for **DiGeorge syndrome** **(22q11.2 deletion syndrome)**.[1][2][3]

DiGeorge syndrome results from defective development of the third and fourth pharyngeal pouches, leading to:

- **Conotruncal cardiac defects** (tetralogy of Fallot, truncus arteriosus, interrupted aortic arch type B)[4][5]
- **Thymic aplasia/hypoplasia** → T-cell immunodeficiency[1]
- **Parathyroid aplasia/hypoplasia** → hypoparathyroidism with **hypocalcemia**[1][2]
- **Palatal abnormalities** (cleft palate, velopharyngeal insufficiency)[2]
- Facial dysmorphism[5]

Hypoparathyroidism is present in approximately 50% of patients and results in clinically significant **hypocalcemia that can manifest as neonatal seizures**, feeding difficulties, jitteriness, and tremors.[1][2] Per the AAP clinical report, seizures in neonates with 22q11.2DS are most often provoked seizures attributable to hypocalcemia and respond to appropriate electrolyte management.[2]

Why the other options are incorrect:

- **B. Catlike cry** — characteristic of Cri-du-chat syndrome (5p deletion), not 22q11.2 deletion
- **C. Hyperthyroidism from transplacental antibodies** — associated with neonatal Graves disease, unrelated to this presentation
- **D. Increased phenylalanine** — characteristic of phenylketonuria (PKU), an inborn error of metabolism unrelated to DiGeorge syndrome

Would you like to explore the recommended neonatal screening and monitoring protocols for infants diagnosed with 22q11.2 deletion syndrome?

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Question 407

A 60-year-old female patient with a history of hypertension presents to an outpatient office for regular check-up and is found to have hypertriglyceridemia. Her physician prescribes high-dose niacin and recommends taking the medication along with aspirin. The side effect the physician is trying to avoid is thought to be mediated by what mechanism?

Answer Choices:

(A) Bile deposition in the dermis
(B) Release of prostaglandins
(C) Mast cell degranulation
(D) T cell activation

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/57c4af31-77aa-43aa-9496-c3e2458c1bd3

OpenEvidence Explanation

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The answer is **B. Release of prostaglandins**.

The side effect in question is **niacin-induced cutaneous flushing**, which is the most common adverse effect of niacin therapy (occurring in up to 71% of patients) and a major cause of treatment discontinuation.[1] This flushing is

mediated by the **release of prostaglandins**, primarily prostaglandin D_2 (PGD_2) and prostaglandin E_2 (PGE_2).

Mechanism: Niacin activates the G protein-coupled receptor GPR109A (HCA_2) on dermal Langerhans cells and keratinocytes. This triggers increased arachidonic acid mobilization and its conversion via cyclooxygenase (COX-1 in Langerhans cells, COX-2 in keratinocytes) to PGD_2 and PGE_2, which then act on vascular DP_1, EP_2, and EP_4 receptors to cause cutaneous vasodilation — manifesting as warmth, redness, and tingling of the face and upper body.[2][3][4]

Why aspirin helps: Aspirin (acetylsalicylic acid) inhibits cyclooxygenase, thereby reducing prostaglandin synthesis. Pretreatment with 325 mg of aspirin 30 minutes before niacin dosing reduces moderate-to-severe flushing events by approximately 30–50%.[5][6][7] The FDA-approved niacin label specifically recommends aspirin pretreatment to mitigate flushing.[7]

The following figure illustrates the dual mechanism of GPR109A activation — therapeutic lipid-lowering effects in adipocytes (top) and prostaglandin-mediated flushing in epidermal cells (bottom):

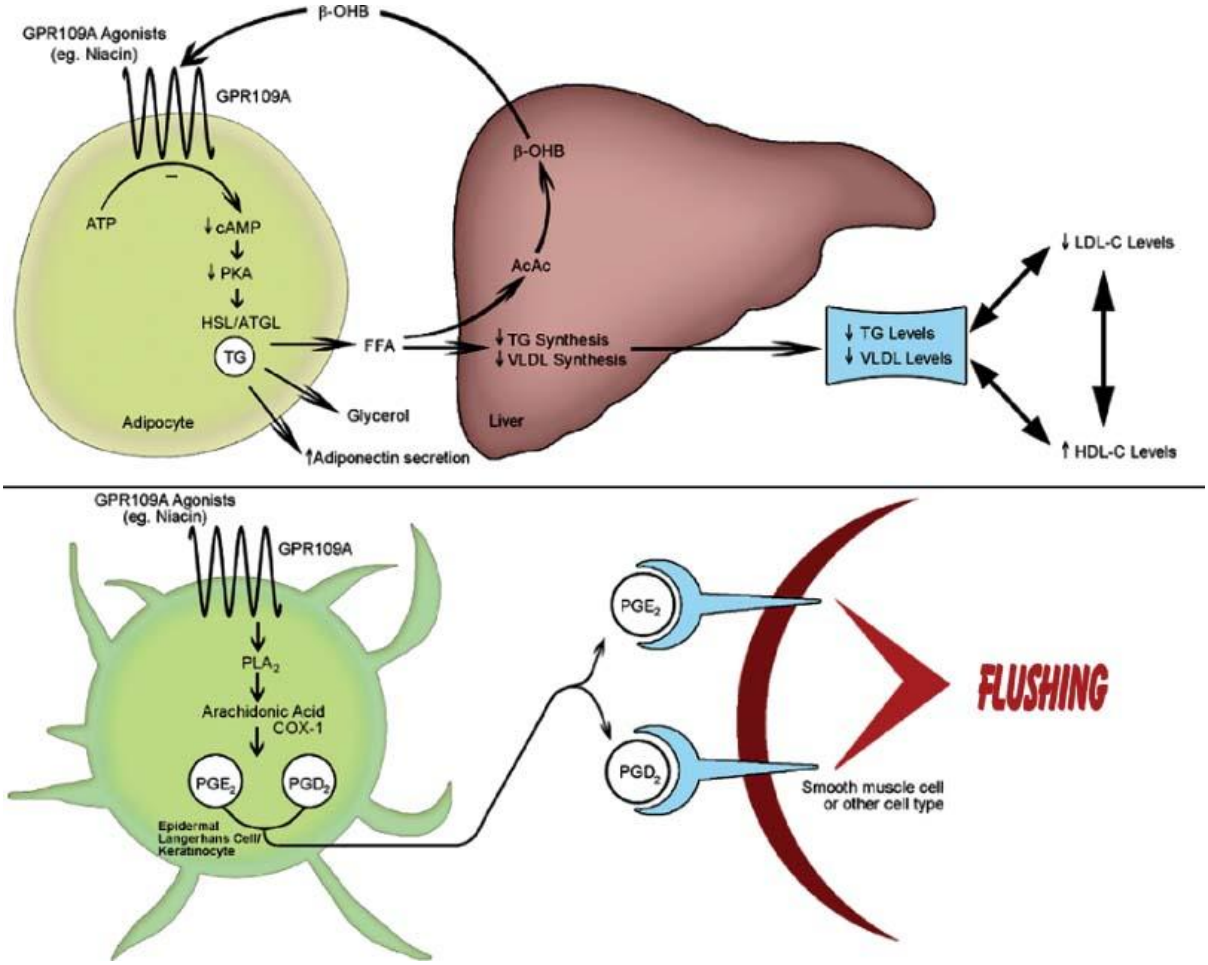


Figure 1. Mechanism of action of GPR109A. GPR109A is a receptor for endogenous (β -OHB) and exogenous (e.g. niacin) ligands. Activation of GPR109A (top panel above) in the adipocyte results in inhibition of adenylate cyclase activity and subsequent reduction in cAMP levels and PKA, HSL/ATGL activity. This results in reduced hydrolysis of TG and subsequent suppression of FFA and glycerol release from the adipocyte. At the same time, adipocyte secretion of adiponectin is increased. The reduction of substrate availability to the liver limits TG and VLDL synthesis and subsequently reduces serum concentrations of TG and LDL-C and increases HDL-C. In epidermal Langerhans cells and keratinocytes (bottom panel above), GPR109A activation results in arachidonic acid-mediated prostaglandin synthesis which will initiate a flushing response. ATP, adenosine triphosphate; cAMP, cyclic adenosine monophosphate; PKA, protein kinase A; HSL, hormone sensitive lipase; ATGL, adipose triglyceride lipase; TG, triglyceride; FFA, free fatty acid; VLDL, very low-density lipoprotein; AcAc, acetoacetate; β -OHB, β -hydroxybutyrate; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; PLA2, phospholipase A2; COX-1, cyclooxygenase-1; PGE2, prostaglandin E2; PGD2, prostaglandin D2.

The other answer choices are incorrect: bile deposition in the dermis (A) relates to cholestatic pruritus, not niacin flushing; mast cell degranulation (C) may play a minor contributory role but is not the primary accepted mechanism; and T cell activation (D) is not involved in this pathway.[9]

Would you like to explore the comparative efficacy of different flushing mitigation strategies, including extended-release formulations versus aspirin pretreatment versus the DP_1 receptor antagonist laropiprant?

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Question 408

A 42-year-old man comes to the physician after elevated liver function tests were found after a routine screening. He has had occasional headaches over the past year, but otherwise feels well. The patient reports that he was involved in a severe car accident 30 years ago. He does not smoke or drink alcohol. He has never used illicit intravenous drugs. He takes no medications and has no known allergies. His father had a history of alcoholism and died of liver cancer. The patient appears thin. His temperature is 37.8°C (100°F), pulse is 100/min, and blood pressure is 110/70 mm Hg. Physical examination shows no abnormalities. Laboratory studies show:
Hemoglobin 14 g/dL
Leukocyte count 10,000/mm3
Platelet count 146,000/mm3
Serum
Glucose 150 mg/dL
Albumin 3.2 g/dL
Total bilirubin 1.5 mg/dL
Alkaline phosphatase 75 U/L
AST 95 U/L
ALT 73 U/L
HIV negative
Hepatitis B surface antigen negative
Hepatitis C antibody positive
HCV RNA positive
HCV genotype 1
A liver biopsy is performed and shows mononuclear infiltrates that are limited to portal tracts and periportal hepatocyte necrosis. Which of the following is the most appropriate next step in management?

> **Answer Choices:**
>
> (A) Sofosbuvir and ledipasvir therapy
> (B) Tenofovir and velpatasvir therapy

(C) Interferon and ribavirin therapy
(D) Tenofovir and entecavir therapy

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/f60a2241-c8ab-4182-a897-8327f9736d55

OpenEvidence Explanation

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The answer is **A. Sofosbuvir and ledipasvir therapy**.

This patient has chronic **HCV genotype 1 infection** confirmed by positive HCV antibody, positive HCV RNA, and genotyping. The liver biopsy shows mononuclear portal infiltrates and periportal hepatocyte necrosis consistent with chronic hepatitis (interface hepatitis) without cirrhosis. The likely route of transmission was a blood transfusion during his severe car accident 30 years ago (before routine HCV screening of blood products, which began in 1992).

Why sofosbuvir/ledipasvir (Harvoni)? This is an FDA-approved direct-acting antiviral (DAA) combination for HCV genotype 1 infection, combining an NS5B polymerase inhibitor (sofosbuvir) with an NS5A inhibitor (ledipasvir).[1] In the ION trials, sofosbuvir/ledipasvir achieved SVR rates of **94–97%** in treatment-naive patients with genotype 1 HCV, including those with cirrhosis.[2] Real-world data confirm SVR rates exceeding 93% for genotype 1.[3][4]

Why the other options are incorrect:

- **B. Tenofovir and velpatasvir** — Tenofovir is an antiviral used for hepatitis B and HIV, not HCV. The correct HCV combination is sofosbuvir/velpatasvir (Epclusa), not tenofovir/velpatasvir. This is a distractor answer.
- **C. Interferon and ribavirin** — This was the prior standard of care but has been replaced by DAA regimens due to superior efficacy (>95% vs. ~50% SVR), shorter treatment duration, and far fewer side effects.[5][6]
- **D. Tenofovir and entecavir** — Both are hepatitis B antivirals (nucleos(t)ide analogues) and have no role in HCV treatment. This patient is HBsAg-negative.

It is worth noting that current AASLD-IDSA guidelines now recommend pangenotypic regimens — **glecaprevir/pibrentasvir** (8 weeks) or **sofosbuvir/velpatasvir** (12 weeks) — as the simplified first-line treatment for treatment-naive adults regardless of genotype.[7] However, among the answer choices provided, sofosbuvir/ledipasvir is the only appropriate DAA regimen for HCV genotype 1.

Would you like to explore the monitoring approach and SVR assessment timeline after initiating DAA therapy for chronic HCV?

Relevant images

(CONTENT OMITTED)

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Question 409

A 44-year-old woman with hypothyroidism comes to the physician because of a 1-month history of tingling in her feet and poor balance. Her only medication is levothyroxine. Physical examination shows conjunctival pallor and an ataxic gait. Proprioception and sense of vibration are decreased in her toes bilaterally. Laboratory studies show macrocytic anemia and normal thyroid hormone levels. Histological evaluation of tissue samples obtained by esophagogastroduodenoscopy reveals atrophic changes of the gastric body and fundus with normal antral mucosa. Which of the following structures is most likely being targeted by antibodies in this patient?

Answer Choices:

(A) Islet cell cytoplasm
(B) Deamidated gliadin peptide
(C) Parietal cells
(D) Smooth muscle

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/ceb6d251-4012-4c7b-9d5f-9721e64175c3

OpenEvidence Explanation

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The answer is **C. Parietal cells**.

This patient presents with a classic picture of **subacute combined degeneration of the spinal cord due to vitamin B12 deficiency** caused by **autoimmune (type A) atrophic gastritis / pernicious anemia**. The key findings supporting this diagnosis include:

- **Neurological features**: Tingling in feet (peripheral neuropathy), poor balance, ataxic gait, and decreased proprioception/vibration sense — all hallmarks of dorsal column and peripheral nerve involvement from B12 deficiency.
- **Macrocytic anemia** with conjunctival pallor.
- **Histology**: Atrophic changes limited to the gastric **body and fundus** with **normal antral mucosa** — this distribution is pathognomonic for autoimmune (type A) gastritis, as parietal cells (and chief cells) are located in the body and fundus.

In autoimmune atrophic gastritis, **anti-parietal cell antibodies** (and anti-intrinsic factor antibodies) destroy the oxyntic mucosa, leading to loss of intrinsic factor production, impaired B12 absorption in the terminal ileum, and ultimately pernicious anemia. The association with hypothyroidism further supports an autoimmune polyglandular syndrome.

Why not the other options?

- **A. Islet cell cytoplasm** — Associated with type 1 diabetes mellitus, not relevant here.
- **B. Deamidated gliadin peptide** — Associated with celiac disease, which causes villous atrophy of the small intestine (not gastric body atrophy) and typically presents with iron deficiency anemia.
- **D. Smooth muscle** — Anti-smooth muscle antibodies are associated with autoimmune hepatitis, which does not explain this presentation.

Would you like to explore the overlap between autoimmune atrophic gastritis and other autoimmune conditions in polyglandular syndromes?

Question 412

A 64-year-old man comes to the emergency department because of a 2-day history of lower back pain, fever, and chills. He has had nausea but no vomiting during this time. He has hypertension, chronic kidney disease, and type 2 diabetes mellitus. Three months ago, he underwent amputation of his left third toe because of a non-healing ulcer. He has smoked a pack of cigarettes daily for 48 years. Current medications include hydrochlorothiazide, metoprolol, and insulin. His temperature is 39.4°C (102.9°F), pulse is 102/min, blood pressure is 150/94 mm Hg, and respirations are 18/min. Examination shows a 1-cm (0.4-in) round ulcer on the sole of his right foot. There is costovertebral angle tenderness on the left side. The abdomen is soft. Laboratory studies show:
Hemoglobin 11.5 g/dL
Leukocyte count 19,000/mm3
Serum
Na+ 140 mEq/L
Cl− 102 mEq/L
K+ 5.0 mEq/L
HCO3− 25 mEq/L
Urea nitrogen 65 mg/dL
Creatinine 2.4 mg/dL
Glucose 240 mg/dL
Urine
Blood 1+
Protein 1+
WBC 100/hpf
Nitrite 2+
WBC casts numerous
Urine and blood samples for culture and sensitivity tests are obtained.
Which of the following is the most appropriate next step in management?

> **Answer Choices:**
>
> (A) Inpatient treatment with intravenous ciprofloxacin
> (B) Outpatient treatment with oral levofloxacin
> (C) Outpatient treatment with trimethoprim-sulfamethoxazole

(D) Initiate hemodialysis

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/851077c6-01e3-41ba-a253-bb30cab2f89f

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OpenEvidence Explanation

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The answer is **A. Inpatient treatment with intravenous ciprofloxacin**.

This patient presents with **complicated acute pyelonephritis** — evidenced by high fever (39.4°C), costovertebral angle tenderness, leukocytosis (19,000/mm³), pyuria with WBC casts, and positive nitrites — in the setting of multiple complicating factors: **diabetes mellitus, chronic kidney disease (creatinine 2.4 mg/dL), and a likely hematogenous or ascending source from a diabetic foot ulcer**. These features mandate **inpatient admission with parenteral antibiotic therapy**.

Why inpatient IV therapy is required:

- Hospital admission is warranted for patients with severe illness or unstable coexisting medical conditions. This patient has poorly controlled diabetes (glucose 240 mg/dL), CKD, high fever, tachycardia, and significant leukocytosis — all indicating a complicated infection with systemic toxicity. [1]

- Patients with diabetes are at increased risk for severe UTI complications, including emphysematous pyelonephritis and atypical pathogens, and fluoroquinolones are a reasonable empiric choice for these patients.[2]
- Fluoroquinolones achieve high concentrations in both urine and renal tissue and have proven clinical efficacy for pyelonephritis.[1]

Why the other options are incorrect:

- **B and C (outpatient therapy):** Outpatient management is appropriate only for mildly ill patients with uncomplicated disease, minimal nausea, no vomiting, and stable comorbidities. This patient's high fever, tachycardia, leukocytosis, CKD, and diabetes make outpatient management inappropriate.[1][3]
- **D (hemodialysis):** While the patient has elevated BUN and creatinine consistent with CKD, there is no indication for emergent hemodialysis (no refractory hyperkalemia, severe acidosis, pulmonary edema, or uremic encephalopathy). The K^+ of 5.0 mEq/L and HCO_3^- of 25 mEq/L do not meet emergent dialysis criteria.

Would you like to explore the specific antibiotic dosing adjustments needed for fluoroquinolones in patients with this degree of renal impairment?

References

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Question 413

A 56-year-old man with a history of pancreatic cancer presents to the surgical intensive care unit following a pancreaticoduodenectomy. Over the next 3 days, the patient's drainage output is noted to exceed 1 liter per day. In the early morning of postoperative day 4, the nurse states that the patient is difficult to arouse. His temperature is 99.5°F (37.5°C), blood pressure is 107/88 mmHg, pulse is 120/min, respirations are 17/min, and oxygen saturation is 98% on room air. His skin and mucous membranes are dry on physical exam. Laboratory values are ordered as seen below.

Serum:
Na+: 154 mEq/L
Cl-: 100 mEq/L
K+: 4.3 mEq/L
HCO3-: 27 mEq/L
BUN: 20 mg/dL
Glucose: 99 mg/dL
Creatinine: 1.1 mg/dL

Which of the following is the best next step in management?

Answer Choices:

(A) 0.9% saline IV
(B) 5% dextrose IV
(C) 5% dextrose IV with 0.45% saline IV
(D) Oral free water replacement

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/80aed5ea-cf43-4bff-bf29-680db366fbd3

OpenEvidence Explanation

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The best next step in management is **A. 0.9% saline IV**.

This question presents a postoperative patient with **hypovolemic hypernatremia** — the key clinical features are high-volume surgical drain losses (>1 L/day), dry skin and mucous membranes, tachycardia (120/min), and a narrowed pulse pressure (107/88 mmHg), all indicating significant **extracellular volume depletion** with hemodynamic compromise. The serum sodium of 154 mEq/L confirms hypernatremia from hypotonic fluid losses through the surgical drain.

Why isotonic saline first? Although hypotonic fluids (D5W, half-normal saline) are the standard treatment for hypernatremia in general, the sole exception is when there is hemodynamic compromise from extracellular volume depletion. As described in the NEJM review by Adrogué and Madias, isotonic saline is indicated when there is "depletion of extracellular-fluid volume that is sufficient to cause substantial hemodynamic compromise".[1] This patient's tachycardia to 120 bpm and narrowed pulse pressure indicate hemodynamic instability requiring initial volume resuscitation with isotonic saline. After circulatory status is stabilized, the fluid should be transitioned to a hypotonic solution (such as D5W or 0.45% saline) to correct the hypernatremia.[1]

Why not the other options?

- **B (D5W) and C (D5W with 0.45% saline):** While these hypotonic fluids would more effectively lower serum sodium, they distribute largely into the intracellular space and are poor volume expanders. In a hemodynamically unstable patient, restoring intravascular volume takes priority over correcting sodium.[1]

- **D (Oral free water):** The patient is obtunded ("difficult to arouse"), making oral administration unsafe due to aspiration risk and impractical for the volume of resuscitation needed.[1]

The management principle is to **stabilize hemodynamics first** with isotonic saline, then transition to hypotonic fluids to correct the hypernatremia at a rate of approximately 10–12 mEq/L per day.[1][2]

Would you like to explore the specific formulas and calculations used to determine the rate and volume of free water replacement once this patient is hemodynamically stabilized?

References

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Question 414

A 46-year-old woman comes to the physician because of a 3-day history of diarrhea, moderate abdominal pain, and weakness. Her symptoms began on the return flight from a 2-week yoga retreat in India, where she stayed at a resort. She was mildly nauseous as she boarded the flight, and diarrhea followed immediately after eating the in-flight meal. Since then, she has had up to five watery stools daily. She has a 1-year history of gastroesophageal reflux disease and is allergic to shellfish. Her only medication is ranitidine. She appears lethargic. Her temperature is 37°C (98.6°F), pulse is 70/min, and blood pressure is 115/72 mm Hg. Abdominal examination shows diffuse tenderness with no guarding or rebound. Bowel sounds are hyperactive. Which of the following is the most likely pathogen?

Answer Choices:

(A) Giardia intestinalis
(B) Shigella species
(C) Staphylococcus aureus
(D) Enterotoxigenic Escherichia coli

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/8afbdf6f-bcae-473b-9de3-e7d1a8a1be28

OpenEvidence Explanation

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The most likely pathogen is **D. Enterotoxigenic Escherichia coli (ETEC)**.

Several clinical features point to ETEC as the causative agent:

- **Travel to India**: ETEC is the most common cause of traveler's diarrhea in South Asia. Diarrheagenic E. coli (most prominently ETEC) account for more than half of traveler's diarrhea cases in the Indian subcontinent. The CDC notes that travelers to India have a >60% likelihood of developing traveler's diarrhea during a 2-week journey.[1][2]
- **Clinical presentation**: Watery, non-bloody diarrhea with abdominal cramping, no fever, and a duration of several days is the hallmark of ETEC infection. The incubation period of 2–10 days fits the timeline of symptom onset near the end of her trip. ETEC outbreaks characteristically show a high prevalence of diarrhea and cramps with low prevalence of vomiting and fever.[3][4]
- **Use of ranitidine (H2 blocker)**: Acid suppression is a recognized risk factor for enteric infections, as reduced gastric acidity lowers the infectious dose threshold.[1]

Why not the other options?

- **Giardia intestinalis** (A): Typically has a longer incubation period (1–2 weeks) and presents with greasy, foul-smelling stools, bloating, and a more chronic course. Three days of illness would be early for symptomatic giardiasis.[3]
- **Shigella** (B): Causes inflammatory/dysenteric diarrhea with bloody stools, fever, and tenesmus — none of which are present here.[5]
- **Staphylococcus aureus** (C): Causes food poisoning via preformed toxin with a very short incubation (2–7 hours), predominantly vomiting, and resolution within 24–48 hours. This patient's 3-day course of predominantly watery diarrhea does not fit S. aureus intoxication.[1][6]

Would you like to explore the role of empiric antibiotic therapy versus supportive care for traveler's diarrhea, including current resistance patterns in South Asia?

Relevant images

(CONTENT OMITTED)

References

1. Bacterial Diarrhea. DuPont HL.. The New England Journal of Medicine. 2009;361(16):1560-9. doi:10.1056/NEJMcp0904162.

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Question 417

A 55-year-old woman with papillary thyroid carcinoma underwent total thyroidectomy. She has no significant medical history. On postoperative day 1, she develops perioral numbness and a tingling sensation, along with paresthesia of the hands and feet. The physical examination reveals that she is anxious and confused. Her pulse is 90/min, the blood pressure is 110/80 mm Hg, the respirations are 22/min, and the temperature is 36.7°C (98.0°F). Latent tetany (carpal spasm) is evident in the right arm. This is observed when the sphygmomanometer cuff pressure is raised above the systolic blood pressure and held for 3 minutes. The laboratory test results are as follows:
Serum calcium 6.7 mg/dL
Serum sodium 143 mEq/L
Serum potassium 4.4 mEq/L
Serum creatinine 0.9 mg/dL
Blood urea 16 mg/dL
Serum magnesium 1.1 mEq/L
What is the most likely cause of this condition?

Answer Choices:

(A) Inadvertent surgical removal of parathyroid glands
(B) DiGeorge syndrome
(C) Chronic hypomagnesemia
(D) Hungry bone syndrome

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/b1c560c9-4c4c-4792-a79d-279f7db69b5a

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OpenEvidence Explanation

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The most likely cause of this patient's condition is **A. Inadvertent surgical removal of parathyroid glands** (post-thyroidectomy hypoparathyroidism).

This patient presents with classic findings of **acute symptomatic hypocalcemia** (serum calcium 6.7 mg/dL) on postoperative day 1 following total thyroidectomy for papillary thyroid carcinoma. The clinical features — perioral numbness, paresthesias of the hands and feet, and a positive **Trousseau sign** (carpal spasm with sphygmomanometer cuff inflation above systolic pressure) — are hallmark manifestations of hypocalcemia due to neuromuscular irritability.[1]

Why hypoparathyroidism from inadvertent parathyroid removal is the best answer:

- Post-thyroidectomy hypoparathyroidism is the **most common complication** of bilateral thyroid surgery, occurring in 20–50% of patients, due to inadvertent excision, devascularization, or mechanical injury to the parathyroid glands. Malignancy and total thyroidectomy are independent risk factors for incidental parathyroidectomy.[2][3][4][5]
- The hypocalcemia typically develops within **24–72 hours** postoperatively, consistent with this patient's presentation on postoperative day 1.[1][6]

Why the other options are less likely:

- **DiGeorge syndrome (B):** This congenital condition involves aplasia/hypoplasia of the parathyroid glands and thymus due to 22q11.2 deletion. It presents in infancy, not in a 55-year-old with no prior history of hypocalcemia.

- **Chronic hypomagnesemia (C):** While the serum magnesium is mildly low (1.1 mEq/L), this is likely a consequence of the acute postoperative state rather than a chronic condition. Chronic hypomagnesemia can impair PTH secretion, but the temporal relationship to surgery makes inadvertent parathyroid removal far more likely.

- **Hungry bone syndrome (D):** This occurs primarily in patients with **preoperative thyrotoxicosis or hyperparathyroidism**, where chronically elevated bone turnover leads to rapid skeletal calcium uptake after surgery. This patient had papillary thyroid carcinoma (not thyrotoxicosis), and hungry bone syndrome occurs essentially exclusively in thyrotoxic patients undergoing thyroidectomy. In euthyroid patients with benign or malignant thyroid nodules, hypoparathyroidism — not hungry bone syndrome — is the predominant cause of postoperative hypocalcemia.[7]

Would you like to explore the optimal management algorithm for acute post-thyroidectomy hypocalcemia, including the role of PTH monitoring for early prediction and discharge planning?

References

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Question 418

A 16-year-old boy is brought to the physician by his parents for the evaluation of fatigue for several weeks. The parents report that their son quit doing sports at school because of low energy. The patient's academic performance has declined recently. He spends most of his time in the basement playing video games and eating bowls of cereal. He has no history of serious illness. His mother has Hashimoto's thyroiditis and his father has major depressive disorder. The patient does not smoke or drink alcohol. His vital signs are within normal limits. Examination shows conjunctival pallor, inflammation and fissuring of the corners of the mouth, and concavity of the finger nails. The remainder of the examination shows no abnormalities. Laboratory studies show:
Hemoglobin 11.5 g/dL
Mean corpuscular volume 76 µm3
Platelet count 290,000/mm3
Red cell distribution width 18% (N = 13%–15%)
Leukocyte count 7,000/mm3
Which of the following is the most appropriate initial step in treatment?

Answer Choices:

(A) Regular blood transfusions
(B) Methylphenidate
(C) Iron supplementation
(D) Allogenic stem cell transplantation

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/27178dbd-939e-4fce-bfb1-d856f75590fb

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OpenEvidence Explanation

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The answer is **C. Iron supplementation**.

This presentation is classic for **iron deficiency anemia (IDA)**. The key findings supporting this diagnosis include:

- **Microcytic anemia**: hemoglobin 11.5 g/dL with MCV 76 μm³ (low)
- **Elevated RDW (18%)**: indicating anisocytosis, characteristic of iron deficiency
- **Physical exam findings**: conjunctival pallor (anemia), **angular cheilitis** (inflammation/fissuring at the corners of the mouth), and **koilonychia** (spoon-shaped/concave nails) — both are classic manifestations of iron deficiency
- **Dietary history**: spending most of his time eating bowls of cereal — a diet predominantly consisting of cereal is low in bioavailable (heme) iron and high in phytates from grains, which inhibit iron absorption

The fatigue, declining academic performance, and withdrawal from sports are all consistent with symptomatic anemia in an adolescent.

Why the other options are incorrect:

- **A. Regular blood transfusions** — Reserved for severe, symptomatic anemia or conditions like thalassemia major. This patient's anemia is mild and correctable with oral iron.
- **B. Methylphenidate** — While the declining school performance and video game use might superficially suggest ADHD, the symptoms are fully explained by iron deficiency anemia.

- **D. Allogeneic stem cell transplantation** — Indicated for severe hematologic disorders (e.g., aplastic anemia, thalassemia major), not simple iron deficiency.

Oral iron supplementation is the standard first-line treatment for iron deficiency anemia, along with dietary counseling to increase intake of iron-rich foods.

Would you like to explore the recommended dosing regimen and duration of oral iron supplementation in adolescents with iron deficiency anemia?

Question 419

A 78-year-old man is brought to the emergency department because of a 1-day history of painful enlarging bruises and skin ulceration over his thighs and external genitalia. He has type 2 diabetes mellitus, mitral regurgitation, and atrial fibrillation. Three days ago, he was started on treatment with warfarin. His only other medications are metformin and lisinopril. His temperature is 37.8°C (100.0°F), pulse is 108/min and irregularly irregular, and blood pressure is 155/89 mm Hg. Examination of the skin shows large purpura, hemorrhagic bullae, and areas of skin necrosis over his anterior legs, gluteal region, and penis. This patient is most likely to benefit from treatment with which of the following?

Answer Choices:

(A) Hyperbaric oxygen
(B) Protein C concentrate
(C) Argatroban
(D) Tranexamic acid

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/45f0f767-3185-43fa-bd83-21ef41a228ed

OpenEvidence Explanation

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The answer is **B. Protein C concentrate**.

This presentation is classic for **warfarin-induced skin necrosis (WISN)**, which typically develops **3–5 days after warfarin initiation** and presents with painful purpura, hemorrhagic bullae, and skin necrosis over adipose-rich areas (thighs, buttocks, breasts, and genitalia).[1][2] The pathophysiology involves a transient hypercoagulable state caused by the rapid decline of **protein C** (a natural anticoagulant with a short half-life of ~8 hours) before the procoagulant factors (II, IX, X) are adequately suppressed, leading to thrombotic occlusion of dermal and subcutaneous microvasculature.[2][3] Patients with underlying hereditary protein C or protein S deficiency are at highest risk.[1][2]

Why Protein C concentrate? Treatment of WISN includes immediate discontinuation of warfarin, administration of vitamin K, initiation of heparin anticoagulation, and **protein C concentrate** to directly replenish the depleted anticoagulant protein driving the microvascular thrombosis.[1][4] Case reports demonstrate that protein C concentrate halts necrosis progression within 24 hours of administration.[4] The FDA-approved protein C concentrate (Ceprotin) carries an indication for treatment of purpura fulminans and warfarin-induced skin necrosis in the setting of protein C deficiency.[5][6]

Why not the other options?

- **A. Hyperbaric oxygen** — Used for certain wound-healing indications (e.g., gas gangrene, chronic non-healing wounds) but does not address the underlying prothrombotic mechanism of WISN.
- **C. Argatroban** — A direct thrombin inhibitor used primarily for heparin-induced thrombocytopenia (HIT). While anticoagulation with heparin is part of WISN management, argatroban does not correct the protein C deficiency driving the pathology.
- **D. Tranexamic acid** — An antifibrinolytic agent that would be contraindicated in this prothrombotic condition, as it could worsen microvascular thrombosis.

Would you like to explore the recommended strategies for safely initiating warfarin in patients with known protein C or protein S deficiency?

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Question 420

A 15-year-old boy is brought to the physician for evaluation of a learning disability. His teachers have reported hyperactivity during class, difficulties with social interaction, and poor scores on reading and writing assessments. Molecular analysis shows an increased number of CGG trinucleotide repeats. Which of the following findings are most likely to be seen on physical examination of this patient?

Answer Choices:

(A) Frontal balding and cataracts
(B) Long face and large everted ears
(C) Almond-shaped eyes and downturned mouth
(D) Thin upper lip and receding chin

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/5df100ce-ed5c-48e1-b646-89498a720284

OpenEvidence Explanation

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The answer is **B. Long face and large everted ears**.

The clinical presentation — a 15-year-old boy with learning disability, hyperactivity, difficulties with social interaction, and an increased number of

CGG trinucleotide repeats — is diagnostic of **Fragile X syndrome (FXS)**. FXS is caused by expansion of CGG repeats (>200 repeats = full mutation) in the 5′ untranslated region of the *FMR1* gene on the X chromosome, leading to silencing of the gene and deficiency of FMRP protein.[1]

The characteristic physical features of Fragile X syndrome include a **long, narrow face**, **large prominent ears**, prominent jaw, high-arched palate, hyperextensible finger joints, soft skin, flat feet, and **macroorchidism** (particularly after puberty).[1][2][3] These craniofacial features become more obvious with age and are often subtle in early childhood.[3][4]

The other answer choices correspond to different conditions:

- **A (Frontal balding and cataracts)** — Myotonic dystrophy (CTG repeat expansion)
- **C (Almond-shaped eyes and downturned mouth)** — Prader-Willi syndrome (chromosome 15q11 deletion)
- **D (Thin upper lip and receding chin)** — Fetal alcohol spectrum disorder

Would you like to explore the behavioral and pharmacologic management strategies for Fragile X syndrome, including newer targeted therapies?

Relevant images

(CONTENT OMITTED)

References

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Question 426

A 51-year-old man presents to his primary care provider complaining of malaise. He returned from a research trip to Madagascar 2 weeks ago and has since developed a worsening fever with a maximum temperature of 102.2°F (39°C). He also reports some swelling around his neck and groin. He works as a zoologist and was in rural Madagascar studying a rare species of lemur. His past medical history is notable for hypertension and gout. He takes lisinopril and allopurinol. His temperature is 101.9°F (38.3°C), blood pressure is 145/85 mmHg, pulse is 110/min, and respirations are 22/min. On exam, he has painful erythematous cervical, axillary, and inguinal lymphadenopathy. Black hemorrhagic eschars are noted on his fingertips bilaterally. The pathogen responsible for this patient's condition produces a virulence factor that has which of the following functions?

Answer Choices:

(A) Cleave immunoglobulin
(B) Inhibit phagocytosis
(C) Inhibit ribosomal function
(D) Trigger widespread inflammation

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/868d1cc9-9b1d-4573-b69a-2ac1552217a3

OpenEvidence Explanation

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B. Inhibit phagocytosis. This presentation is most consistent with **bubonic plague** due to **Yersinia pestis**: fever after travel to rural Madagascar, painful cervical/axillary/inguinal buboes, and acral black hemorrhagic lesions. The key virulence factor tested here is the **F1 antiphagocytic capsule**, which helps the organism **resist phagocytosis**.[1][2]

Why this fits:

- **Madagascar** is a well-known plague-endemic region.[1]
- **Painful erythematous lymphadenopathy** in multiple nodal basins is classic for **buboes** in bubonic plague.[1][2]
- **Black hemorrhagic eschars/necrotic acral lesions** are compatible with plague-associated ischemic/hemorrhagic skin findings, historically linked to the "Black Death" phenotype.[1]
- Zoologic field exposure in rural endemic settings raises risk through **flea bites or contact with infected mammals**.[1][2]

Why the other choices are less likely:

- **A. Cleave immunoglobulin**: classically associated with IgA proteases from organisms such as Neisseria, H influenzae, and S pneumoniae, not Y pestis.
- **C. Inhibit ribosomal function**: suggests exotoxins such as diphtheria toxin, Shiga toxin, or Pseudomonas exotoxin A.
- **D. Trigger widespread inflammation**: endotoxin/LPS can contribute to sepsis, but the classic named virulence factor tested for Y pestis is its **antiphagocytic capsule/Yops-mediated immune evasion**, making **inhibit phagocytosis** the best answer.[1][2]

High-yield microbiology point:

- Y pestis virulence is mediated by **F1 capsule** and **type III secretion Yops**, which impair phagocytic host defenses and promote survival in tissue and lymph nodes.[1][2]

Would you like to explore the highest-yield differentiating features between **plague, tularemia, anthrax, and melioidosis** in travel/exposure vignettes?

References

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Question 427

A 45-year-old African-American male presents to the family medicine physician to assess the status of his diabetes. After reviewing the laboratory tests, the physician decides to write the patient a prescription for miglitol and states that it must be taken with the first bite of the meal. Which of the following bonds will no longer be cleaved when the patient takes miglitol?

Answer Choices:

(A) Phosphodiester bonds
(B) Glycosidic bonds
(C) Cystine bonds
(D) Hydrogen bonds

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/4398cc67-b821-47a7-a220-51926b36bdb0

OpenEvidence Explanation

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The answer is **B. Glycosidic bonds**.

Miglitol is an **alpha-glucosidase inhibitor** that works by reversibly inhibiting membrane-bound intestinal α-glucoside hydrolase enzymes in the brush border

of the small intestine.[1] These enzymes normally hydrolyze the **α-1,4-glycosidic bonds** in oligosaccharides and disaccharides, breaking them down into glucose and other monosaccharides.[1][2] By inhibiting this enzymatic cleavage, miglitol delays glucose absorption and reduces postprandial hyperglycemia.

This is why miglitol must be taken with the first bite of a meal — it needs to be present in the gut lumen at the same time as dietary carbohydrates to competitively inhibit the brush border enzymes before they can cleave the glycosidic bonds.[1][3]

The other answer choices are not relevant to miglitol's mechanism:

- **Phosphodiester bonds** link nucleotides in DNA/RNA — unrelated to carbohydrate digestion.
- **Cystine (disulfide) bonds** are covalent bonds between cysteine residues in proteins — unrelated to carbohydrate metabolism.
- **Hydrogen bonds** are weak noncovalent interactions found throughout biological molecules — not specifically targeted by miglitol.

Would you like to explore how alpha-glucosidase inhibitors compare to other oral antihyperglycemic agents in terms of efficacy and cardiovascular outcomes?

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Question 428

A previously healthy 24-year-old man comes to the physician 1 day after the onset of burning pain, swelling, and multiple blisters over the left index finger. He works as a dental assistant and is concerned about not being able to work. The patient wonders if the symptoms might be related to a hunting trip he returned from 1 week ago because he remembers seeing a lot of poison oak. He is sexually active with one female partner, and they do not use condoms. His father has a history of thromboangiitis obliterans. He has smoked one pack of cigarettes daily for 5 years. He drinks two to four beers on social occasions. Vital signs are within normal limits. Physical examination shows swelling and erythema of the pulp space of the left index finger; there are multiple 3-mm vesicles. Laboratory studies show a leukocyte count of 12,000 cells/mm3. In addition to supportive therapy, which of the following is the most appropriate next step in management?

Answer Choices:

(A) Oral acyclovir
(B) Oral cephalexin
(C) Smoking cessation
(D) Washing thoroughly

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/7952533e-02ad-4b01-a4a6-1286b4fd14ec

OpenEvidence Explanation

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The answer is **A. Oral acyclovir**. This presentation is classic for **herpetic whitlow** — an HSV infection of the distal finger — and the most appropriate next step in management is oral antiviral therapy with acyclovir.

Why herpetic whitlow? The combination of burning pain, swelling, erythema of the pulp space, and multiple small vesicles on the finger of a dental assistant (occupational exposure to oral secretions) is the hallmark presentation. Dental and medical healthcare workers are at elevated risk for herpetic whitlow due to contact with patients' oral mucosa and secretions.[1][2] HSV-1 infection of the hand in healthcare workers may last 21–28 days and be associated with severe pain and lymphangitis.[1]

Why not the other options?

- **Oral cephalexin (B):** This would be appropriate for a bacterial paronychia or cellulitis, but the vesicular nature of the lesions and the clinical context point to a viral etiology. Incision and drainage or antibiotics for a misdiagnosed bacterial infection is a common pitfall with herpetic whitlow and can worsen outcomes.[3]
- **Smoking cessation (C):** While relevant to his father's history of thromboangiitis obliterans and his own smoking history, this does not address the acute presentation.
- **Washing thoroughly (D):** This would be appropriate for poison oak/contact dermatitis, but the localized vesicular eruption on the pulp space of a single finger with burning pain is inconsistent with contact dermatitis, which typically presents with diffuse, pruritic, linear streaks.

Treatment: Both primary and recurrent herpetic whitlow respond to oral acyclovir.[4] Prompt initiation of antiviral therapy leads to faster healing, decreased pain, and shorter duration of viral shedding.[2] Standard dosing for mucocutaneous HSV is acyclovir 400 mg three times daily for 5–10 days.[5][6]

Would you like to explore the occupational health recommendations for healthcare workers with herpetic whitlow, including return-to-work guidelines?

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Question 429

A 63-year-old man presents to the ambulatory medical clinic with symptoms of dysphagia and 'heartburn', which he states have become more troublesome over the past year. His past medical history is significant for hypertension and GERD. He takes lisinopril for hypertension and has failed multiple different therapies for his GERD. On physical exam, he is somewhat tender to palpation over his upper abdomen. Barium swallow demonstrates a subdiaphragmatic gastroesophageal junction, with herniation of the gastric fundus into the left hemithorax. Given the following options, what is the most appropriate next step in the management of this patient's underlying condition?

Answer Choices:

(A) Lifestyle modification
(B) Combined antacid therapy
(C) Continue on Omeprazole
(D) Surgical gastropexy

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/5be3d5f3-9d1d-42e1-8da9-0d8aa99ab4df

OpenEvidence Explanation

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The answer is **D. Surgical gastropexy**.

The barium swallow findings — a subdiaphragmatic gastroesophageal (GE) junction with herniation of the gastric fundus into the left hemithorax — describe a **type II (paraesophageal) hiatal hernia**, in which the GE junction remains in its normal position but the gastric fundus herniates through the hiatus alongside the esophagus. This patient has symptomatic disease (dysphagia, heartburn) that has **failed multiple medical therapies**, making surgical intervention the appropriate next step.

Why surgical management is indicated:

- The ACG guidelines recommend antireflux surgery for patients with objective evidence of GERD who have large hiatal hernias and persistent, troublesome symptoms, particularly when medical management has failed. [1]
- Paraesophageal hernias specifically carry risk of progression to gastric volvulus, obstruction, or ischemia, and symptomatic paraesophageal hernias warrant surgical repair. Emergent repair carries up to a sevenfold increase in mortality compared to elective repair, and outcomes are significantly better when performed electively.[2][3][4][5]
- **Gastropexy** — suturing the stomach to the anterior abdominal wall — is a recognized surgical technique used in paraesophageal hernia repair to anchor the reduced stomach in the abdomen and reduce recurrence. A recent randomized clinical trial in JAMA Surgery evaluated anterior gastropexy as an adjunct to minimally invasive paraesophageal hernia repair.[3][6]

Why the other options are incorrect:

- **A (Lifestyle modification)** and **B (Combined antacid therapy)**: These are conservative measures appropriate for uncomplicated GERD or type I (sliding) hiatal hernias. This patient has already failed multiple medical therapies, and a paraesophageal hernia with symptomatic herniation requires surgical correction — medical therapy alone does not address the anatomic defect.[7][8]

- **C (Continue Omeprazole)**: Continuing a PPI does not address the underlying paraesophageal hernia and has already proven insufficient for symptom control in this patient.

Would you like to explore the specific surgical techniques and outcomes data comparing different approaches to paraesophageal hernia repair (e.g., fundoplication vs. gastropexy, mesh vs. no mesh)?

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Question 430

A 63-year-old man is admitted to the intensive care unit for hemodynamic instability. Several days prior, he had been swimming in the Gulf coast when he stepped on a sharp rock and cut his right foot. Three days ago, the patient presented to the emergency room after noticing painful redness spreading along his skin up from his right foot and was subsequently admitted for antibiotic treatment. Currently, his temperature is 101.8°F (38.8°C), blood pressure is 84/46 mmHg with a mean arterial pressure of 59 mmHg, pulse is 104/min, and respirations are 14/min. His telemetry shows sinus tachycardia. His blood cultures are pending, but Gram stain demonstrated gram-negative bacilli. Which of the following best describes the form of shock and the skin exam?

Answer Choices:

(A) Distributive shock with warm skin
(B) Hypovolemic shock with warm skin
(C) Neurogenic shock with cold skin
(D) Obstructive shock with cold skin

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/0187f6da-8e1a-4d06-bb9a-229669c449c7

OpenEvidence Explanation

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The correct answer is **A. Distributive shock with warm skin**.

This patient presents with **septic shock**, which is a form of **distributive shock**. The clinical scenario — a foot laceration sustained in Gulf coast waters, spreading cellulitis with gram-negative bacilli on Gram stain, fever, hypotension (MAP 59 mmHg), and tachycardia — is classic for gram-negative sepsis, possibly from organisms such as *Vibrio vulnificus* (a well-known pathogen associated with Gulf coast water exposure and wound infections).

Why distributive shock with warm skin?

Septic shock is the prototypical distributive shock, characterized by inappropriate peripheral vasodilation due to the release of inflammatory mediators (cytokines, nitric oxide, prostaglandins). This vasodilation leads to decreased systemic vascular resistance and, in the early ("warm") phase, results in **warm, flushed skin** with a bounding pulse and increased cardiac output.[1][2] This is in contrast to hypovolemic, cardiogenic, or obstructive shock, which present with cold, clammy skin due to compensatory vasoconstriction.[2]

The pathophysiology of septic shock progresses through recognizable phases:[1][3]

- **Early ("warm") shock**: Vasodilation with decreased SVR, increased cardiac output, warm peripheries, and a bounding pulse
- **Late ("cold") shock**: Progressive cardiovascular decompensation with vasoconstriction, decreased cardiac output, and cold, clammy skin
- **Refractory shock**: Profound acidemia, vascular hyporesponsiveness, and multiorgan failure

The following figure illustrates this pathophysiological cascade from warm to cold shock in sepsis:

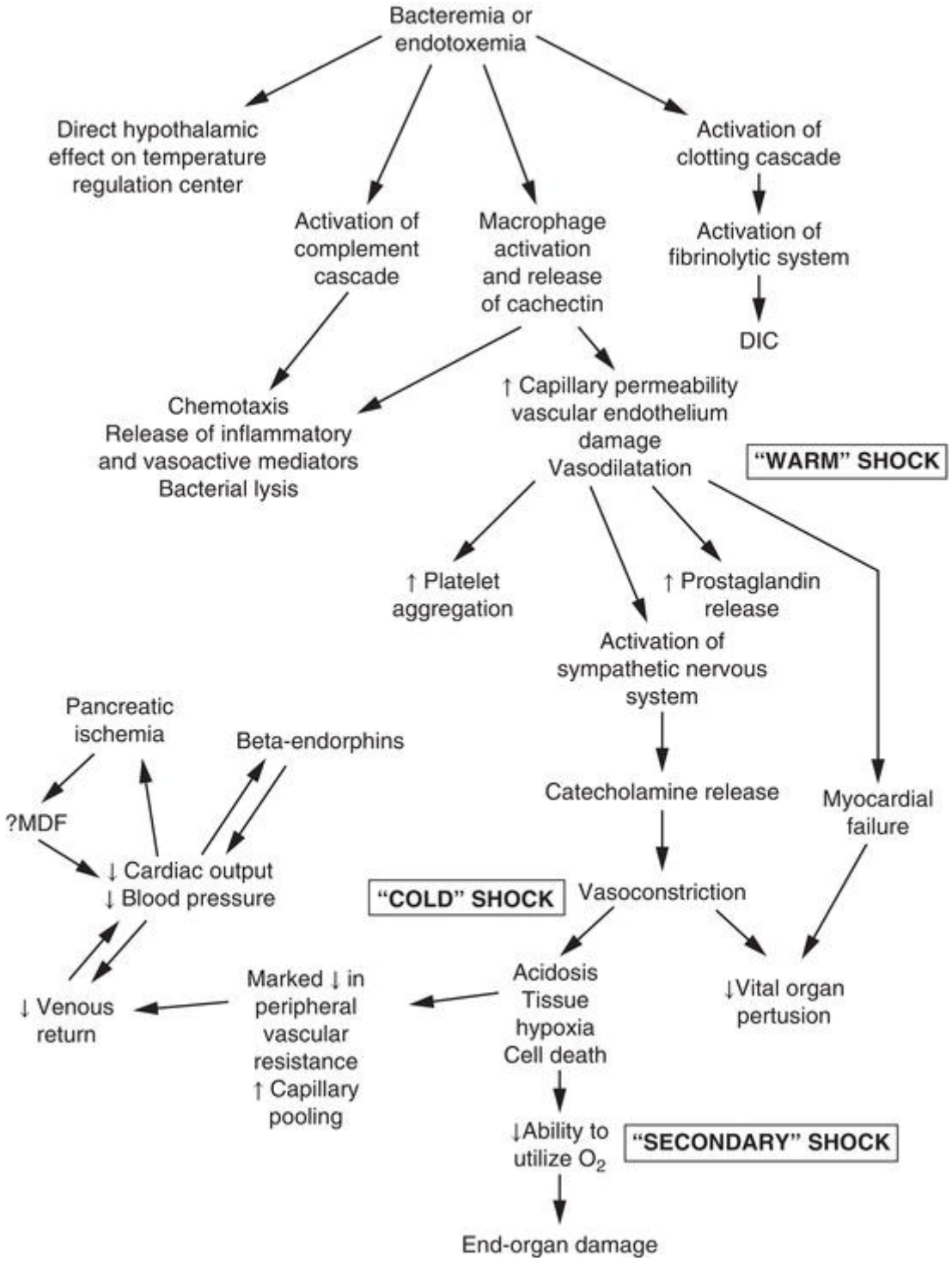


Figure 1. Pathophysiology of septic shock. DIC, disseminated intravascular coagulopathy; MDF, myocardial depressant factor; O 2 , oxygen.

The other answer choices are incorrect because:

- **B (Hypovolemic shock)** — would present with cold, clammy skin from compensatory vasoconstriction, and the clinical picture here is driven by infection, not volume loss

- **C (Neurogenic shock)** — results from loss of sympathetic tone (e.g., spinal cord injury), not infection
- **D (Obstructive shock)** — caused by mechanical obstruction to blood flow (e.g., tension pneumothorax, cardiac tamponade, massive PE), not applicable here

Would you like to explore the specific antibiotic management of *Vibrio vulnificus* wound infections and the role of early surgical debridement in necrotizing soft tissue infections?

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Question 432

A 54-year-old woman is brought to the physician by her brother for confusion and agitation. She is unable to personally give a history. Her brother says she has a problem with alcohol use and that he found an empty bottle of vodka on the counter at her home. She appears disheveled. Her temperature is 37°C (98.6°F), pulse is 85/min, and blood pressure is 140/95 mm Hg. On mental status examination, she is confused and oriented only to person. She recalls 0 out of 3 words after 5 minutes. She cannot perform serial sevens and is unable to repeat seven digits forward and five in reverse sequence. Neurologic examination shows horizontal nystagmus on lateral gaze. She has difficulty walking without assistance. Laboratory studies show:
Hemoglobin 11 g/dL
Mean corpuscular volume 110 µm3
Platelet count 280,000/mm3
Which of the following is most appropriate initial treatment for this patient?

Answer Choices:

(A) Intravenous thiamine
(B) Oral naltrexone
(C) Intravenous vitamin B12
(D) Intravenous glucose

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/ee10f315-15df-4b9f-9e12-d7752932e50e

OpenEvidence Explanation

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The correct answer is **A. Intravenous thiamine**.

This patient presents with the classic triad of **Wernicke encephalopathy (WE)**: encephalopathy (confusion, disorientation, impaired memory), oculomotor dysfunction (horizontal nystagmus), and gait ataxia (difficulty walking) — all in the setting of chronic alcohol use disorder.[1][2] The macrocytic anemia (MCV 110 μm^3) further supports nutritional deficiency associated with chronic alcohol use.

Why intravenous thiamine is the correct initial treatment:

- WE is a medical emergency caused by thiamine (vitamin B1) deficiency, and prompt parenteral thiamine replacement is the cornerstone of treatment. Oral thiamine is inadequate due to erratic gastrointestinal absorption in malnourished patients with alcohol use disorder.[1][3][4]
- Acute thiamine replacement is typically given at **100–500 mg IV**, with recent evidence favoring higher doses (e.g., 500 mg IV three times daily for 2–3 days).[3][5][6]

Why not the other options:

- **D. Intravenous glucose** — Glucose administration in a thiamine-depleted patient can precipitate or worsen WE, as carbohydrate metabolism consumes thiamine as a cofactor. Thiamine must be given **before or concurrently with** glucose.[3][6]
- **B. Oral naltrexone** — Naltrexone is used for long-term treatment of alcohol use disorder to reduce cravings, not for acute management of WE.
- **C. Intravenous vitamin B12** — While B12 deficiency can also cause macrocytic anemia, it does not explain the acute triad of encephalopathy, nystagmus, and ataxia seen here. B12 replacement is not the priority in this acute presentation.

Without treatment, approximately **80% of patients with WE progress to Korsakoff syndrome**, an irreversible condition characterized by profound amnesia and confabulation.[1][4]

Would you like to explore the optimal dosing regimens for IV thiamine in Wernicke encephalopathy and the evidence comparing standard-dose versus high-dose protocols?

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Question 433

An 18-year-old woman makes an appointment with a gynecologist for her first gynecologic examination. She did not disclose her past medical history, but her sexual debut occurred with her boyfriend 3 weeks ago. She is now complaining of a yellow-green, diffuse, malodorous vaginal discharge that she noticed 1 week ago for the first time. She also reported mild pelvic and abdominal pain. cervical motion tenderness was noted during the pelvic examination. The gynecologist also noticed a pink and inflamed nulliparous cervix with a preponderance of small red punctate spots. There was a frothy white discharge with a malodorous odor in the vaginal vault. A wet mount was prepared for a light microscopic examination, which revealed numerous squamous cells and motile organisms. The gynecologist concluded that this was a sexually-transmitted infection. What is the causative organism?

Answer Choices:

(A) Chlamydia trachomatis
(B) Ureaplasma urealyticum
(C) Trichomonas vaginalis
(D) Enterobius vermicularis

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/50948b00-371f-4797-8e1f-cde8de4d228f

OpenEvidence Explanation

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The answer is **C. Trichomonas vaginalis**.

The clinical presentation is classic for **trichomoniasis**, caused by the flagellated protozoan *Trichomonas vaginalis*:

- **"Strawberry cervix"** — the pink, inflamed cervix with small red punctate spots (colpitis macularis) is a pathognomonic finding, present in a minority of cases but highly specific for trichomoniasis.
- **Frothy, malodorous, yellow-green vaginal discharge** — the frothy quality is characteristic of *T. vaginalis* infection.
- **Motile organisms on wet mount** — *T. vaginalis* is a motile, pear-shaped, flagellated protozoan readily identified on saline wet prep by its jerky, tumbling motility. The "numerous squamous cells" alongside motile organisms is the hallmark microscopic finding.
- **Cervical motion tenderness and pelvic pain** — while more commonly associated with PID, trichomoniasis can cause cervicitis and upper tract irritation.

Why not the other options?

- **A. Chlamydia trachomatis** — an obligate intracellular bacterium that cannot be seen on wet mount as motile organisms. It typically causes mucopurulent cervicitis or may be asymptomatic.
- **B. Ureaplasma urealyticum** — a tiny bacterium (Mollicutes class) not visible on light microscopy wet mount; it does not produce frothy discharge or strawberry cervix.
- **D. Enterobius vermicularis** — pinworm; causes perianal pruritus, not a sexually transmitted vaginitis with motile organisms on wet prep.

Would you like to explore the recommended treatment regimens for trichomoniasis, including the updated CDC guidelines on metronidazole dosing?

Question 434

A 70-year-old man is brought to the physician by his daughter because of increasing forgetfulness over the past 3 years. Initially, he used to forget his children's names or forget to lock the house door. During the past year, he has gotten lost twice while returning from the grocery store and was unable to tell passersby his address. One time, he went to the park with his granddaughter and returned home alone without realizing he had forgotten her. His daughter says that over the past year, he has withdrawn himself from social gatherings and avoids making conversation. He does not sleep well at night. His daughter has hired a helper to cook and clean his home. On mental status examination, he is oriented only to person. He describes his mood as fair. Short- and long-term memory deficits are present. He appears indifferent about his memory lapses and says this is normal for someone his age. The most appropriate initial pharmacotherapy for this patient is a drug that acts on which of the following neurotransmitters?

Answer Choices:

(A) γ-aminobutyric acid
(B) Acetylcholine
(C) Dopamine
(D) Glutamate

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/59cbca5b-794e-41d7-a457-108c993f6365

OpenEvidence Explanation

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The correct answer is **B. Acetylcholine**.

This patient presents with a classic picture of **moderate-to-severe Alzheimer disease** (AD): progressive memory loss over 3 years, getting lost in familiar places, inability to recall his address, impaired judgment (leaving his granddaughter at the park), social withdrawal, and orientation only to person. The **initial pharmacotherapy** for AD targets the **cholinergic system** through **acetylcholinesterase inhibitors** (donepezil, rivastigmine, or galantamine), which increase acetylcholine availability at the synaptic cleft.[1][2][3]

The rationale is based on the **cholinergic hypothesis**: degeneration of cholinergic neurons in the basal forebrain leads to decreased acetylcholine levels, contributing to the memory and cognitive deficits seen in AD.[4] Acetylcholinesterase inhibitors are the **first-line** pharmacologic treatment across mild, moderate, and severe stages of AD.[5][6]

Why not the other options?

- **A. GABA** — No GABA-targeting drugs are approved for AD treatment. Drugs targeting the GABAergic system have not shown cognitive benefits in AD.[5]
- **C. Dopamine** — While dopaminergic deficits exist in AD, drugs targeting dopamine have not demonstrated cognitive improvement.[5]
- **D. Glutamate** — Memantine, an NMDA receptor antagonist that modulates glutamate activity, is approved for **moderate-to-severe** AD but is not the initial pharmacotherapy. It is typically added to a cholinesterase inhibitor rather than used as first-line monotherapy.[6][7]

Would you like to explore the evidence comparing cholinesterase inhibitors head-to-head for efficacy and tolerability in Alzheimer disease?

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Question 435

A 45-year-old mechanic presents to the emergency department complaining of acute-onset shortness of breath while repairing a plowing tractor for his neighbor. The patient denies having any history of asthma or respiratory symptoms, and does not smoke. His temperature is 99.8°F (37.7°C), pulse is 65/min, blood pressure is 126/86 mmHg, and respirations are 20/min. His oxygen saturation is 97%. On exam, he is pale and diaphoretic. His pupils are contracted. Diffuse wheezes are noted in all lung fields. What is the best treatment for his condition?

Answer Choices:

(A) Succinylcholine
(B) Inhaled ipratropium and oxygen
(C) Atropine and pralidoxime
(D) Inhaled albuterol and oxygen

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/ad367c79-ceac-44d8-81c8-2ea1d70d7d09

OpenEvidence Explanation

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The correct answer is **C. Atropine and pralidoxime**.

This presentation is classic for **organophosphate poisoning**. The clinical scenario — a mechanic working on a plowing tractor (agricultural equipment likely treated with organophosphate pesticides) — combined with the constellation of **miosis** (contracted pupils), **diaphoresis**, **diffuse wheezing** (bronchospasm), and **low-grade fever** represents a cholinergic toxidrome from acetylcholinesterase inhibition.[1][2]

The muscarinic features here (miosis, bronchospasm, diaphoresis) are remembered by the mnemonic **SLUDGE** (Salivation, Lacrimation, Urination, Defecation, GI cramping, Emesis) plus the "killer B's" (Bradycardia, Bronchospasm, Bronchorrhea).[3]

Why atropine and pralidoxime? Per AHA guidelines, the cornerstones of treatment for organophosphate poisoning are **atropine** (blocks muscarinic overstimulation, relieving bronchospasm, bronchorrhea, and bradycardia) and **pralidoxime** (an oxime that reactivates acetylcholinesterase, reversing nicotinic effects such as muscle weakness and paralysis).[1] Early atropine administration improved survival in a clinical trial, and high-dose pralidoxime regimens have been associated with greater survival and lower rates of pneumonia.[4]

Why not the other options?

- **A. Succinylcholine** — Contraindicated. Succinylcholine is metabolized by butyrylcholinesterase (pseudocholinesterase), which is inhibited by organophosphates. Its use can result in **prolonged neuromuscular blockade lasting several hours**.[4]
- **B. Inhaled ipratropium and oxygen** — While ipratropium is an anticholinergic bronchodilator, it only addresses local airway muscarinic effects and does not treat the systemic cholinergic crisis. It is not the definitive treatment.
- **D. Inhaled albuterol and oxygen** — This would be appropriate for asthma or reactive airway disease, but the miosis, diaphoresis, and occupational context point to organophosphate toxicity requiring systemic antidotal therapy, not just bronchodilation.

Would you like to explore the specific atropine dosing protocol and titration endpoints for organophosphate poisoning?

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Question 438

A 45-year-old man comes to his primary-care doctor with his wife for a 4-week history of constipation. The patient reports that his bowel habits have changed from every day to every 3 or 4 days. He also now has to strain to pass stool. On further questioning, his wife has also noticed that he has seemed fatigued, with little interest in going on their usual afternoon walks. Medical history is notable for hypertension and hyperlipidemia, both managed medically. He was last seen for follow-up of these conditions 1 month ago. Physical examination is unremarkable. Which of the following is the cellular target of the medicine that is most likely responsible for this patient's symptoms?

Answer Choices:

(A) Angiotensin-II receptors in the membranes of vascular smooth muscle cells
(B) Angiotensin-converting enzyme
(C) Na+/Cl- cotransporter in the membranes of epithelial cells in the distal convoluted tubule
(D) Na+/K+/2Cl- transporters in the membranes of epithelial cells in the ascending loop of Henle

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/9054f2e4-f44b-4e54-9226-c5eb754f40ea

OpenEvidence Explanation

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The answer is **C. Na+/Cl- cotransporter in the membranes of epithelial cells in the distal convoluted tubule**.

This patient presents with new-onset **constipation**, **fatigue**, and **decreased interest in activities** — a constellation consistent with **hypercalcemia** secondary to a **thiazide diuretic** (e.g., hydrochlorothiazide), which is commonly prescribed for hypertension and was likely initiated at his visit 1 month ago. Thiazide diuretics decrease calcium excretion and can cause hypercalcemia, which classically manifests with constipation, fatigue, and psychiatric symptoms (the classic mnemonic: "stones, bones, groans, and psychiatric moans"). Constipation is also a directly listed adverse reaction of hydrochlorothiazide.[1][2][3]

Mechanism of action: Thiazide diuretics inhibit the **Na+/Cl- cotransporter (NCC)** located on the apical membrane of epithelial cells in the **distal convoluted tubule** (DCT).[4][5][6] By blocking this electroneutral symporter, thiazides reduce sodium and chloride reabsorption, promoting natriuresis and diuresis.[1] The reduced intracellular sodium also enhances basolateral Na+/Ca2+ exchange, leading to increased calcium reabsorption — explaining the hypocalciuric and potentially hypercalcemic effect.[7]

Why not the other options:

- **A (Angiotensin-II receptors)** — ARBs are associated with diarrhea rather than constipation, and have placebo-like tolerability with possible mood-protective effects.[8][9][10]
- **B (ACE)** — ACE inhibitors are most notably associated with dry cough and angioedema; they are not typically linked to constipation or the symptom complex described.[11]
- **D (Na+/K+/2Cl- transporters in the ascending loop of Henle)** — This is the target of loop diuretics (e.g., furosemide), which cause hypercalciuria (the opposite of thiazides) and would not explain hypercalcemia-related symptoms.

Would you like to explore the workup and management of thiazide-induced hypercalcemia, including when to suspect an underlying primary hyperparathyroidism unmasked by thiazide use?

Relevant images

(CONTENT OMITTED)

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Question 439

A 23-year-old man presents to the office for a circular, itchy rash over the abdomen that has been slowly getting worse for the past 2 weeks. The patient has a medical history of chronic dermatitis and chronic sinusitis for which he has prescriptions of topical hydrocortisone and fexofenadine. He smokes one-half pack of cigarettes every day. His vital signs include: blood pressure 128/76 mm Hg, heart rate 78/min, and respirations 12/min. On physical examination, the patient appears tired but oriented. Examination of the skin reveals a 2 x 2 cm round and erythematous, annular plaque on the abdomen 3 cm to the left of the umbilicus. There are no vesicles, pustules, or papules. Auscultation of the heart reveals a 1/6 systolic murmur. Breath sounds are mildly coarse at the bases. A KOH preparation from the skin scraping confirms the presence of hyphae. Which of the following is the next best step in the management of this patient?

Answer Choices:

(A) Itraconazole
(B) Griseofulvin
(C) Topical clindamycin
(D) Doxycycline

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/1f8cf210-762a-4adc-a586-797c198158a9

OpenEvidence Explanation

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The best next step is **A. Itraconazole**. This patient has a KOH-confirmed dermatophyte infection (tinea corporis) that has been **worsening despite ongoing use of topical hydrocortisone**, which can exacerbate fungal infections by suppressing local immune responses and promoting dermatophyte growth.[1][2]

Why oral antifungal therapy is appropriate here:

The patient's tinea corporis has been progressively worsening over 2 weeks in the setting of chronic topical corticosteroid use. Topical corticosteroids can mask symptoms while allowing fungal proliferation and deeper tissue invasion.[2] Oral antifungal agents are indicated when tinea corporis has failed to respond to (or been worsened by) prior treatment, or when there are complicating factors such as concurrent immunosuppressive therapy.[3] Itraconazole 100 mg daily for 2 weeks is an effective regimen for tinea corporis.[4][5]

Why not the other options:

- **B. Griseofulvin** — While FDA-approved for tinea corporis, griseofulvin has demonstrated inferior cure rates compared to itraconazole (14% vs. 66% at 8 weeks in one trial) and is generally considered less effective.[6]
- **C. Topical clindamycin** — Clindamycin is an antibacterial agent with no antifungal activity; it would be inappropriate for a confirmed dermatophyte infection.
- **D. Doxycycline** — Doxycycline is an antibacterial/anti-inflammatory agent and has no role in treating dermatophyte infections.

The following table summarizes common antifungal options for tinea infections:

TABLE 4

Common Antifungals for the Treatment of Tinea Infections

Medication	Formulation	Uses*	Dosage and duration*	Cost†
Terbinafine	Oral	Label: onychomycosis of the toenail or fingernail caused by dermatophytes Off-label: dermatophyte folliculitis (eg, tinea barbae, Majocchi granuloma), tinea capitis, tinea corporis, tinea cruris, tinea manuum, tinea pedis	250 mg once daily 6-12 weeks for onychomycosis; 4-6 weeks for tinea capitis	$20 for 30 tablets
	Topical	Label: tinea corporis, tinea cruris, tinea pedis Off-label: tinea manuum	1% once daily 1-2 weeks	$15 for a 30-g tube at Walgreens
Itraconazole	Oral	Label: onychomycosis of the toenail, with or without fingernail involvement, and onychomycosis of the fingernail caused by dermatophytes (tinea unguium) in nonimmunocompromised patients Off-label: fungal folliculitis, tinea capitis, tinea corporis, tinea cruris, tinea manuum, tinea pedis	200 mg twice daily 6-12 weeks for onychomycosis; 2-12 weeks for tinea capitis; 1-2 weeks for tinea infections besides onychomycosis (some patients, such as those with *Trichophyton indotineae* infection, may require longer treatment)	$40 for 30 capsules
Fluconazole	Oral	Off-label: onychomycosis, tinea capitis, tinea corporis, tinea cruris, tinea pedis	150-450 mg once weekly 6-12 weeks for onychomycosis; 2-6 weeks for other types of tinea infection	$30 for 2 tablets (150 mg)
Clotrimazole	Topical	Label: tinea corporis, tinea cruris, tinea pedis Off-label: tinea manuum	1% twice daily 1-4 weeks	$15 for a 30-g tube
Ketoconazole	Topical	Label:, tinea corporis, tinea cruris, tinea pedis Off-label: tinea manuum	2% once daily 2-4 weeks	$30 for a 60-g tube
Griseofulvin	Oral	Label: tinea barbae, tinea capitis, tinea corporis, tinea cruris, tinea pedis, tinea unguium Off-label: tinea manuum	500-1,000 mg once daily 6-12 weeks for tinea capitis	$105 for 30 tablets
Butenafine	Topical	Label: tinea corporis, tinea cruris, tinea pedis Off-label: tinea manuum	1% once daily 1-4 weeks	$10 for a 30-g tube
Efinaconazole (Jublia)	Topical	Label: mild to moderate onychomycosis of the toenail	10% once daily 48 weeks	$800 for a 4-mL bottle of Jublia (not available as generic)
Ciclopirox	Topical	Label: tinea corporis (cream or suspension), tinea cruris, tinea pedis; topical treatment in immunocompetent patients with mild to moderate onychomycosis (lacquer) Off-label: tinea manuum	8% once daily (lacquer), 0.77% twice daily (cream) Up to 48 weeks for onychomycosis; 1-4 weeks for other tinea infections	$20 for a 30-g tube of cream $35 for a 30-mL bottle of suspension $25 for 1 bottle of lacquer
Tavaborole	Topical	Label: onychomycosis of the toenails	5% once daily Up to 48 weeks	$100 for a 10-mL bottle

*—Indication by US Food and Drug Administration label status. Information obtained from https://UpToDate.com. Accessed March 13, 2025.

Table 4. Common Antifungals for the Treatment of Tinea Infections

Would you like to explore the role of topical corticosteroids in exacerbating dermatophyte infections and the concept of "tinea incognito"?

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Question 441

A 40-year-old female presents to your office complaining of a tender neck and general lethargy. Upon further questioning, she reports decreased appetite, fatigue, constipation, and jaw pain. Her pulse is 60 bpm and her blood pressure is 130/110 mm Hg. Biopsy of her thyroid reveals granulomatous inflammation and multinucleate giant cells surrounding fragmented colloid. Which of the following likely precipitated the patient's condition:

> **Answer Choices:**
>
> (A) Iodine deficiency
> (B) Thryoglossal duct cyst
> (C) Infection
> (D) Chronic renal disease

> **Correct Answer:**
>
> (C)
>
> **OpenEvidence Response:**
>
> (C) ✓

OpenEvidence Link: https://openevidence.com/ask/a678fd2e-0d9d-4886-9ddc-c8e0cff3b482

OpenEvidence Explanation

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The correct answer is **C. Infection**.

This clinical presentation — a 40-year-old woman with a tender neck, fatigue, constipation, jaw pain, bradycardia, and biopsy showing **granulomatous inflammation with multinucleate giant cells surrounding fragmented colloid** — is classic for **subacute granulomatous thyroiditis (de Quervain thyroiditis)** in its hypothyroid phase. The patient's symptoms of bradycardia, constipation, fatigue, and decreased appetite are consistent with hypothyroidism, which follows the initial thyrotoxic phase of this triphasic disease.

Why infection is the precipitant: Subacute granulomatous thyroiditis is thought to be a sequela of a **viral upper respiratory tract infection** involving the thyroid gland.[1][2] Viruses commonly implicated include Coxsackievirus, adenovirus, Epstein-Barr virus, mumps, measles, influenza, and SARS-CoV-2.[1][3] The condition frequently follows an upper respiratory infection by 2–8 weeks, with peak incidence in late summer and fall correlating with enterovirus seasonality.[4][5] The pathogenesis is believed to involve either direct viral injury to thyroid follicular cells or a T-cell-mediated hypersensitivity reaction to follicular epithelial cells carrying viral antigens.[4]

Why the other options are incorrect:

- **A. Iodine deficiency** — causes endemic goiter, not granulomatous thyroiditis.
- **B. Thyroglossal duct cyst** — a congenital midline neck mass, unrelated to granulomatous inflammation of the thyroid.
- **D. Chronic renal disease** — can cause secondary/tertiary hyperparathyroidism and nonthyroidal illness syndrome, but does not cause granulomatous thyroiditis.

The neck pain radiating to the jaw, the characteristic biopsy findings of multinucleated giant cells with granulomatous inflammation around fragmented colloid, and the demographic (middle-aged woman) are all hallmarks of de Quervain thyroiditis.[2][5]

Would you like to explore the triphasic clinical course of subacute thyroiditis and how management differs in each phase?

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Question 442

A 24-year-old man is brought to the emergency room by the police after a fall. The patient smells of alcohol and is slurring his words. You find out that he has recently been fired from his job as a salesperson for months of tardiness and poor performance. The police tell you that his girlfriend, who was there at the time of the fall, mentioned that the patient has been struggling with alcohol for at least a year. Upon physical examination, the patient becomes agitated and starts yelling. He accuses his ex-boss of being a cocaine addict and says he couldn't keep up sales percentages compared to someone using cocaine. Which of the following psychiatric defense mechanisms is the patient demonstrating?

Answer Choices:

(A) Denial
(B) Displacement
(C) Projection
(D) Regression

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/b09e16c1-233c-4951-aa11-16d3d0d0b8f0

OpenEvidence Explanation

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The answer is **C. Projection**.

Projection is the defense mechanism in which a person attributes their own unacceptable thoughts, feelings, or behaviors to someone else.[1][2][3] In this scenario, the patient has a well-documented alcohol problem — fired for poor performance, a year-long history of alcohol use per his girlfriend, and presenting intoxicated to the ED. Rather than acknowledging his own substance use disorder and its consequences, he accuses his ex-boss of being a cocaine addict and blames the boss's supposed drug use for his own inability to keep up at work. He is projecting his own substance abuse onto another person.

Why the other options are incorrect:

- **Denial** would involve the patient simply refusing to acknowledge his alcohol problem altogether (e.g., "I don't have a drinking problem") without attributing it to someone else.[1][4]
- **Displacement** involves redirecting emotions from a threatening target to a less threatening one (e.g., yelling at a nurse instead of the boss). While the patient is angry, the key feature here is the attribution of substance abuse to the boss, not merely redirected anger.[5][6]
- **Regression** involves reverting to behaviors characteristic of an earlier developmental stage (e.g., throwing a tantrum like a child). Although the patient is agitated, his behavior centers on accusing someone else of his own problem, which is characteristic of projection rather than regression.[6]

Projection functions through at least three cognitive steps: differentiating internal from external experience, comparing a thought or feeling against internal standards, and then attributing the unacceptable thought or feeling to an external source — thereby avoiding shame or guilt.[1]

Would you like to explore how defense mechanisms are formally assessed in clinical settings, such as with the Defense Style Questionnaire or observer-rated methods?

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Question 444

A 61-year-old man complaining of unexplained bleeding by from the mouth is escorted to the emergency department by corrections officers. Upon examination patient states he feels nauseated as he begins to retch violently and vomit bright red blood. His past medical history is remarkable for cirrhosis secondary to alcohol abuse and untreated hepatitis C. His current blood pressure is 90/50 mm Hg, heart rate is 128/min, and oxygen saturation in room air is 88%. On further questioning, he states that he is scared to die and wants everything done to save his life. IV fluids are initiated and packed RBCs are ordered. You begin to review his labs and notice and he has elevated beta-hydroxybutyrate, ammonia, and lactate. What would be the appropriate response to the patient?

Answer Choices:

(A) Consult an ethics committee to determine whether to resuscitate the patient
(B) Accept the patient's wishes and appoint and get a psych evaluation.
(C) Accept the patient's wishes and ensure he receives appropriate care.
(D) Obtain an emergency order from a judge to initiate resuscitation.

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/50f0d77f-f6b4-4458-bc00-39ffa70b7a25

OpenEvidence Explanation

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The correct answer is **C. Accept the patient's wishes and ensure he receives appropriate care.**

This patient is presenting with an acute variceal hemorrhage in the setting of cirrhosis, is hemodynamically unstable, and is **explicitly requesting full resuscitative efforts** — stating he "wants everything done to save his life." The appropriate response is to honor his clearly expressed wishes and provide aggressive, appropriate care.

Several key principles support this answer:

Patient autonomy and decision-making capacity. Under the ethical principle of respect for autonomy, competent patients have the right to make decisions about their own medical care, including both refusing and requesting treatment.[1][2] This patient is conscious, communicating clearly, and expressing a consistent, unambiguous desire for life-saving intervention. His incarcerated status does not diminish his right to make medical decisions. Patients with decision-making capacity retain the right to accept or refuse medical interventions regardless of their legal status.[3]

No ethical or legal barrier to treatment here. There is no conflict between the patient's wishes and the clinical team's obligations — the patient wants treatment, and treatment is indicated for acute variceal hemorrhage. An ethics committee consultation (option A) would be appropriate when there is a dispute or ethical dilemma, but none exists here.[4] A psychiatric evaluation (option B) is unnecessary because the patient is not refusing care or expressing suicidal ideation — he is requesting appropriate treatment. A court order (option D) would only be relevant in scenarios involving treatment refusal or disputes over decision-making authority, neither of which applies.[5]

Clinical urgency. Acute variceal hemorrhage carries a 6-week mortality of 10–15% and requires timely resuscitation, vasoactive medications, and endoscopic intervention.[6] The patient's hemodynamic instability (BP 90/50, HR 128, SpO2 88%) and laboratory derangements (elevated lactate, ammonia, beta-

hydroxybutyrate) underscore the need for immediate, aggressive management consistent with his expressed wishes.

Would you like to explore the evidence-based management algorithm for acute variceal hemorrhage in decompensated cirrhosis, including the role of vasoactive agents, antibiotic prophylaxis, and early endoscopy?

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Question 445

Three days after undergoing a laparoscopic Whipple's procedure, a 43-year-old woman has swelling of her right leg. She does not have pain. She has nausea but has not vomited. She was diagnosed with pancreatic cancer 1 month ago. She has been using an incentive spirometer every 6 hours since recovering from her surgery. Prior to admission, her only medications were a multivitamin and an herbal weight-loss preparation. She appears uncomfortable. Her temperature is 38°C (100.4°F), pulse is 90/min, and blood pressure is 118/78 mm Hg. Examination shows mild swelling of the right thigh to the ankle; there is no erythema or pitting edema. Homan's sign is negative. The abdomen is soft and shows diffuse tenderness to palpation. There are five abdominal laparoscopic incisions with no erythema or discharge. The lungs are clear to auscultation. The remainder of the examination shows no abnormalities. Which of the following is the most appropriate next step in management?

Answer Choices:

(A) CT pulmonary angiography
(B) Compression ultrasonography
(C) D-dimer level
(D) 2 sets of blood cultures

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/46ecc91d-614c-48b9-aa82-25a2f0c2e5b6

OpenEvidence Explanation

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The answer is **B. Compression ultrasonography**.

This postoperative patient with **pancreatic cancer** and **unilateral right leg swelling** 3 days after a Whipple procedure has a high pretest probability for **deep vein thrombosis (DVT)**. Multiple major risk factors are present: active malignancy, recent major abdominal surgery, and postoperative immobilization. The most appropriate next step is **compression ultrasonography**, which is the first-line imaging test for suspected DVT.[1][2][3]

Why not the other options?

- **D-dimer level (C)** — D-dimer testing has limited utility in this scenario for two reasons. First, D-dimer specificity is markedly reduced in cancer patients due to the hypercoagulable state associated with malignancy. Second, D-dimer is expected to be elevated after major surgery, making it essentially non-informative. Both NCCN and JAMA reviews recommend proceeding directly to imaging rather than D-dimer testing in cancer patients with suspected DVT. An individual participant data meta-analysis confirmed that clinical models followed by D-dimer testing fail to efficiently rule out DVT in cancer patients, and direct referral for compression ultrasonography is the preferred approach.[2][3][4][5]

- **CT pulmonary angiography (A)** — While this patient is at risk for pulmonary embolism, the clinical presentation (leg swelling without respiratory symptoms, clear lungs, no hypoxemia or chest pain) points to DVT rather than PE. The appropriate initial step is to evaluate the presenting complaint with venous ultrasonography. If DVT is confirmed, PE evaluation may follow based on clinical judgment.

- **Blood cultures (D)** — The low-grade fever (38°C) could be postoperative in nature, and the surgical incisions show no signs of infection. While infection should remain on the differential, the unilateral leg swelling is the dominant finding requiring urgent evaluation, and DVT is far more likely in this clinical context.

Would you like to explore the recommended anticoagulation strategies for cancer-associated DVT in the postoperative setting?

Relevant images

(CONTENT OMITTED)

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Question 449

A 38-year-old woman undergoes a partial thyroidectomy for an enlarged thyroid gland compressing the trachea. During surgery, a young surgeon ligates the inferior thyroid arteries as close to the poles as possible to prevent intraoperative hemorrhage. 2 weeks later, the patient presents to the outpatient clinic with hoarseness. What could be the most likely cause of her hoarseness?

> **Answer Choices:**
>
> (A) Internal laryngeal nerve injury
> (B) Recurrent laryngeal nerve injury
> (C) External laryngeal nerve injury
> (D) Laryngeal edema

> **Correct Answer:**
>
> **(B)**
>
> **OpenEvidence Response:**
>
> **(B)** ✓

OpenEvidence Link: https://openevidence.com/ask/2f3395bc-149b-45e9-ba8f-6f74d8d1f3bf

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OpenEvidence Explanation

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The most likely cause of hoarseness is **B. Recurrent laryngeal nerve (RLN) injury**.

The **recurrent laryngeal nerve** has an intimate and highly variable anatomical relationship with the **inferior thyroid artery (ITA)**, making it the structure most vulnerable to iatrogenic injury during ligation of this vessel. The RLN may course anterior to, posterior to, or between the branches of the ITA.[1][2] Ligating the ITA "as close to the poles as possible" — rather than on its terminal branches immediately adjacent to the gland — places the RLN at significant risk of being included in the ligature, compressed, or stretched.

The following figure illustrates the three main configurations of the RLN relative to the ITA, highlighting why careless ligation can injure the nerve:

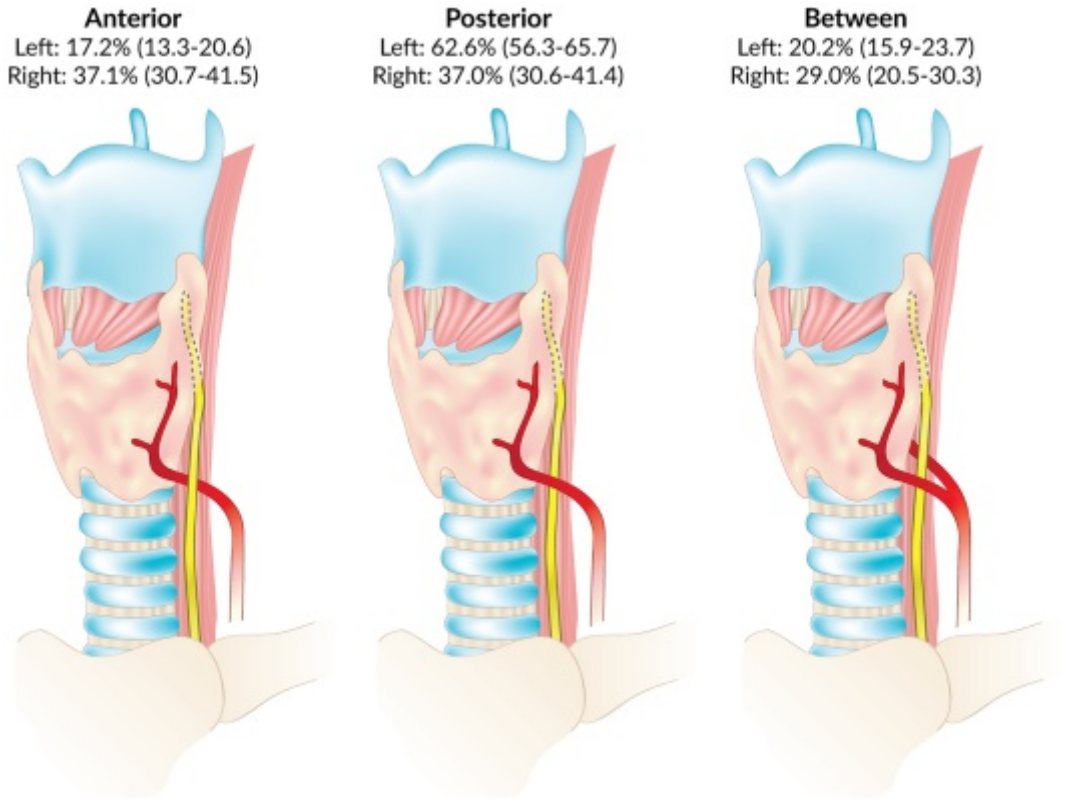


Figure 4. The 3 main types of recurrent laryngeal nerve to inferior thyroid artery relationships, comparing pooled prevalence rates for the left and right sides. Prevalence rate % (95% confidence interval). [Color figure can be viewed at wileyonlinelibrary.com]

Key points distinguishing the answer choices:

- **Recurrent laryngeal nerve injury** causes **vocal cord paralysis** and presents with hoarseness, breathy voice, and potentially aspiration — consistent with this patient's presentation.[3][4]
- **Internal laryngeal nerve** is a sensory branch of the superior laryngeal nerve supplying the supraglottic mucosa. Injury causes loss of the cough reflex and aspiration risk, but not hoarseness.

- **External laryngeal nerve** (external branch of the superior laryngeal nerve) innervates the cricothyroid muscle. Injury causes subtle voice changes — loss of high-pitched phonation and vocal fatigue — rather than frank hoarseness.[4][5]

- **Laryngeal edema** would typically present in the immediate postoperative period (hours to days), not at 2 weeks, and would more likely cause stridor than isolated hoarseness.

The RLN crosses the ITA anteriorly in up to ~46% of right-sided nerves and ~17% of left-sided nerves, and passes between ITA branches in ~29% and ~20%, respectively.[1] These high-risk configurations mean that ligation of the ITA trunk without first identifying the RLN carries substantial risk of nerve injury — the three primary mechanisms being traction, compression from a ligature, and direct sharp or thermal trauma.[4]

Would you like to explore the techniques for intraoperative RLN identification and the role of intraoperative nerve monitoring in reducing injury rates during thyroidectomy?

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Question 450

A 17-year-old man presents to his family physician for an evaluation about the size of his penis. He feels increasingly anxious during physical education (PE) class as he has noticed that the size of his penis is significantly smaller when compared to his peers. Based on the physical examination, he is Tanner stage 1. The weight and height are 60 kg (132 lb) and 175 cm (5 ft 9 in), respectively. The cardiopulmonary examination is normal; however, the patient has difficulty identifying coffee grounds by smell. Which of the following explains the pathophysiology underlying this patient's disorder?

Answer Choices:

(A) Expansion of a CTG trinucleotide repeat
(B) Isolated gonadotropin-releasing hormone (GnRH) deficiency
(C) Sex-specific epigenetic imprinting
(D) Non-disjunction of sex chromosomes

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/00d21ff1-d14e-47b6-b194-fec2c7c01be0

OpenEvidence Explanation

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The correct answer is **B. Isolated gonadotropin-releasing hormone (GnRH) deficiency**.

This clinical presentation — a 17-year-old male at **Tanner stage 1** (absent pubertal development) with a small penis and **impaired olfaction** (inability to identify coffee grounds by smell) — is classic for **Kallmann syndrome**, a form of isolated GnRH deficiency associated with anosmia/hyposmia.

Pathophysiology of Kallmann Syndrome

During embryonic development, GnRH-producing neurons originate in the olfactory placode (nasal region) and migrate along olfactory axons into the hypothalamus.[1][2] Genetic mutations (in genes such as ANOS1, FGFR1, FGF8, CHD7, PROK2, PROKR2) disrupt this migratory process, causing both:

- **GnRH deficiency** → hypogonadotropic hypogonadism → absent puberty (Tanner stage 1, micropenis, cryptorchidism)
- **Olfactory neuron migration failure** → olfactory bulb aplasia/hypoplasia → anosmia or hyposmia[3][4]

This shared embryologic origin of olfactory and GnRH neurons explains the co-occurrence of anosmia and hypogonadism, which is the hallmark distinguishing Kallmann syndrome from other forms of hypogonadotropic hypogonadism.[3][5]

Why the other options are incorrect:

- **A. CTG trinucleotide repeat expansion** — This causes myotonic dystrophy, which can be associated with hypogonadism but presents with myotonia, muscle weakness, and cataracts, not anosmia at Tanner stage 1.
- **C. Sex-specific epigenetic imprinting** — This relates to conditions like Prader-Willi syndrome, which causes hypogonadism but is characterized by obesity, hyperphagia, and intellectual disability — not isolated anosmia with normal BMI.
- **D. Non-disjunction of sex chromosomes** — This causes Klinefelter syndrome (47,XXY), which presents with hypergonadotropic hypogonadism. Importantly, boys with Klinefelter syndrome typically enter puberty normally before testosterone production stalls mid-puberty, and anosmia is not a feature.[6]

Would you like to explore the genetic testing approach and treatment strategies for Kallmann syndrome, including fertility preservation options?

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Question 451

A 63-year-old man is aiming to improve his health by eating a well balanced diet, walking daily, and quitting smoking following a 45-year smoking history. While on his daily walks he notices a strong cramping pain in his calves that consistently appears after a mile of walking. He sees his physician and a diagnosis of peripheral artery disease with intermittent claudication is made. To improve his symptoms, cilostazol is prescribed. What is the mechanism of action of this medication?

Answer Choices:

(A) Irreversible cyclooxygenase inhibitor
(B) Thromboxane synthase inhibitor
(C) Adenosine diphosphate receptor inhibitor
(D) Phosphodiesterase inhibitor

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/cec39af2-916d-4eb6-9210-25500c83cc24

OpenEvidence Explanation

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The correct answer is **D. Phosphodiesterase inhibitor**.

Cilostazol is a **phosphodiesterase III (PDE-III) inhibitor** that is FDA-approved for the treatment of intermittent claudication in peripheral artery disease.[1][2][3] By inhibiting PDE-III, cilostazol increases intracellular cyclic AMP (cAMP) levels, which produces vasodilation (particularly in femoral arteries), antiplatelet effects, and antithrombotic activity.[2][3]

The other answer choices represent different drug mechanisms:

- **A. Irreversible cyclooxygenase inhibitor** — aspirin
- **B. Thromboxane synthase inhibitor** — ozagrel
- **C. Adenosine diphosphate receptor inhibitor** — clopidogrel, prasugrel, ticagrelor

An important clinical consideration: because the PDE-III inhibitor milrinone was associated with increased mortality in patients with severe heart failure, cilostazol carries a **black box warning** and is contraindicated in patients with heart failure of any severity.[1][2]

Per the 2024 ACC/AHA PAD guidelines, cilostazol receives a **Class I, Level of Evidence A** recommendation for improving leg symptoms and increasing walking distance in patients with claudication.[1]

Would you like to explore how cilostazol compares with supervised exercise therapy for improving walking distance in patients with intermittent claudication?

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Question 453

A 34-year-old man presents to the emergency department complaining of headache, fever, chills, cough, shortness of breath, and chest pain for the past 4 days. He smokes 2 packs per day and drinks 2–3 beers every day. He denies any previous medical problems except for seasonal allergies for which he takes diphenhydramine on occasions. At the hospital, the vital signs include: temperature 40.0°C (104.0°F), blood pressure 140/80 mm Hg, heart rate 98/min, and respiratory rate 28/min. On physical exam, he is thin and poorly kept. His clothes appear dirty. Small scars are visible in the decubitus region of both arms. The lung sounds are equal with bilateral crackles, and heart auscultation reveals a systolic murmur that radiates to the left axilla. Petechiae are seen on the hard palate and palms of his hands. A chest X-ray and blood cultures are ordered. What is the most likely organism causing his symptoms?

Answer Choices:

(A) Streptococci viridans
(B) Staphylococcus aureus
(C) Aspergillus fumigatus
(D) Staphylococcus epidermidis

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/3209d2c9-d55c-42c4-b989-df6aa4dc96fc

OpenEvidence Explanation

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The answer is **B. Staphylococcus aureus**.

This patient presents with classic features of **infective endocarditis in a person who injects drugs (PWID)**. Key clinical clues include:

- **Track marks** (scars in the antecubital fossae), poor hygiene, and a thin, poorly kept appearance — all suggestive of intravenous drug use
- **High fever** (40°C), cough, shortness of breath, and chest pain — consistent with septic pulmonary emboli from right-sided endocarditis
- **Systolic murmur radiating to the left axilla** — suggesting mitral valve involvement (left-sided endocarditis can also occur in PWID)
- **Petechiae on the hard palate and palms** — classic peripheral vascular/embolic manifestations of endocarditis

Why Staphylococcus aureus?

S. *aureus* is the predominant pathogen in PWID-associated endocarditis, causing **43–69% of cases** in this population worldwide and approximately **85% of right-sided IE cases** in PWID.[1][2] This is in stark contrast to non-PWID endocarditis, where S. *aureus* accounts for only ~28% of cases.[1] The acute presentation with high fever and rapid symptom onset over just 4 days is also characteristic of S. *aureus* endocarditis, which tends to follow a more fulminant course.[3]

Why not the other options?

- **Streptococcus viridans** (A) is the most common cause of native valve endocarditis in non-PWID patients and typically presents subacutely. It accounts for only 5–10% of PWID-associated IE.[1][4]
- **Aspergillus fumigatus** (C) is a rare cause of fungal endocarditis, typically seen in immunocompromised patients, and accounts for <1–5% of PWID-IE.[1]

- **Staphylococcus epidermidis** (D) is the predominant organism in early prosthetic valve endocarditis (within 2 months of surgery), not native valve endocarditis in PWID.[5]

Would you like to explore the recommended empiric antibiotic regimens and diagnostic workup for suspected infective endocarditis in people who inject drugs?

Relevant images

(CONTENT OMITTED)

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Question 456

A three-day-old, full-term infant born by uncomplicated vaginal delivery is brought to a pediatrician by his mother, who notes that her son's skin appears yellow. She reports that the child cries several times per day, but sleeps 7-8 hours at night, uninterrupted. She has been breastfeeding the infant but feels the latch has been poor and is unsure how much milk he has been consuming but feels it is not enough. A lactation consult was called for the patient and it was noted that despite proper instruction the observed latch was still poor. When asked the mother stated that the baby is currently making stools 2 times per day. Which of the following is the most likely etiology of the patient's presentation?

Answer Choices:

(A) Breast milk jaundice
(B) Breastfeeding jaundice
(C) Sepsis
(D) Physiologic hyperbilirubinemia

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/f02e3b97-8c62-4b73-9454-e5de734edde2

OpenEvidence Explanation

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The answer is **B. Breastfeeding jaundice**.

Practice Guideline

The American Academy of Pediatrics (AAP) distinguishes two categories of jaundice in breastfed infants based on timing and mechanism:[1]

- **Breastfeeding jaundice** (suboptimal intake hyperbilirubinemia) typically peaks on **days 3–5** after birth and is caused by inadequate milk intake, leading to decreased stool frequency and increased enterohepatic circulation of bilirubin. Breastfeeding fewer than 8 times per day has been associated with higher TSB concentrations. This infant's presentation at day 3 with a poor latch, perceived insufficient intake, and only 2 stools per day (along with sleeping 7–8 hours uninterrupted at night, suggesting infrequent feeds) is classic for this entity.[1]
- **Breast milk jaundice**, in contrast, is a prolonged unconjugated hyperbilirubinemia that persists despite adequate milk intake and appropriate weight gain, lasting up to 3 months. It occurs in a healthy, thriving infant who is stooling frequently and is almost always nonpathologic.[1][2]

The key distinguishing features in this case that point to breastfeeding jaundice rather than breast milk jaundice include:

1. **Timing** — day 3 of life, within the classic window for suboptimal intake jaundice[1]
2. **Evidence of poor intake** — poor latch confirmed by lactation consultant, mother's concern about insufficient milk consumption[1]
3. **Decreased stool frequency** — only 2 stools per day, consistent with low caloric intake and increased enterohepatic circulation[1]
4. **Prolonged sleep** — 7–8 hours uninterrupted at night suggests the infant is not feeding frequently enough (AAP recommends at least 8 feeds in 24 hours)[1]

Why not the other options?

- **Breast milk jaundice (A)** occurs later (typically after the first week) in well-nourished, thriving infants with adequate weight gain and stooling — the opposite of this clinical picture.[2][3]
- **Sepsis (C)** would typically present with additional systemic signs such as temperature instability, lethargy, poor feeding beyond just a latch issue, respiratory distress, or hemodynamic instability. The vignette describes an otherwise well-appearing infant with an identifiable feeding problem.
- **Physiologic hyperbilirubinemia (D)** does peak around days 2–5 in term infants, but the clinical scenario specifically highlights suboptimal intake (poor latch, low stool output, prolonged sleep intervals), making breastfeeding jaundice the more precise and most likely etiology rather than the normal physiologic process.[1]

Would you like to explore the AAP's updated 2022 phototherapy thresholds and neurotoxicity risk factors for managing neonatal hyperbilirubinemia?

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Question 458

A 20-year-old healthy man is running on a treadmill for the last 30 minutes. He is in good shape and exercises 3 times per week. He takes no medications and denies smoking cigarettes, drinking alcohol, and illicit drug use. Prior to starting his run, his heart rate was 70/min, and the blood pressure was 114/74 mm Hg. Immediately after stopping his run, the heart rate is 130/min, and the blood pressure is 145/75 mm Hg. Which of the following is most likely responsible for the change in his heart rate and blood pressure?

Answer Choices:

(A) Baroreceptor reflex
(B) Increased activation of the vagal nuclei
(C) Sympathetic nervous system activation
(D) Vasopressin release from the pituitary

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/8024a8fe-1aa1-4b7b-b1f7-90b542e99043

OpenEvidence Explanation

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Sympathetic nervous system activation (C) is most likely responsible for the observed changes in heart rate and blood pressure during exercise.

During sustained aerobic exercise, the cardiovascular response is predominantly driven by **increased sympathetic outflow and withdrawal of parasympathetic (vagal) tone**. This produces the following hemodynamic effects:

- **Increased heart rate** (70 → 130 bpm): Sympathetic activation releases norepinephrine at cardiac sympathetic nerve terminals and epinephrine from the adrenal medulla, both acting on cardiac β_1-adrenergic receptors to increase chronotropy (heart rate) and inotropy (contractility).
- **Increased systolic blood pressure** (114 → 145 mmHg): Enhanced cardiac output (from increased heart rate and stroke volume) raises systolic pressure.
- **Maintained or slightly decreased diastolic blood pressure** (74 → 75 mmHg): Sympathetic-mediated vasodilation in exercising skeletal muscle (via β_2 receptors and local metabolites) decreases total peripheral resistance, which offsets the rise in diastolic pressure. This pattern of **widened pulse pressure** is the classic hemodynamic signature of dynamic exercise.

Why the other options are incorrect:

- **A. Baroreceptor reflex** — The baroreceptor reflex acts to counteract changes in blood pressure (e.g., lowering heart rate when BP rises). During exercise, the baroreflex set point is actually reset upward by central command, but the baroreflex itself is not the primary driver of the exercise response — it modulates it.
- **B. Increased activation of vagal nuclei** — The opposite occurs: vagal tone is withdrawn during exercise, which is one of the earliest mechanisms contributing to the initial rise in heart rate. Increased vagal activation would slow the heart rate.
- **D. Vasopressin release from the pituitary** — Vasopressin (ADH) plays a role in fluid retention and vasoconstriction during prolonged or dehydrating exercise, but it is not the primary mechanism responsible for the acute heart rate and blood pressure changes seen here.

Would you like to explore how the baroreflex set point is centrally reset during exercise ("central command") and its interaction with the exercise pressor reflex?

Question 459

A 14-year-old obese boy presents with severe right hip and knee pain. The patient says that he has been limping with mild pain for the past three weeks, but the pain acutely worsened today. He describes the pain as severe, non-radiating, sharp and aching in character, and localized to the right hip and knee joints. The patient denies recent illness, travel, trauma, or similar symptoms in the past. No significant past medical history and no current medications. The patient is not sexually active and denies any alcohol, smoking or drug use. The vital signs include: temperature 37.0°C (98.6°F), blood pressure 110/70 mm Hg, pulse 72/min, respiratory rate 15/min, and oxygen saturation 99% on room air. Body mass index (BMI) is 32 kg/m2. On physical examination, the patient is alert and cooperative. The right leg is externally rotated, and there is a limited range of motion in the right hip. Strength is 4 out of 5 at the right hip joint and 5 out of 5 elsewhere. There is no tenderness to palpation. No joint erythema, edema or effusion present. Sensation is intact. Deep tendon reflexes are 2+ bilaterally. Laboratory tests are unremarkable. Plain radiographs of the right hip joint are significant for displacement of the right femoral head inferoposterior off the femoral neck. Which of the following is the most appropriate course of treatment for this patient?

Answer Choices:

(A) Reassess in 3 months
(B) Intra-articular corticosteroid injection of the right hip joint
(C) Pavlik harness
(D) Surgical pinning of the right hip

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/bda9c478-dfe2-44a6-8471-254b6a06901f

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OpenEvidence Explanation

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The correct answer is **D. Surgical pinning of the right hip**.

This presentation is classic for **slipped capital femoral epiphysis (SCFE)** — the most common hip disorder in adolescents. The key features pointing to this diagnosis include the patient's age (14 years), obesity (BMI 32), chronic limp with acute worsening of hip and knee pain, external rotation of the affected leg, limited hip range of motion, and radiographic findings showing inferoposterior displacement of the femoral head off the femoral neck.[1][2][3]

Why surgical pinning is the correct treatment:

SCFE is treated surgically with **in situ screw fixation** (pinning), which is the standard of care for both stable and unstable SCFE.[1][2][4] After diagnosis, the patient should be made non-weight-bearing and urgently referred to an orthopedic surgeon, with surgery ideally performed within 24 hours.[1] The goals of treatment are to prevent further slip progression and avoid complications such as avascular necrosis, chondrolysis, and femoroacetabular impingement.[2]

Why the other options are incorrect:

- **A. Reassess in 3 months** — SCFE requires urgent surgical intervention. Delay risks further slippage, avascular necrosis, and worsening deformity.[1]
- **B. Intra-articular corticosteroid injection** — SCFE is a mechanical/structural problem of the physis, not an inflammatory condition. Corticosteroid injection has no role in management.
- **C. Pavlik harness** — This is used for developmental dysplasia of the hip (DDH) in infants, not for SCFE in adolescents.[2]

This patient's presentation — with a 3-week prodrome of limping followed by acute worsening — represents an **acute-on-chronic SCFE**, which is the most common pattern.[5] Forceful reduction should be avoided due to the risk of avascular necrosis.[1]

Would you like to explore the approach to evaluating the contralateral hip in SCFE, given the 25–80% rate of bilateral involvement?

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Question 460

A 32-year-old man comes to the physician because of a progressive development of tender breast tissue over the past 18 months. He used to ride his bicycle for exercise 4 times a week but stopped after he had an accident and injured his left testicle 3 months ago. He has gained 5 kg (11 lb) during this period. For the last 10 years, he drinks one to two beers daily and sometimes more on weekends. He occasionally takes pantoprazole for heartburn. He is 171 cm (5 ft 7 in) tall and weighs 87 kg (192 lb); BMI is 30 kg/m2. Vital signs are within normal limits. Examination shows bilaterally symmetrical, mildly tender gynecomastia. A nontender 1.5-cm mass is palpated in the left testis; transillumination test is negative. The remainder of the examination shows no abnormalities. Which of the following is the most likely underlying cause of these findings?

Answer Choices:

(A) Leydig cell tumor
(B) Obesity
(C) Klinefelter syndrome
(D) Trauma to testis

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/eb0bf9db-9321-454f-85c2-a0fde43e15b7

OpenEvidence Explanation

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The correct answer is **A. Leydig cell tumor**.

The combination of **progressive tender gynecomastia** and a **palpable, nontender testicular mass** that is **transillumination-negative** (solid, not cystic) in a 32-year-old man is classic for a **Leydig cell tumor**. These tumors directly secrete estradiol, creating an estrogen-androgen imbalance that drives breast tissue proliferation.[1][2][3]

Why Leydig cell tumor fits best:

- Leydig cell tumors are sex cord-stromal tumors that occur most commonly in men aged 20–60 years. Approximately **15–30% present with gynecomastia**, which is the most common endocrinologic manifestation and often precedes detection of the testicular mass.[2][3]
- These tumors produce excess estradiol, lowering the testosterone-to-estradiol ratio and stimulating breast tissue growth. The gynecomastia in this case has been progressive over 18 months — consistent with the slow growth of a hormone-secreting tumor.[4][5]
- The negative transillumination test confirms a **solid mass**, ruling out a hydrocele or spermatocele.

Why the other options are less likely:

- **Obesity (B):** While obesity increases aromatase activity and can contribute to gynecomastia through peripheral estrogen conversion, it does not explain the palpable solid testicular mass. The BMI of 30 and recent weight gain are distractors; the gynecomastia preceded the weight gain (18 months vs. 3 months).[1]
- **Klinefelter syndrome (C):** This would typically present earlier in life with small, firm testes, tall stature, and infertility — not with a discrete testicular mass.[1]
- **Trauma to testis (D):** The bicycle accident occurred only 3 months ago, whereas the gynecomastia has been developing for 18 months. Trauma does not cause a persistent solid testicular mass; rather, the trauma likely brought the pre-existing mass to clinical attention.

The following diagnostic algorithm illustrates the systematic workup for gynecomastia, highlighting how elevated estradiol should prompt testicular ultrasound to evaluate for Leydig or Sertoli cell tumors.

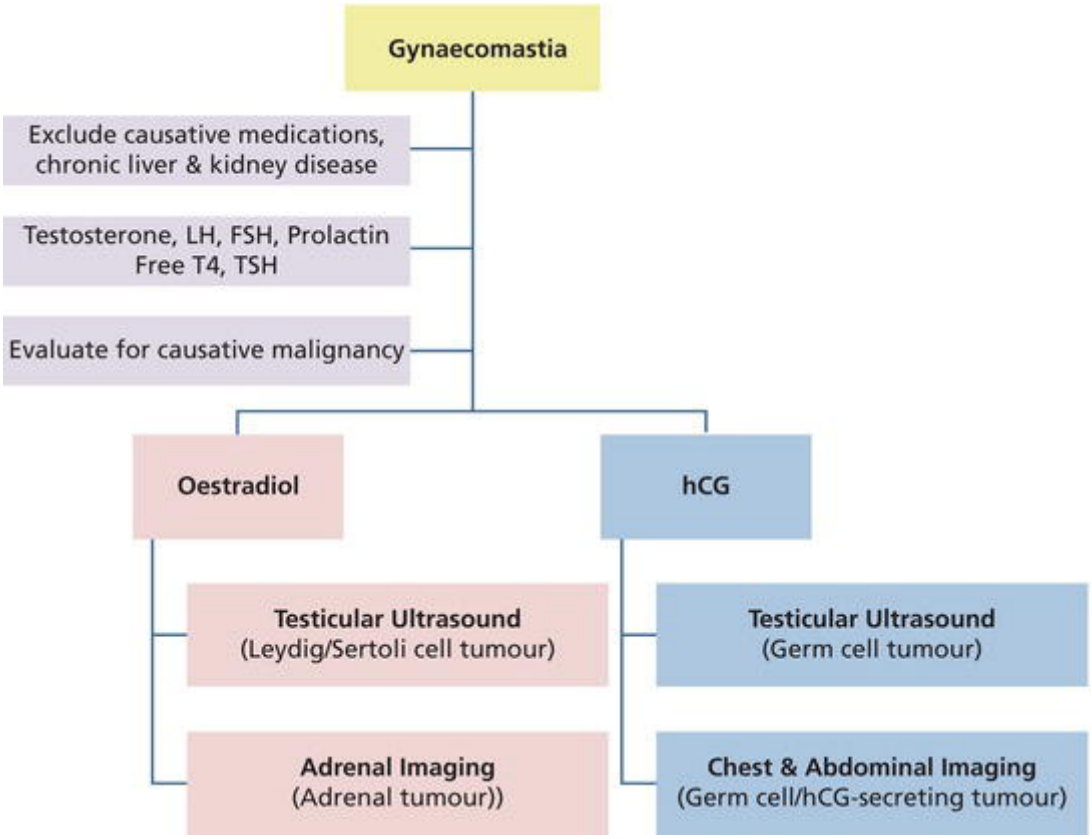


Figure 2. Investigation of gynaecomastia. Source: Ali, S. N., et al. 2017/John Wiley & Sons.

Would you like to explore the hormonal workup and management approach for suspected Leydig cell tumors, including the role of testicular ultrasound and tumor markers?

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Question 462

A 5-year-old male presents to the pediatrician with a 10-day history of cough that is worse at night. The patient has a history of mild intermittent asthma and has been using his albuterol inhaler without relief. He has also been complaining of headache and sore throat, and his mother has noticed worsening rhinorrhea. The patient's past medical history is otherwise unremarkable, and he has no known drug allergies. In the office, his temperature is 101.8°F (38.8°C), blood pressure is 88/65 mmHg, pulse is 132/min, and respirations are 16/min. The patient has purulent mucus draining from the nares, and his face is tender to palpation over the maxillary sinuses. His pharynx is erythematous with symmetric swelling of the tonsils. On lung exam, he has moderate bilateral expiratory wheezing.

Which of the following is the best next step in management?

> **Answer Choices:**
>
> (A) Amoxicillin
> (B) Amoxicillin-clavulanic acid
> (C) Clindamycin
> (D) Levofloxacin

> **Correct Answer:**
>
> **(B)**
>
> **OpenEvidence Response:**
>
> **(B)** ✓

OpenEvidence Link: https://openevidence.com/ask/d36e3ea8-83a8-4dde-a508-5d452b61cabd

OpenEvidence Explanation

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The best next step in management is **B. Amoxicillin-clavulanic acid**.

This child meets clinical criteria for **acute bacterial sinusitis** — persistent symptoms for ≥10 days (cough, rhinorrhea, headache, sore throat), purulent nasal discharge, fever, and maxillary sinus tenderness. The Infectious Diseases Society of America (IDSA) recommends **amoxicillin-clavulanate** as first-line empirical therapy for pediatric acute bacterial sinusitis.[1][2] The AAP guideline allows either amoxicillin or amoxicillin-clavulanate, but several factors in this case favor amoxicillin-clavulanate:[3]

- **Age <5 years** — a risk factor for penicillin-nonsusceptible organisms and β-lactamase-producing pathogens[1]
- **Underlying asthma** — the AAP guideline specifically notes that children with asthma should generally be managed with antibiotic therapy (rather than observation) and may warrant broader coverage[3]
- The three predominant organisms (*S. pneumoniae*, nontypeable *H. influenzae*, and *M. catarrhalis*) include two that frequently produce β-lactamases, which clavulanate inhibits[4]

Why not the other options?

- **Amoxicillin alone (A)** is a reasonable alternative per AAP guidelines but provides less comprehensive coverage against β-lactamase-producing organisms, which is particularly relevant in a young child with an underlying condition.[1][3]
- **Clindamycin (C)** lacks activity against *H. influenzae* and *M. catarrhalis* and is reserved for penicillin-allergic patients, typically in combination with a cephalosporin.[3]
- **Levofloxacin (D)** is reserved for children with type I penicillin hypersensitivity; fluoroquinolones are generally avoided in pediatrics due to concerns about musculoskeletal toxicity.[1][3]

The recommended dosing is high-dose amoxicillin-clavulanate (90 mg/kg/day of the amoxicillin component, divided twice daily) for 10–14 days.[1][2]

Would you like to explore the management of the concurrent asthma exacerbation in this patient, including whether the sinusitis treatment alone may improve the wheezing?

Relevant images

(CONTENT OMITTED)

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Question 464

A 22-year-old woman presents to the emergency department for abdominal pain. The patient has been trying to get pregnant and was successful recently, but now she is experiencing abdominal pain, contractions, and a bloody vaginal discharge. According to her last appointment with her primary care provider, she is 10 weeks pregnant. The patient has a past medical history of constipation, anxiety, and substance abuse. She is not currently taking any medications. Her temperature is 99.5°F (37.5°C), blood pressure is 107/58 mmHg, pulse is 90/min, respirations are 17/min, and oxygen saturation is 98% on room air. Physical exam is notable for a bloody vaginal discharge and an open cervix. The patient is initially extremely grateful for the care she is receiving and thanks the doctor and the nursing staff for saving her baby. Upon hearing the news that she is having a spontaneous abortion, the patient becomes angry and aggressive and states that her physician and the medical staff are incompetent, evil, and she is going to sue all of them. The patient is left to grieve but upon entering the room again you notice that the patient has new lacerations over her wrists and that some of the medical equipment in the room is broken. Which of the following is the most likely diagnosis?

Answer Choices:

(A) Antisocial personality disorder
(B) Borderline personality disorder
(C) Normal grief response
(D) Post-traumatic stress disorder

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/43d12565-575d-4351-a124-2e137662acc3

OpenEvidence Explanation

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The most likely diagnosis is **B. Borderline personality disorder**.

This vignette illustrates several hallmark features of borderline personality disorder (BPD) as defined by the DSM-5:[1][2]

- **Idealization and devaluation (splitting):** The patient initially idealizes the medical staff ("extremely grateful," "thanking the doctor and nursing staff for saving her baby"), then rapidly shifts to devaluing them ("incompetent, evil," threatening to sue). This alternation between extremes of idealization and devaluation of caregivers is a core criterion of BPD.[1]
- **Self-mutilating behavior:** The new wrist lacerations discovered upon re-entering the room represent self-harm, which is strongly associated with BPD. Nonsuicidal self-injury has historically been regarded as nearly pathognomonic of BPD.[1][2]
- **Inappropriate, intense anger:** The explosive rage and destruction of medical equipment reflect the criterion of inappropriate intense anger or difficulty controlling anger.[2]
- **Impulsivity and substance abuse:** The history of substance abuse is consistent with the impulsivity criterion of BPD, which includes potentially self-damaging behaviors such as substance use.[2]
- **Affective instability:** The rapid emotional shift from gratitude to rage to self-harm demonstrates marked reactivity of mood.[1][2]

Why the other options are less likely:

- **Antisocial personality disorder** — characterized by a pervasive pattern of disregard for and violation of others' rights, deceitfulness, and lack of remorse. The idealization-devaluation pattern and self-harm are not typical features.[1]
- **Normal grief response** — while grief is expected after pregnancy loss, self-mutilation, destruction of property, and the dramatic splitting behavior go well beyond a normal grief reaction.[3]
- **PTSD** — requires at least 1 month of symptoms following a traumatic event and features re-experiencing, avoidance, negative cognitions, and hyperarousal. This acute presentation with splitting and self-harm is more consistent with BPD.[1]

Would you like to explore the recommended acute management approach for patients with BPD who present with self-injurious behavior in the emergency department?

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Question 465

A 45-year-old female presents to the emergency department with gross hematuria and acute, colicky flank pain. She denies any previous episodes of hematuria. She reports taking high doses of acetaminophen and aspirin over several weeks due to persistent upper back pain. The patient's blood pressure and temperature are normal, but she is found to have proteinuria. Physical examination is negative for palpable flank masses. Which of the following is the most likely diagnosis:

> **Answer Choices:**
>
> (A) Diffuse cortical necrosis
> (B) Chronic pyelonephritis
> (C) Papillary necrosis
> (D) Acute Nephrolithiasis

> **Correct Answer:**
>
> (C)
>
> **OpenEvidence Response:**
>
> (C) ✓

OpenEvidence Link: https://openevidence.com/ask/b4f0d126-ad89-4205-acdc-56170d5ee0b7

OpenEvidence Explanation

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The most likely diagnosis is **C. Papillary necrosis**.

This patient's presentation — gross hematuria, acute colicky flank pain, and proteinuria in the setting of **chronic high-dose acetaminophen and aspirin use** — is classic for **analgesic nephropathy with renal papillary necrosis**. The combination of at least two antipyretic analgesics (acetaminophen + aspirin) taken over several weeks is the hallmark risk factor for this condition.[1][2]

Why papillary necrosis fits best:

- **Analgesic nephropathy** is characterized by renal papillary necrosis and chronic interstitial nephritis, resulting from daily use of mixtures containing at least two antipyretic analgesics. The renal papilla is particularly vulnerable to ischemic necrosis due to its relatively hypoxic environment and peculiar blood supply arrangement.[1][3][4]
- Early clinical symptoms include **renal colic** (from sloughing of necrotic papillary tissue causing ureteral obstruction), **gross hematuria** (from papillary sloughing), and **proteinuria** — all present in this patient.[1][3][5]
- The mnemonic for causes of papillary necrosis is often recalled as "**POSTCARDS**": Pyelonephritis, Obstruction, Sickle cell disease, Tuberculosis, Chronic liver disease, Analgesic abuse, Renal transplant rejection, Diabetes mellitus, Systemic vasculitis.[4]

Why the other options are less likely:

- **A. Diffuse cortical necrosis** — Typically occurs in the setting of obstetric complications (e.g., abruptio placentae), septic shock, or DIC, not analgesic use. It presents with acute renal failure and oliguria/anuria rather than colicky pain.
- **B. Chronic pyelonephritis** — Would typically present with fever, pyuria, and a history of recurrent urinary tract infections. This patient has normal temperature and no infectious symptoms.
- **D. Acute nephrolithiasis** — While it can cause colicky flank pain and hematuria, the history of chronic combined analgesic use with proteinuria points more specifically to papillary necrosis. Sloughed papillary fragments can mimic stone passage clinically, but the analgesic history is the key distinguishing feature.[1][4]

Would you like to explore the imaging modalities best suited for diagnosing renal papillary necrosis and distinguishing it from nephrolithiasis?

Relevant images

(CONTENT OMITTED)

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Question 466

A 40-year-old man presents to the clinic with complaints of increased bilateral pain in his knees. The pain developed over time and now limits his mobility. He states that the pain is worse at the end of the day, though he does have some early-morning stiffness lasting about 20 minutes. He used to have some success with over-the-counter NSAIDs; however, they no longer help. The patient also has been taking metformin for the past 2 years and is severely obese, with a BMI of 41 kg/m2. Additionally, he states that he has felt increasingly tired during the day, often dozes off during work, and no longer feels refreshed when he wakes up in the morning. Upon examination, there is no tenderness on palpation or erythema; however, some crepitus is felt. He has no other complaints but has a family history of rheumatoid arthritis (RA) on his mother's side. Which of the following factors is the underlying cause of the patient's pain, as well as the rest of his complaints?

Answer Choices:

(A) Medication side effect
(B) Excess weight
(C) Infection
(D) Occult malignancy

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/b3474e34-0dfc-470b-8834-3d0f69b97290

OpenEvidence Explanation

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The answer is **B. Excess weight**. This patient's severe obesity (BMI 41 kg/m²) is the single underlying factor that unifies all of his complaints — bilateral knee pain consistent with osteoarthritis, and excessive daytime sleepiness with unrefreshing sleep consistent with obstructive sleep apnea (OSA).

Knee osteoarthritis from obesity: The clinical presentation — bilateral knee pain that worsened gradually, is worse at the end of the day, has brief morning stiffness (<30 minutes), crepitus on exam, and absence of erythema or tenderness — is classic for osteoarthritis (OA) rather than rheumatoid arthritis (despite the family history of RA).[1][2] Obesity is one of the strongest modifiable risk factors for knee OA, with a pooled odds ratio of **2.66** (95% CI, 2.15–3.28).[1] At a BMI ≥36, the risk of knee OA increases to approximately **13.6-fold** compared to a BMI of 24.[3] The mechanism involves both excessive biomechanical loading — forces across the knee approximate 2–3 times body weight during walking — and systemic metabolic effects from inflammatory adipokines.[4][5]

Obstructive sleep apnea from obesity: The daytime fatigue, dozing off at work, and unrefreshing sleep are hallmark symptoms of OSA.[6] OSA prevalence among individuals with class III obesity (BMI ≥40) ranges from **50% to 98%**, with a relative risk ≥10 compared to normal-weight individuals.[3][7] Obesity promotes OSA through fatty tissue deposition in the pharyngeal airway, reduced upper airway muscle protective force, and mass effect of the abdomen on chest wall mechanics.[7]

Why not the other options:

- **A (Medication side effect):** Metformin does not cause joint pain or excessive daytime sleepiness; its most common side effects are gastrointestinal.
- **C (Infection):** Septic arthritis typically presents acutely with erythema, warmth, tenderness, and effusion — none of which are present here.

- **D (Occult malignancy):** There are no red-flag features such as night pain, constitutional symptoms (weight loss, night sweats), or focal bone tenderness to suggest malignancy.

Would you like to explore the evidence for weight loss interventions (behavioral, pharmacologic, or surgical) in simultaneously improving both knee OA symptoms and OSA severity in patients with class III obesity?

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Question 473

A 5-year-old male is brought to the pediatrician with complaints of a painful mouth/gums, and vesicular lesions on the lips and buccal mucosa for the past 4 days. The patient has not been able to eat or drink due to the pain and has been irritable. The patient also reports muscle aches. His vital signs are as follows: T 39.1, HR 110, BP 90/62, RR 18, SpO2 99%. Physical examination is significant for vesicular lesions noted on the tongue, gingiva, and lips, with some vesicles having ruptured and ulcerated, as well as palpable cervical and submandibular lymphadenopathy. Which of the following is the most likely causative organism in this patient's presentation?

Answer Choices:

(A) CMV
(B) HIV
(C) HSV-1
(D) HSV-2

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/36aab5aa-7810-4269-b603-b96eabdb205f

OpenEvidence Explanation

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The correct answer is **C. HSV-1**.

This presentation is classic for **primary herpetic gingivostomatitis (PHGS)**, which is caused principally by **herpes simplex virus type 1 (HSV-1)**.[1][2] The key features pointing to this diagnosis include:

- **Age**: PHGS has a peak incidence in children between **6 months and 5 years of age**, making this 5-year-old fall squarely within the typical age range.[1][2][3]
- **Oral findings**: Painful vesicular lesions on the tongue, gingiva, and lips, with vesicles rupturing to form ulcers, are the hallmark of PHGS. Vesicles appear on the gingiva, hard palate, and entire oral mucosa, then burst and become irregular painful ulcers.[3][4]
- **Systemic symptoms**: Fever (39.1°C), irritability, myalgias, and inability to eat are characteristic accompanying features. Cervical and submandibular lymphadenopathy is a common finding.[2][5]
- **Decreased oral intake**: Inability to eat or drink due to pain is a well-recognized complication, with dehydration being a common sequela of PHGS.[1][6]

Why not the other options:

- **CMV (A)**: CMV can cause oral ulcers but typically in immunocompromised patients; it does not present with this classic vesicular gingivostomatitis pattern.
- **HIV (B)**: HIV does not cause acute vesicular oral lesions. HIV-associated oral findings include candidiasis, hairy leukoplakia, and Kaposi sarcoma, not vesicular gingivostomatitis.
- **HSV-2 (D)**: While HSV-2 can rarely cause oral lesions, primary herpetic gingivostomatitis is caused **principally by HSV-1 and only rarely by HSV-2**, with HSV-2 oral involvement affecting mostly adults rather than children.[2][3]

Would you like to explore the evidence for acyclovir treatment in pediatric primary herpetic gingivostomatitis, including optimal timing and dosing?

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Question 474

A patient is unresponsive in the emergency department following a motor vehicle accident. The patient's written advance directive states that he does not wish to be resuscitated in the event of a cardiac arrest. The patient's wife arrives and demands that everything be done to keep him alive because she can't go on living without him. The patient's adult son is on his way to the hospital. If the patient arrests, which of the following should occur?

> **Answer Choices:**
>
> (A) Respect the wife's wishes and resuscitate the patient
> (B) Respect the patient's prior wishes and do not resuscitate
> (C) Consult a judge for the final decision on whether or not to resuscitate
> (D) Consult the hospital ethics committee

> **Correct Answer:**
>
> **(B)**
>
> **OpenEvidence Response:**
>
> **(B)** ✓

OpenEvidence Link: https://openevidence.com/ask/0821679a-d7ec-4d6a-a55c-8636b92e236e

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OpenEvidence Explanation

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The answer is **B. Respect the patient's prior wishes and do not resuscitate**.

A written advance directive represents the patient's autonomous wishes expressed while the patient had decision-making capacity, and these wishes take **precedence over the preferences of surrogate decision-makers**, including family members. This is a foundational principle in medical ethics and law.

The 2025 AHA Guidelines for CPR and Emergency Cardiovascular Care explicitly address this scenario: "The patient's wishes, as expressed in person or via ACP, are principal, and a surrogate's preference should be honored [only] if the patient's wishes are uncertain".[1] In this case, the patient's wishes are not uncertain — there is a written advance directive clearly stating he does not wish to be resuscitated.

Multiple professional society position statements reinforce this hierarchy of decision-making for incapacitated patients:[2][3]

1. **First priority**: Known preferences expressed by the patient when competent (i.e., advance directive or clear oral statement)
2. **Second**: Substituted judgment by surrogates (what the patient would have wanted)
3. **Third**: Best interests standard (used only when patient wishes are unknown)

The wife's request is based on her own emotional needs ("she can't go on living without him"), not on the patient's values or wishes. Surrogates are ethically obligated to decide as the patient would, not based on their own desires.[2][4] There is no need to consult a judge or ethics committee when a valid advance directive clearly addresses the clinical scenario, as the directive itself provides the legal and ethical authority to guide care.[5]

Would you like to explore the nuances of when an advance directive may be appropriately overridden, such as when the clinical situation does not match the scenario contemplated in the directive?

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Question 476

A 14-year-old boy presents with right upper quadrant abdominal pain and is found on ultrasound to have a gallstone. Based on clinical suspicion, a CBC, a Coombs test, and a bilirubin panel are obtained to determine the etiology of the gallstone. These tests reveal a mild normocytic anemia with associated reticulocytosis as well as an increased RDW. In addition there is an indirect hyperbilirubinemia and the Coombs test results are negative. To confirm the diagnosis, an osmotic fragility test is performed which shows increased fragility in hypotonic solution. In this patient, what findings would most likely be anticipated if a blood smear were obtained?

Answer Choices:

(A) Hypersegmented neutrophils
(B) Sideroblasts
(C) Spherocytes
(D) Dacrocytes

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/7aa0664e-f75d-4fe7-9ad7-2fd9f2a30c01

OpenEvidence Explanation

(CONTENT OMITTED)

The answer is **C. Spherocytes**.

This clinical presentation is classic for **hereditary spherocytosis (HS)**, the most common inherited hemolytic anemia in individuals of Northern European descent. The key findings that point to this diagnosis include:

- **Normocytic hemolytic anemia** with reticulocytosis and indirect hyperbilirubinemia — indicating extravascular hemolysis
- **Negative Coombs test** — ruling out autoimmune hemolytic anemia and pointing toward an intrinsic RBC membrane defect
- **Increased osmotic fragility** — the confirmatory finding, reflecting spherocytes' reduced surface-area-to-volume ratio, which makes them lyse more readily in hypotonic solutions
- **Pigmented gallstones** in a young patient — a well-recognized complication of chronic hemolysis due to excess bilirubin

HS results from defects in RBC membrane proteins (most commonly **ankyrin, band 3, or spectrin**), causing loss of membrane surface area and transformation of biconcave discs into **spherocytes**. These rigid, spherical cells are trapped and destroyed in the splenic cords, producing the characteristic extravascular hemolysis. On peripheral blood smear, spherocytes appear as **small, round, densely staining RBCs lacking central pallor**.

Why not the other options?

- **A. Hypersegmented neutrophils** — seen in megaloblastic anemias (B12/folate deficiency), which cause macrocytic anemia, not normocytic.
- **B. Sideroblasts** — ringed sideroblasts are characteristic of sideroblastic anemia, which typically presents with microcytic anemia and would not show increased osmotic fragility.
- **D. Dacrocytes (teardrop cells)** — associated with myelofibrosis or marrow infiltrative processes, not hemolytic anemia with increased osmotic fragility.

Would you like to explore the current diagnostic approach to hereditary spherocytosis, including the role of eosin-5-maleimide (EMA) binding test versus traditional osmotic fragility testing?

Question 479

A 63-year-old patient presents to the emergency department because of severe left leg pain and tingling. His condition started suddenly 30 minutes ago. He has had hypertension for the past 10 years for which he takes bisoprolol. He does not smoke or drink alcohol. His temperature is 37.1°C (98.7°F), the blood pressure is 130/80 mm Hg, and the pulse is 100/min and irregular. On physical examination, the patient appears in severe pain and his left leg is pale and cool. The popliteal pulse is weaker on the left side compared to the right side. Which of the following is the most common cause of this patient's condition?

Answer Choices:

(A) Vasculitis
(B) Hyperhomocysteinemia
(C) Arterial emboli
(D) Arterial trauma

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/895254ac-ea0b-46ef-b37f-d51068a24295

OpenEvidence Explanation

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The correct answer is **C. Arterial emboli**.

This patient presents with classic **acute limb ischemia (ALI)** — sudden onset of severe leg pain, pallor, cool extremity, diminished pulse, and paresthesias (the "6 Ps"). The key clinical clue pointing to the etiology is the **irregular pulse at 100/min**, which is highly suggestive of **atrial fibrillation**. Approximately **80% of peripheral emboli originate from the heart**, with atrial fibrillation being the most common cardiac source.[1] Thrombus forms in the left atrial appendage and embolizes to the peripheral arterial circulation, most commonly lodging at bifurcation points.

The 2024 ACC/AHA PAD Guidelines identify cardiac embolization — particularly from atrial fibrillation — as a major cause of ALI, with atrial fibrillation found in 30% of patients with non-PAD-related ALI and a presumed major cardioembolic cause identified in 44% of such cases.[2][3] An NEJM review similarly lists embolism from the heart or a diseased artery among the primary clinical events causing ALI.[4]

Why not the other options?

- **Vasculitis (A):** A rare cause of ALI, typically presenting with systemic inflammatory features rather than an isolated acute embolic event.
- **Hyperhomocysteinemia (B):** A risk factor for atherosclerosis and thrombosis but not a common cause of acute arterial occlusion.
- **Arterial trauma (D):** No history of injury, instrumentation, or catheterization to suggest traumatic arterial occlusion.

The following figure illustrates the etiologic classification of ALI, highlighting the distinction between thrombotic and embolic mechanisms:

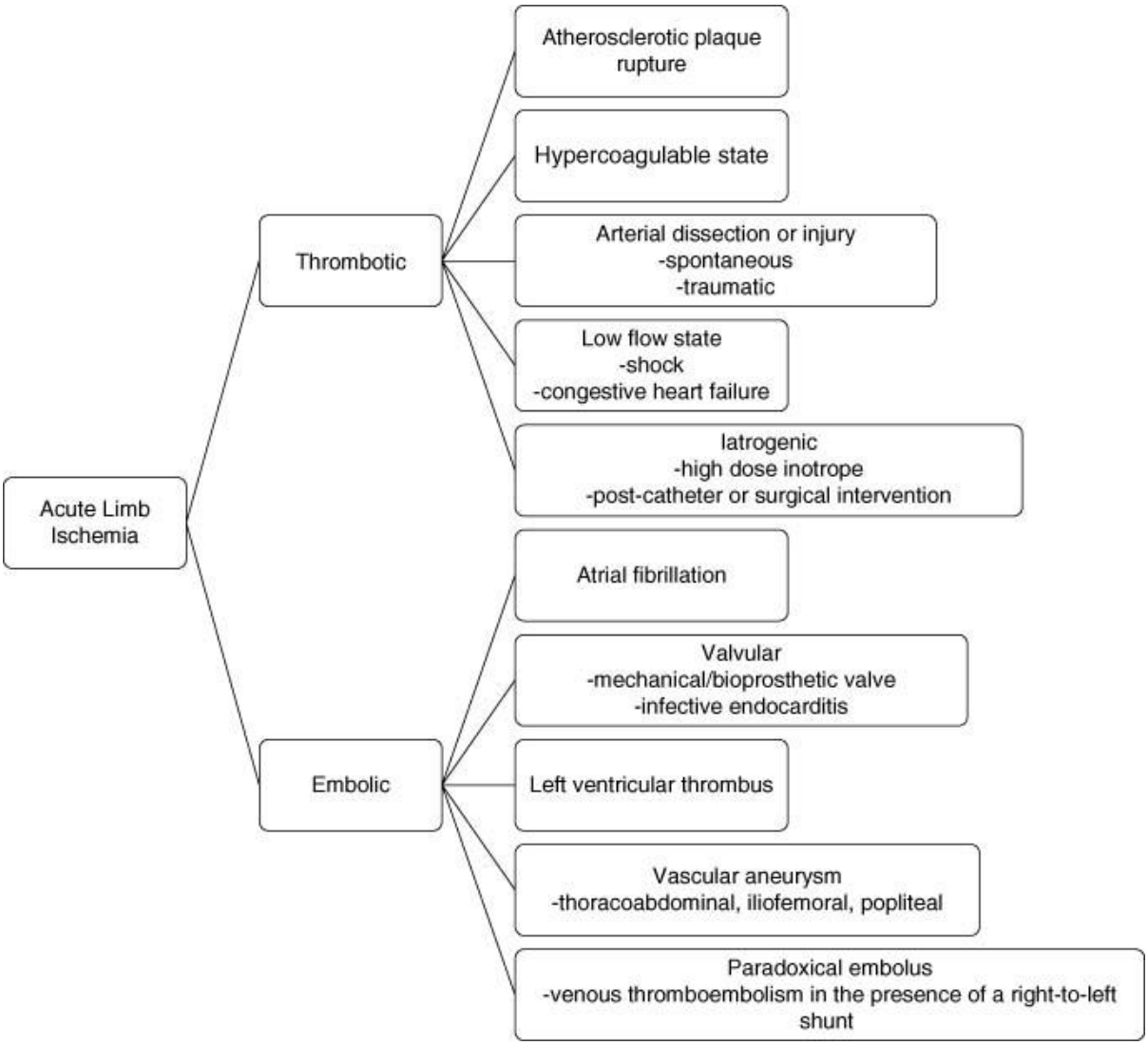


Figure 1. Etiologies of acute limb ischemia.

Would you like to explore the initial management algorithm for acute limb ischemia, including anticoagulation and revascularization strategies?

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Association Joint Committee on Clinical Practice Guidelines. Gornik HL, Aronow HD, Goodney PP, et al.. Journal of the American College of Cardiology. 2024;83(24):2497-2604. doi:10.1016/j.jacc.2024.02.013.

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Question 481

Current recommendations state that a single hemoglobin A1c value of greater than 6.5% is diagnostic of diabetes mellitus. If this 6.5% cut-off is to be increased to 7.0%, which of the following would be true?

Answer Choices:

(A) Increase in false negative test results
(B) Increase in false positive test results
(C) Decrease in true negative test results
(D) Increase in true positive test results

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/58dd7ee6-b64e-4c55-a6a3-1886e556b506

OpenEvidence Explanation

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Increasing the diagnostic threshold from 6.5% to 7.0% would result in an increase in false negative test results (Answer A).

This is a fundamental concept in diagnostic test characteristics related to shifting a cutoff point:

Effect of raising the diagnostic threshold:

- By raising the HbA1c cutoff from 6.5% to 7.0%, the test becomes **more specific but less sensitive**. Individuals with true diabetes who have HbA1c values between 6.5% and 7.0% would now be classified as "not diabetic" — these are **false negatives** (people with the disease who test negative).

Why the other options are incorrect:

- **B (Increase in false positives):** False positives would actually *decrease*. A higher threshold means fewer non-diabetic individuals will be incorrectly labeled as diabetic.
- **C (Decrease in true negatives):** True negatives would actually *increase*. More truly non-diabetic individuals will correctly fall below the higher cutoff.
- **D (Increase in true positives):** True positives would *decrease*, as some genuinely diabetic patients (those with HbA1c 6.5–7.0%) would no longer meet the diagnostic criterion.

General principle: Raising a diagnostic cutoff increases **specificity** (fewer false positives, more true negatives) at the cost of decreased **sensitivity** (more false negatives, fewer true positives). Conversely, lowering a cutoff increases sensitivity at the expense of specificity. This trade-off is a core concept in interpreting ROC curves and selecting optimal diagnostic thresholds.

Would you like to explore how different HbA1c thresholds perform across various populations in terms of sensitivity and specificity for diagnosing diabetes?

Question 482

Patients with the diagnosis of sickle cell anemia make a specific type of hemoglobin known as HgbS. This mutation results in the sickling of their red blood cells when exposed to inciting factors such as hypoxic conditions. Patients are often treated with hydroxyurea, which has which of the following direct effects on their hemoglobin physiology?

Answer Choices:

(A) Decreases oxygen carrying capacity of hemoglobin
(B) Increases levels of fetal hemoglobin (HgbF)
(C) Decreases levels of HgbS
(D) Decreases levels of fetal hemoglobin (HgbF)

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/c9414ee3-d913-4938-b54e-88211c90ec86

OpenEvidence Explanation

(CONTENT OMITTED)

The correct answer is **B. Increases levels of fetal hemoglobin (HgbF)**.

Hydroxyurea is a ribonucleotide reductase inhibitor that **induces fetal hemoglobin (HbF) production**, which is normally suppressed shortly after birth. [1][2] HbF directly inhibits intracellular HbS polymerization — the fundamental

pathological event in sickle cell disease — thereby reducing red cell rigidity, sickling, and hemolysis.[1][3] Randomized controlled trials have demonstrated a statistically significant increase in HbF levels with hydroxyurea compared to placebo (pooled mean difference ~9.88%).[3]

The mechanism of HbF induction involves hydroxyurea's cytostatic activity killing rapidly cycling erythroid precursors, which triggers stress erythropoiesis and favors production of F cells (red cells with high HbF content) from more primitive progenitors.[2][4] Additional beneficial effects include increased nitric oxide bioavailability, decreased red cell adhesion, and reduced leukocyte counts.[1][3]

The following figure illustrates how hydroxyurea shifts red cell production toward protective F cells, reducing sickling and downstream vaso-occlusive complications:

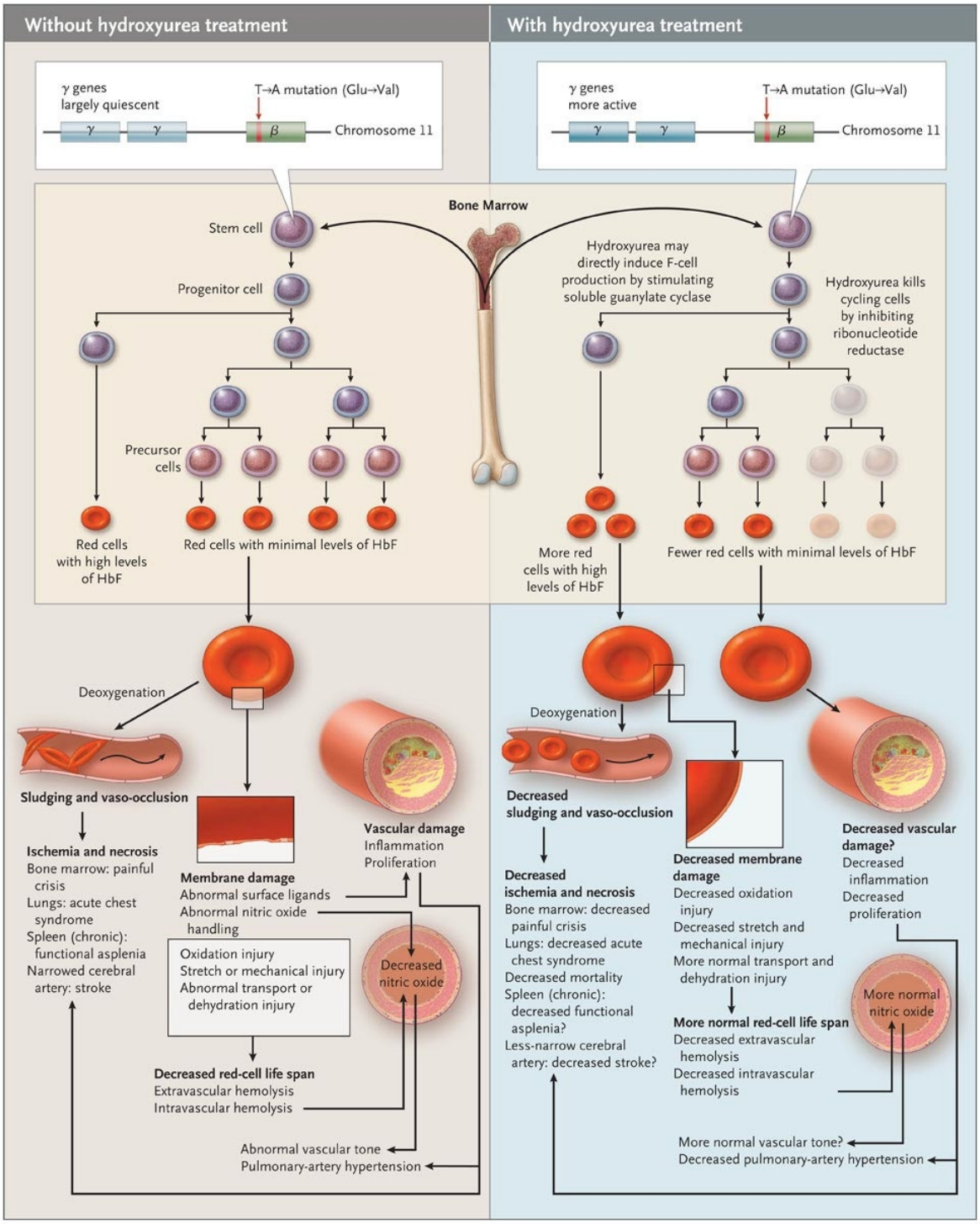


Figure 1. Pathophysiological Characteristics of Sickle Cell Anemia and the Effect of Hydroxyurea.

Used under license from The New England Journal of Medicine.

Regarding the other answer choices: hydroxyurea does not decrease oxygen-carrying capacity (A) — it actually improves anemia by reducing hemolysis. It does not directly decrease HbS levels (C); rather, the proportion of HbS decreases as HbF increases. And it increases, not decreases, HbF (D).[1][3]

Would you like to explore the specific dosing strategies and monitoring parameters for hydroxyurea in pediatric versus adult sickle cell disease patients?

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Question 486

A 2-year-old boy in respiratory distress is brought to the emergency department by his parents. They state that approximately one hour after putting their child to sleep, a hacking cough was heard from his bedroom. After entering his room the parents state their child appeared to be in distress, making a high pitched noise with every breath. Beyond a runny nose for the past few days, the child has been healthy. He has no toys in his bed or access to any other small objects. Physical exam demonstrates a 2-year-old child in respiratory distress.

Which of the following choices is the proper management for this patient?

Answer Choices:

(A) Humidified oxygen and dexamethasone; discharge if the patient improves
(B) Dexamethasome, racemic epinephrine and observation for 4 hours; discharge if stridor remits
(C) Broncoscopy to remove a foreign body in the upper airway then discharge
(D) Empiric intravenous (IV) antibiotics, intubate and admission

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/38f9cf30-1db4-49ec-965e-656d8f8844be

OpenEvidence Explanation

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The correct answer is **B. Dexamethasone, racemic epinephrine, and observation for 4 hours; discharge if stridor remits.**

This presentation is classic for **croup** (acute laryngotracheobronchitis): a 2-year-old with a preceding viral prodrome (runny nose), abrupt nocturnal onset of a barking/hacking cough, and inspiratory stridor. The key clinical features — age group (6 months to 3 years), URI prodrome, nighttime onset, barking cough, and stridor — are hallmarks of croup.[1][2]

Why B is correct: This child has moderate-to-severe croup given the respiratory distress and stridor. Guidelines recommend **corticosteroids as first-line treatment regardless of severity**, with **nebulized epinephrine added for moderate-to-severe presentations**.[2] After nebulized epinephrine, children should be monitored for **2 to 4 hours** due to its short half-life and risk of symptom recurrence (rebound effect).[2][3] Discharge is appropriate if stridor resolves and the child improves.

Why the other answers are incorrect:

- **A (Humidified oxygen and dexamethasone alone):** This would be appropriate for mild croup, but this child is in respiratory distress with stridor, indicating moderate-to-severe disease requiring nebulized epinephrine in addition to dexamethasone.[2][4]
- **C (Bronchoscopy for foreign body):** Foreign body aspiration typically presents with sudden onset and no prodrome or fever, and hoarseness/barking cough are usually absent. This child had a viral prodrome (runny nose) and no access to small objects, making croup far more likely.[5]
- **D (IV antibiotics, intubation, admission):** This would be appropriate for bacterial tracheitis or epiglottitis, which present with toxic appearance, high fever, and drooling — none of which are described here.[5][6]

  "Children with severe symptoms should be treated with nebulized epinephrine (0.5 ml of 2.25% racemic epinephrine in 4.5 ml of normal

saline). If treatment is given in an outpatient setting, it should be followed by at least 2 hours of observation for a return of obstructive symptoms before discharge."

—James D. Cherry, M.D., M.Sc., UCLA. Croup. N Engl J Med. January 24, 2008.

Used under license from The New England Journal of Medicine.

Would you like to explore the Westley croup scoring system and how it guides treatment escalation decisions?

Relevant images

(CONTENT OMITTED)

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Question 488

A 38-year-old woman presents with eye dryness and a foreign body sensation in the eyes. On physical examination, the oral cavity shows mucosal ulceration and atrophy. Biopsy of the lower lip shows marked lymphocytic infiltration of the minor salivary glands. Which of the following is most likely seen in this patient?

Answer Choices:

(A) Anti-Sjögren's syndrome type B (SS-B) antibody
(B) Anti-centromere antibody
(C) Anti-Jo-1 antibody
(D) Anti-Scl-70 antibodies

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/d84181d1-eba1-42f2-96c6-1f79d5e040e2

OpenEvidence Explanation

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The answer is **A. Anti-Sjögren's syndrome type B (SS-B) antibody**.

This clinical presentation — eye dryness (keratoconjunctivitis sicca), oral mucosal ulceration/atrophy, and **marked lymphocytic infiltration of the minor salivary glands** on lip biopsy — is classic for **Sjögren syndrome**. The hallmark

autoantibodies in this disease are **anti-SSA (anti-Ro)** and **anti-SSB (anti-La)**, which are found in approximately 70% of patients with primary Sjögren syndrome.[1][2] Anti-SSB antibodies are strongly associated with Sjögren syndrome and are rarely found without concomitant anti-SSA positivity.[3]

Among the other options:

- **Anti-centromere antibody (B)** is associated with **limited cutaneous systemic sclerosis** (CREST syndrome), not Sjögren syndrome.[1]
- **Anti-Jo-1 antibody (C)** is associated with **antisynthetase syndrome/polymyositis**, characterized by interstitial lung disease, myositis, and mechanic's hands.
- **Anti-Scl-70 (anti-topoisomerase I) antibody (D)** is associated with **diffuse cutaneous systemic sclerosis**.

The 2017 ACR-EULAR classification criteria for primary Sjögren syndrome assign equal weight (3 points each) to a salivary gland biopsy with a focus score ≥1 and the presence of anti-SSA antibodies, underscoring the central role of these serologic and histologic findings in diagnosis.[4]

Would you like to explore the systemic complications and lymphoma risk stratification in Sjögren syndrome based on autoantibody profiles?

References

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Question 489

A 62-year-old man with a history of chronic bronchitis comes to the physician because of a 1-month history of worsening shortness of breath and cough productive of thick sputum. He smoked one pack of cigarettes daily for 20 years but quit 5 years ago. Physical examination shows an increased anteroposterior chest diameter and coarse crackles in the lower lung fields bilaterally. Treatment with a drug that directly antagonizes the effects of vagal stimulation on the airways is begun. Which of the following drugs was most likely started?

> **Answer Choices:**
>
> (A) Fluticasone
> (B) Montelukast
> (C) Tiotropium
> (D) Cromolyn

> **Correct Answer:**
>
> (C)
>
> **OpenEvidence Response:**
>
> (C) ✓

OpenEvidence Link: https://openevidence.com/ask/8bb2362e-ab88-40c1-bb02-14f188a2c15f

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OpenEvidence Explanation

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The answer is **C. Tiotropium**.

Tiotropium is a long-acting muscarinic antagonist (LAMA) that directly blocks the action of acetylcholine — the neurotransmitter released by vagal (parasympathetic) nerve fibers — at M3 muscarinic receptors on airway smooth muscle. This is the drug that "directly antagonizes the effects of vagal stimulation on the airways."

Clinical reasoning in this case:

This patient presents with a classic picture of **COPD** (chronic bronchitis phenotype): long smoking history, productive cough, increased anteroposterior chest diameter (barrel chest from hyperinflation), and coarse crackles. The question stem specifically asks for a drug that counteracts vagal/parasympathetic tone in the airways.

- Vagal stimulation releases acetylcholine → activates muscarinic receptors → bronchoconstriction and mucus secretion.
- Tiotropium competitively and irreversibly binds M3 receptors, producing sustained bronchodilation and reducing mucus hypersecretion — making it a cornerstone of COPD maintenance therapy.

Why not the others?

- **A. Fluticasone** — An inhaled corticosteroid; reduces airway inflammation via glucocorticoid receptor activation, not a vagal antagonist.
- **B. Montelukast** — A leukotriene receptor antagonist; blocks cysteinyl leukotrienes, not acetylcholine.
- **D. Cromolyn** — A mast cell stabilizer; prevents degranulation and mediator release, not a muscarinic antagonist.

Would you like to explore the current GOLD guidelines on stepwise pharmacotherapy for COPD, including when to add ICS to bronchodilator therapy?

Question 490

A 14-year-old boy is brought to the physician for evaluation of his sense of smell. Two days ago, his mother found that he had left the gas on in the kitchen, and he was unable to smell the odor of the gas. As a child, he was consistently in the 40th percentile for height; now he is in the 15th percentile. He had bilateral orchidopexy for cryptorchidism as an infant. The patient is unable to identify several common odors when presented with them. Physical examination shows sparse axillary and pubic hair and Tanner stage 1 genitals. Which of the following is the most likely underlying cause of the patient's condition?

Answer Choices:

(A) Compression of pituitary stalk
(B) Hyperprolactinemia
(C) Impaired migration of GnRH neurons
(D) Decreased thyroxine production

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/3efdde10-d739-4521-93cb-81f4c8392b9b

OpenEvidence Explanation

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The correct answer is **C. Impaired migration of GnRH neurons**.

This clinical presentation is classic for **Kallmann syndrome**, which is characterized by the triad of **anosmia** (inability to smell), **hypogonadotropic hypogonadism** (delayed/absent puberty with prepubertal genitalia), and often **cryptorchidism** — all of which are present in this patient.[1][2]

Pathophysiology: During embryonic development, GnRH-producing neurons originate in the olfactory placode (nasal region) and must migrate along olfactory axons to reach the hypothalamus. In Kallmann syndrome, genetic mutations (in genes such as *ANOS1/KAL1*, *FGFR1*, *FGF8*, *CHD7*, *PROK2*, among others) disrupt this migratory process, causing GnRH neurons to fail to reach the hypothalamus.[2][3][4] Because the olfactory neurons share this developmental pathway, their migration is also impaired, resulting in olfactory bulb hypoplasia/aplasia and anosmia.[3][5]

The GnRH deficiency leads to low gonadotropins (LH and FSH), which in turn causes failure of pubertal development — explaining this patient's Tanner stage 1 genitalia, sparse secondary sexual hair, growth deceleration (loss of the pubertal growth spurt), and history of cryptorchidism.[2][6]

Why the other options are incorrect:

- **A (Compression of pituitary stalk):** A mass lesion (e.g., craniopharyngioma) could cause hypogonadotropic hypogonadism but would not explain congenital anosmia or cryptorchidism.
- **B (Hyperprolactinemia):** Elevated prolactin can suppress GnRH pulsatility and cause hypogonadism, but does not cause anosmia or cryptorchidism.
- **D (Decreased thyroxine production):** Hypothyroidism can cause growth delay and pubertal delay but does not cause anosmia or cryptorchidism in this pattern.

Would you like to explore the diagnostic workup and hormonal replacement strategies for Kallmann syndrome in adolescent males?

Relevant images

(CONTENT OMITTED)

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Question 491

A 26-year-old woman comes to the physician for a follow-up vaccination 1 week after being bitten by a rodent while camping. She received appropriate post-exposure prophylaxis in the emergency department and has already received 2 doses of the rabies vaccine. The same physician has been managing the post-exposure care regimen. After the physician administers the third dose of the rabies vaccine, the patient asks him if he would like to join her for a movie and dinner. The physician is interested in going on a date with her. Which of the following is the most appropriate reaction for the physician to have to the patient's invitation?

Answer Choices:

(A) Inform the patient that romantic relationships with current patients are unethical.
(B) Inform the patient that he will go on a date with her because her case is uncomplicated and does not require decision-making on his part.
(C) Inform the patient that dating her will never be appropriate even once the physician-patient relationship has been terminated.
(D) Inform the patient that he will go on a date with her, but that she will have to transfer her care to a different physician.

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/e64feb21-7ae4-42dc-af62-706a99487e2d

OpenEvidence Explanation

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The correct answer is **A. Inform the patient that romantic relationships with current patients are unethical.**

The physician-patient relationship is currently active — the patient is still receiving her rabies post-exposure prophylaxis series, and the physician is actively managing her care. Romantic or sexual relationships between a physician and a **current patient are always unethical**, regardless of whether the patient initiates the interaction.[1][2][3]

Why the other options are incorrect:

- **B (uncomplicated case, no decision-making):** The complexity of the medical case is irrelevant. The ethical prohibition applies to all physician-patient relationships, not just those involving complex decision-making. The inherent power imbalance and potential to exploit patient trust exist regardless of case complexity.[2][3]
- **C (dating will never be appropriate):** This is too absolute. While romantic relationships with current patients are prohibited, relationships with **former** patients may be permissible under certain circumstances after the physician-patient relationship has been appropriately terminated and a sufficient period of time has passed. The AMA Council on Ethical and Judicial Affairs concluded that romantic relationships with former patients "may be unethical under certain circumstances" — not that they are categorically prohibited forever. Permanent prohibition applies specifically to vulnerable patients or those with psychiatric disorders.[1][3]
- **D (date her but transfer care):** Simply transferring care to pursue a romance is itself considered unethical. Terminating the physician-patient relationship specifically to pursue a romantic relationship is still problematic and may be unlawful, as it can exploit trust, knowledge, or influence derived from the professional relationship.[1]

The key ethical principle is that a patient's apparent consent does not make the relationship permissible, because the inherent power imbalance in the physician-patient relationship makes true voluntary consent uncertain.[2]

Would you like to explore the specific ethical guidelines around when, if ever, a romantic relationship with a former patient may become permissible after termination of the physician-patient relationship?

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Question 494

A 2050-g (4.5-lb) female newborn and a 2850-g (6.3-lb) female newborn are delivered at 37 weeks' gestation to a 23-year-old, gravida 2, para 1 woman. The mother had no prenatal care. Examination of the smaller newborn shows a flattened nose and left-sided clubfoot. The hematocrit is 42% for the smaller newborn and 71% for the larger newborn. This pregnancy was most likely which of the following?

Answer Choices:

(A) Monochorionic-diamniotic monozygotic
(B) Dichorionic-diamniotic dizygotic
(C) Monochorionic-monoamniotic monozygotic
(D) Conjoined twins

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/0f196c42-3963-476d-9a43-24ac4bea9181

OpenEvidence Explanation

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The answer is **A. Monochorionic-diamniotic monozygotic**.

This clinical scenario describes **twin-to-twin transfusion syndrome (TTTS)** or **twin anemia-polycythemia sequence (TAPS)**, which are complications unique to

monochorionic-diamniotic (MCDA) twin pregnancies. Several key findings point to this diagnosis:

Hematocrit discordance: The smaller twin has a hematocrit of 42% (donor/anemic twin), while the larger twin has a hematocrit of 71% (recipient/polycythemic twin). This significant intertwin hematocrit difference results from unbalanced blood transfusion through shared placental vascular anastomoses, which are characteristic of monochorionic placentas.[1][2]

Growth discordance: The weight difference between the twins (2050 g vs. 2850 g, approximately 28% discordance) is consistent with unequal placental sharing, commonly seen in MCDA pregnancies.[3][4]

Deformation findings in the smaller twin: The flattened nose and clubfoot in the donor twin result from **oligohydramnios** (reduced amniotic fluid due to decreased urine output from hypovolemia), causing the "stuck twin" phenomenon with compressive deformities.[5][6]

Why not the other options:

- **B (Dichorionic-diamniotic dizygotic)**: Dizygotic twins have separate placentas without shared vascular anastomoses, so TTTS/TAPS cannot occur.[5]
- **C (Monochorionic-monoamniotic monozygotic)**: TTTS is very uncommon in monoamniotic twins because they typically have large bidirectional arterioarterial anastomoses that balance blood flow. Additionally, the oligohydramnios sequence causing deformations in one twin would not occur in a shared amniotic cavity.[5]
- **D (Conjoined twins)**: This would present with physically connected twins, not the findings described here.

TTTS complicates approximately **10–15% of MCDA pregnancies** and results from arteriovenous anastomoses in the shared monochorionic placenta that create an imbalanced fetal-placental circulation.[1][4]

Would you like to explore the Quintero staging system for TTTS and the role of fetoscopic laser coagulation in management?

Relevant images

(CONTENT OMITTED)

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Question 496

A 24-year-old woman is brought to the physician because of agitation, confusion, and lethargy. She has also had progressive recurring headaches and visual impairment over the last month. Three days ago, she had a seizure but has not seen a physician. She is oriented only to person. Her temperature is 36.7°C (98.1°F), pulse is 90/min, and blood pressure is 110/80 mm Hg. Capillary refill time is more than 3 seconds. Her laboratory studies show:
Hemoglobin 11.2 g/dL
Leukocyte count 7000/mm3
Serum
Na+ 148 mEq/L
Cl- 100 mEq/L
K+ 3.8 mEq/L
HCO3- 26 mEq/L
Urea nitrogen 18 mg/L
Glucose 90 mg/L
Creatinine 0.8 mg/L
Osmolality 300 mOsmol/kg H2O
Urine osmolality 240 mOsm/kg H2O
Which of the following is the most likely explanation for this patient's hypernatremia?

Answer Choices:

(A) Increased water intake
(B) Increased adrenocorticotropin hormone secretion
(C) Decreased antidiuretic hormone secretion
(D) Decreased adrenocorticotropin hormone secretion

Correct Answer:

(C)

OpenEvidence Response:

> (C) ✓

OpenEvidence Link: https://openevidence.com/ask/61e10032-e4f5-45af-bb74-2cb6319efc15

OpenEvidence Explanation

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The correct answer is **C. Decreased antidiuretic hormone secretion**.

This patient's presentation — progressive headaches, visual impairment, seizure, confusion, and lethargy in a young woman — is consistent with a **central nervous system lesion** (likely a hypothalamic/pituitary mass such as a craniopharyngioma or other sellar/suprasellar tumor) causing **central diabetes insipidus** through decreased ADH (vasopressin) secretion.

The key laboratory findings that confirm this mechanism:

- **Serum Na^+ of 148 mEq/L** (hypernatremia) with **serum osmolality of 300 mOsm/kg** (elevated)
- **Urine osmolality of 240 mOsm/kg**, which is inappropriately **dilute** relative to the serum hyperosmolality

Under normal physiology, when serum sodium exceeds ~145 mmol/L, vasopressin levels should be high enough to produce maximally concentrated urine (~1200 mOsm/kg).[1] The presence of dilute urine in the setting of hypernatremia implies either **deficient vasopressin secretion** (central diabetes insipidus) or renal resistance to vasopressin (nephrogenic diabetes insipidus).[1] The neurological symptoms (headaches, visual changes, seizure) point to a central cause.

Why the other options are incorrect:

- **A (Increased water intake)** — Polydipsia would cause hyponatremia, not hypernatremia.

- **B (Increased ACTH secretion)** — Cushing syndrome can cause mild hypernatremia but would not explain the dilute urine or the neurological presentation in this pattern.
- **D (Decreased ACTH secretion)** — Adrenal insufficiency from ACTH deficiency typically causes hyponatremia (due to impaired free water excretion and increased ADH release), not hypernatremia.

The prolonged capillary refill time (>3 seconds) further supports dehydration from ongoing free water losses, which in the setting of impaired consciousness limits the patient's ability to compensate through thirst-driven water intake.[2] [3]

Would you like to explore the diagnostic workup for central diabetes insipidus, including the role of copeptin testing versus the traditional water deprivation test?

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Question 497

A 29-year-old woman presents to the physician with a blurred vision of her right eye for 2 days. She has pain around her right eye during eye movement. She takes no medications. At the clinic, her blood pressure is 110/70 mm Hg, the pulse is 72/min, respirations are 15/min, and the temperature is 36.5°C (97.7°F). On physical examination, illumination of the left eye results in bilateral pupillary constriction while illumination of the right eye results in a mild bilateral pupillary dilation. Fundoscopic examination shows optic disk swelling in the right eye. The color vision test shows decreased perception in the right eye. The remainder of the physical examination shows no abnormalities. Specific additional history should be obtained regarding which of the following?

Answer Choices:

(A) Dry eyes
(B) High-risk sexual behaviour
(C) Oral ulcers
(D) Sensory loss

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/5d1fe5b8-710a-410d-aa2c-4dab8af68d2f

OpenEvidence Explanation

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The answer is **D. Sensory loss**.

This patient presents with a classic case of **optic neuritis**: a young woman with acute painful monocular visual loss, pain with eye movement, a **relative afferent pupillary defect** (RAPD — demonstrated by the bilateral pupillary dilation when the right eye is illuminated, i.e., a positive swinging flashlight test), optic disc swelling, and decreased color vision.[1][2] Optic neuritis is the presenting feature of **multiple sclerosis (MS)** in 15–20% of cases and occurs at some point during the disease course in over 50% of MS patients.[1][2]

Given the strong association between optic neuritis and MS, the most important additional history to obtain is regarding **sensory loss** (e.g., limb paresthesias, numbness, banding dysesthesias), which would suggest prior or concurrent demyelinating episodes in other CNS regions. Classic MS presentations include extremity and torso sensory disturbances, weakness, ataxia, and brainstem syndromes.[3] Identifying such symptoms would support dissemination in space and time — the hallmark diagnostic criteria for MS.

Why the other options are less appropriate:

- **A. Dry eyes** — associated with Sjögren syndrome, which can rarely cause optic neuropathy but is not the primary concern in this classic presentation.
- **B. High-risk sexual behavior** — relevant for syphilitic optic neuritis, but this presentation is typical of demyelinating optic neuritis, not infectious.
- **C. Oral ulcers** — associated with Behçet disease, which can cause optic neuropathy but is far less common than MS-associated optic neuritis in this demographic.

Would you like to explore the recommended workup for a first episode of optic neuritis, including the role of brain MRI in stratifying MS risk?

Relevant images

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Question 498

A 25-year-old woman presents to her physician with complaints of cyclic vomiting for 3 days. The vomitus is watery and contains undigested food particles. She also complains of feeling tired and having the “sniffles”. She has not felt like eating or drinking since her symptoms started, and she has not taken any medications. Her concern now is that she immediately gets dizzy when she stands up. Vitals signs include: pulse 120/min, respiratory rate 9/min, and blood pressure 100/70 mm Hg. Her eyes are sunken, and her tongue appears dry. Which set of lab values would best correspond to this patient’s condition?

Answer Choices:

(A) pH = 7.5, Pco2 = 50 mm Hg, HCO32- = 38 mEq/L
(B) pH = 7.2, Pco2 = 25 mm Hg, HCO32- = 30 mEq/L
(C) pH = 7.5, Pco2 = 34 mm Hg, HCO32- = 38 mEq/L
(D) pH = 7.5, Pco2 = 30 mm Hg, HCO32- = 24 mEq/L

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/b8bb8780-7c56-4e8d-97ec-0c8671548b57

OpenEvidence Explanation

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The answer is **A: pH = 7.5, PCO2 = 50 mm Hg, HCO_3^- = 38 mEq/L**, which represents a **metabolic alkalosis with appropriate respiratory compensation** (compensatory hypoventilation).

Why metabolic alkalosis? This patient has been vomiting for 3 days, losing gastric acid (HCl). Loss of hydrogen and chloride ions from the stomach generates metabolic alkalosis, characterized by elevated pH and elevated HCO_3^-. Volume depletion (sunken eyes, dry tongue, orthostatic hypotension, tachycardia) further maintains the alkalosis by impairing renal bicarbonate excretion.[1][2] A nearly identical clinical vignette published in NEJM — a 31-year-old woman vomiting for 2 days with hypotension — showed pH 7.54, PCO2 48 mm Hg, and HCO_3^- 40 mmol/L.[3]

Why is PCO2 elevated? The expected respiratory compensation for metabolic alkalosis is hypoventilation, which raises PCO2. The compensation formula is: **Expected PCO2 = 0.7 × (HCO_3^- − 24) + 40 ± 2 mm Hg**.[4] For an HCO_3^- of 38: expected PCO2 = 0.7 × 14 + 40 = **49.8 mm Hg**, which closely matches the 50 mm Hg in option A. This is also consistent with the patient's low respiratory rate of 9/min, reflecting compensatory hypoventilation.[5]

Why not the other options?

- **B (pH 7.2, PCO2 25, HCO_3^- 30):** An acidemic pH with elevated bicarbonate is internally inconsistent and does not fit any recognized acid-base pattern for vomiting.
- **C (pH 7.5, PCO2 34, HCO_3^- 38):** While the pH and HCO_3^- suggest metabolic alkalosis, the PCO2 of 34 is inappropriately low (expected ~50), indicating a concurrent respiratory alkalosis rather than appropriate compensation.
- **D (pH 7.5, PCO2 30, HCO_3^- 24):** A normal bicarbonate with low PCO2 represents a primary respiratory alkalosis, not the metabolic alkalosis expected from vomiting.

Would you like to explore the management of contraction alkalosis, including fluid and electrolyte replacement strategies?

Relevant images

(CONTENT OMITTED)

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Question 502

A 45-year-old woman comes into your office with complaints of lump she found on her neck while showering. She denies any other symptoms and states that she has not gained any weight. On exam, you notice a 2 cm nodule on her anterior neck. Her TSH level is normal and radionucleotide scan reveals a cold nodule. Fine needle aspiration biopsy (FNAB) reveals follicular architecture suspicious for malignancy. What is the next best step?

> **Answer Choices:**
>
> (A) Punch biopsy
> (B) Surgical excision
> (C) Thyroxine administration
> (D) Ultrasound

> **Correct Answer:**
>
> **(B)**
>
> **OpenEvidence Response:**
>
> **(B)** ✓

OpenEvidence Link: https://openevidence.com/ask/61008411-2fc7-4a8b-9c51-a616bef70e7a

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OpenEvidence Explanation

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The answer is **B. Surgical excision** (lobectomy or thyroidectomy). When FNAB of a thyroid nodule reveals follicular architecture suspicious for malignancy, surgical excision is the next best step because the definitive diagnosis of

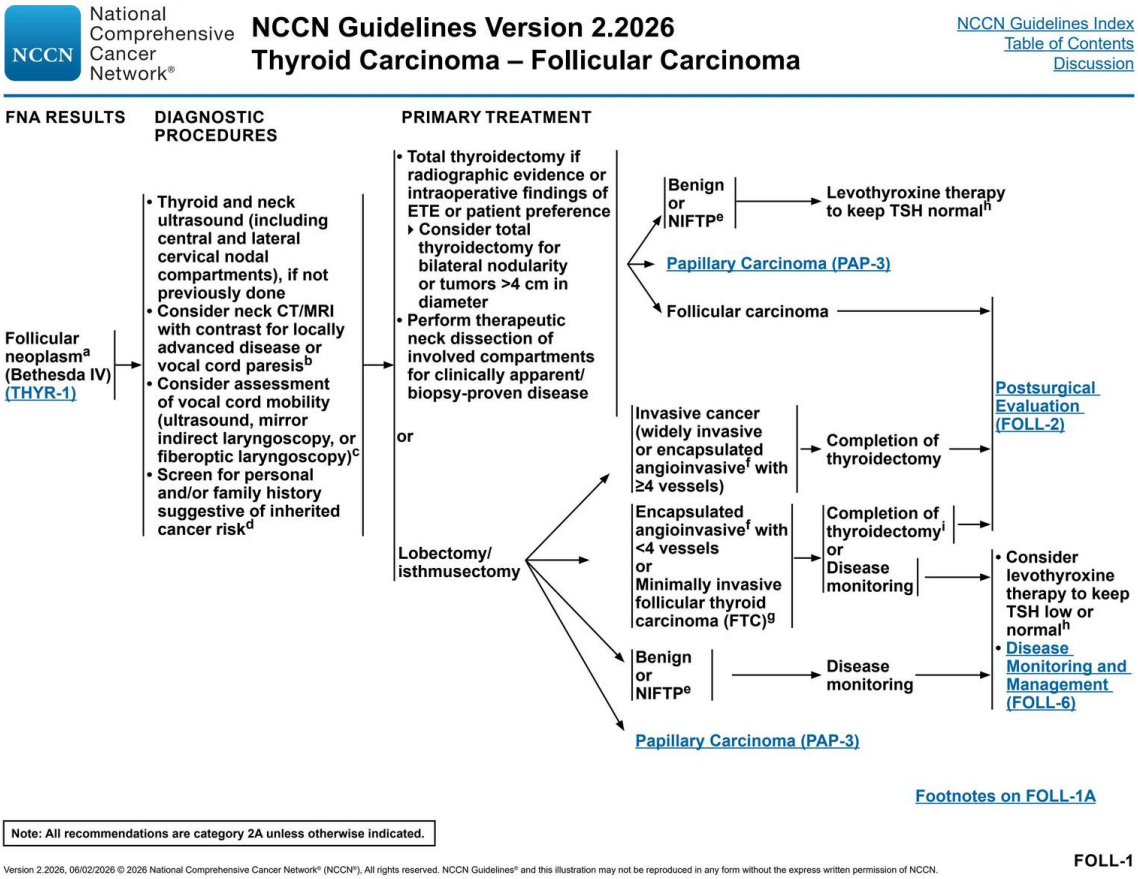
follicular carcinoma requires histologic evidence of vascular or capsular invasion, which **cannot be determined by FNA alone**.[1]

Why surgical excision is necessary: Follicular neoplasm on FNA corresponds to Bethesda category IV, which carries a mean risk of malignancy of approximately 30% (range 23–34%).[1] The distinction between follicular adenoma and follicular carcinoma hinges on demonstrating capsular or vascular invasion on permanent histologic sections — something no cytologic or imaging modality can provide.[1][2] The NCCN Thyroid Carcinoma Guidelines recommend **lobectomy/isthmusectomy** as the primary surgical approach for Bethesda IV nodules, with total thyroidectomy reserved for cases with extrathyroidal extension, bilateral nodularity, or tumors >4 cm.[1] The AACE/ACE guidelines similarly state that surgical excision with histologic examination should be performed in most cases of follicular neoplasm.[3]

Why the other options are incorrect:

- **A. Punch biopsy** — Punch biopsy is a dermatologic technique and has no role in thyroid nodule evaluation.
- **C. Thyroxine administration** — Thyrotropin-suppressive therapy with thyroid hormone is **not recommended** for euthyroid patients with thyroid nodules. This patient already has a normal TSH.[2][4]
- **D. Ultrasound** — While thyroid ultrasound is an important part of the initial workup, this patient has already undergone radionuclide scanning and FNAB. Ultrasound would not change the need for surgical excision given the cytologic findings suspicious for malignancy. Although NCCN guidelines do recommend ultrasound as part of the diagnostic workup if not previously done, the question stem implies the workup has progressed to the point where the next definitive step is surgery.[1]

The following NCCN algorithm illustrates the management of follicular neoplasm (Bethesda IV), showing the pathway from FNA results through diagnostic procedures to primary treatment with lobectomy or total thyroidectomy:



FOLL-1. Follicular Carcinoma: FNA Results, Diagnostic Procedures, and Primary Treatment for Follicular Neoplasm (Bethesda IV) — NCCN Guidelines® — Thyroid Carcinoma p. 27 (v2.2026)

Would you like to explore the role of molecular testing (e.g., gene expression classifier, mutational analysis) in refining the management of indeterminate thyroid nodules and potentially avoiding unnecessary surgery?

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Question 504

A 3-year-old boy is brought to the physician for a well-child examination. Over the past 8 months, his mother reports difficulty understanding the boy's speech. On occasion during this period, she has noticed that he does not respond when called by name and cannot follow 1-step instructions. He has a history of recurrent ear infections treated with antibiotics since birth. He is at the 60th percentile for length and 50th percentile for weight. Vital signs are within normal limits. His speech is quiet and difficult to understand. Otoscopic examination shows retracted tympanic membranes bilaterally that are immobile on pneumatic otoscopy. Nasopharyngoscopy shows mild adenoid hypertrophy. Pure tone audiometry shows a conductive hearing loss of 26 dB on the right side and 28 dB on the left side. Which of the following is the most appropriate next step in management?

Answer Choices:

(A) Adenoidectomy
(B) Tympanostomy tube insertion
(C) Antihistamine therapy
(D) Corticosteroid therapy

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/9b11c873-9476-4853-a286-fd5b91f94df1

OpenEvidence Explanation

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The most appropriate next step is **B. Tympanostomy tube insertion**.

This child presents with classic findings of **chronic bilateral otitis media with effusion (OME)**: retracted, immobile tympanic membranes bilaterally, a history of recurrent ear infections, and **bilateral mild conductive hearing loss** (26–28 dB) with associated speech and language difficulties over 8 months. Per the **AAO-HNS Clinical Practice Guideline on Tympanostomy Tubes in Children**, clinicians should offer bilateral tympanostomy tube insertion to children with bilateral OME for ≥3 months AND documented hearing difficulties.[1][2] This child clearly meets both criteria — bilateral effusion well beyond 3 months and documented hearing loss in the mild range (16–40 dB) with functional impairment (unintelligible speech, inability to follow commands).[1]

Why not the other options?

- **Adenoidectomy alone (A):** While mild adenoid hypertrophy is noted, adenoidectomy alone is not the preferred initial surgical intervention for OME. Guidelines recommend adenoidectomy as an adjunct to tympanostomy tubes, primarily in children **≥4 years old**; it is not recommended as a standalone treatment for middle ear disease in children under 4 years without symptoms directly related to the adenoid (obstruction or infection).[1][3]

- **Antihistamine therapy (C):** Antihistamines, decongestants, and similar medical therapies have not been shown to improve outcomes in OME and are not recommended.[4]

- **Corticosteroid therapy (D):** Oral and nasal corticosteroids offer limited short-term benefit for OME and are not routinely recommended, particularly in a child with chronic bilateral effusion and documented hearing loss who meets surgical criteria.[4][5]

Would you like to explore the perioperative considerations and expected outcomes following tympanostomy tube insertion in young children?

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Question 505

A 42-year-old man is admitted to the intensive care unit with decreased consciousness and convulsions. His wife reports that 30 min following the onset of her husband's condition, which started approximately 6 hours ago, he treated his garden bed with pesticides against mice. He developed nausea, vomiting, and abdominal cramps. The patient noted facial muscle twitching and developed a tonic-clonic seizure that lasted 3 minutes, 4 hours following the onset of his condition. His past medical history is insignificant for any seizure disorders, and he does not take any medications. His blood pressure is 95/60 mm Hg, heart rate is 104/min, respiratory rate is 10/min, and the temperature is 37.0°C (98.6°F). On physical examination, the patient's consciousness is decreased with a Glasgow Coma Scale score of 13. He is pale and sweaty. His lung sounds are normal, cardiac sounds are decreased, and no murmurs are present. Abdominal palpation reveals epigastric tenderness. Neurological examination shows rapid downbeating nystagmus, facial muscle twitching, and symmetrically decreased sensation to all the sensory modalities on both the upper and lower extremities. Further discussion reveals that the patient was using sodium fluoroacetate as a pesticide, which is known to form fluorocitrate in the cells of aerobic organisms. Which of the following substances will accumulate in the patient's cells?

Answer Choices:

(A) Fumarate
(B) Citrate
(C) Malate
(D) Succinate

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/9187da1a-9635-404a-9ea8-bce0296a53db

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OpenEvidence Explanation

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The answer is **B. Citrate**.

Sodium fluoroacetate undergoes "lethal synthesis" in the body: it is converted to **fluorocitrate**, which potently inhibits the enzyme **aconitase** (aconitate hydratase) in the tricarboxylic acid (TCA) cycle.[1][2] Aconitase normally catalyzes the conversion of citrate to isocitrate. When this enzyme is blocked, **citrate accumulates** in the cells because it cannot proceed to the next step of the cycle.

This mechanism has been directly confirmed experimentally — fluoroacetate exposure increased cardiac citrate concentrations by **4.2-fold** in a rat model.[3] The accumulation of citrate is considered the primary toxic effect, likely through chelation of free calcium ions (leading to hypocalcemia), which contributes to the neurological symptoms (seizures, muscle twitching) and cardiac toxicity seen in this patient.[2][4]

The other answer choices — fumarate, malate, and succinate — are TCA cycle intermediates that occur downstream of the aconitase step and would not accumulate from this specific enzymatic blockade.

Would you like to explore the clinical management and antidotal strategies for sodium fluoroacetate poisoning, including the roles of calcium gluconate and sodium succinate?

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Question 507

A 68-year-old man comes to the emergency department because of a cough, dyspnea, and fever for 1 day. The cough is productive of small amounts of green phlegm. He has metastatic colon cancer and has received three cycles of chemotherapy with 5-fluorouracil, leucovorin, and oxaliplatin; his last chemotherapy session was 2.5 months ago. He has chronic obstructive pulmonary disease and has been treated with antibiotics and prednisolone for acute exacerbations three times in the past year. His medications include a fluticasone-salmeterol inhaler and a tiotropium bromide inhaler. He has smoked one pack of cigarettes daily for 48 years. His temperature is 39.1°C (103.1°F), pulse is 112/min, respirations are 32/min, and blood pressure is 88/69 mm Hg. Pulse oximetry on room air shows an oxygen saturation of 88%. Pulmonary examination shows diffuse crackles and rhonchi. An x-ray of the chest shows a left upper-lobe infiltrate of the lung. Two sets of blood cultures are obtained. Endotracheal aspirate Gram stain shows gram-negative rods. Two large bore cannulas are inserted and intravenous fluids are administered. Which of the following is the most appropriate pharmacotherapy?

Answer Choices:

(A) Ceftriaxone and azithromycin
(B) Ertapenem
(C) Colistin
(D) Cefepime and levofloxacin

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/ce14fb6e-12fe-4bcf-8e0f-34afff20981c

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OpenEvidence Explanation

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The most appropriate pharmacotherapy is **D. Cefepime and levofloxacin**, as this patient requires empiric broad-spectrum coverage with **antipseudomonal activity** given his multiple risk factors for Pseudomonas aeruginosa infection.

Why antipseudomonal coverage is necessary: This patient has several key risk factors that mandate antipseudomonal empiric therapy:

- **Immunocompromised state** from chemotherapy for metastatic colon cancer (FOLFOX regimen)
- **Structural lung disease** (COPD with frequent exacerbations)
- **Chronic corticosteroid use** (fluticasone inhaler, repeated prednisolone courses)
- **Repeated antibiotic exposure** (three courses in the past year)
- **Severe presentation** with sepsis (fever, tachycardia, tachypnea, hypotension, hypoxia)
- **Gram-negative rods** on endotracheal aspirate Gram stain, consistent with Pseudomonas

The ATS/IDSA guidelines recommend that when risk factors for P. aeruginosa are present, empiric coverage should include an antipseudomonal beta-lactam (such as **cefepime**, piperacillin-tazobactam, or a carbapenem) combined with an antipseudomonal fluoroquinolone (such as **levofloxacin**).[1] The NCCN guidelines for cancer-related infections similarly recommend cefepime (Category 1) as empiric therapy for febrile neutropenia with broad-spectrum antipseudomonal coverage.[2]

Why the other options are incorrect:

- **A. Ceftriaxone and azithromycin** — This is the standard regimen for community-acquired pneumonia without risk factors for resistant organisms. Ceftriaxone lacks antipseudomonal activity, making it inadequate here.[1]
- **B. Ertapenem** — Although a carbapenem, ertapenem specifically **lacks antipseudomonal activity**, as noted in the NCCN guidelines. It would be inappropriate when Pseudomonas is a concern.[2]
- **C. Colistin** — This is a last-resort agent reserved for multidrug-resistant gram-negative infections when no other alternatives are available. Guidelines recommend against using colistin unless agents with adequate gram-negative activity are unavailable. It is not appropriate as first-line empiric therapy.[3][4]

The combination of cefepime (antipseudomonal cephalosporin) plus levofloxacin (antipseudomonal fluoroquinolone) provides appropriate dual antipseudomonal coverage for this severely ill, immunocompromised patient with gram-negative pneumonia.[1][5]

Would you like to explore the approach to de-escalation of antibiotics once culture and sensitivity results return in this clinical scenario?

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Question 508

A 21-year-old old college student is brought to the emergency department by his roommates because he has been acting strangely. Over the last 7 months, he has claimed to hear voices telling him that he must prepare for the end of the world. He used to be a straight A student but started failing exams recently due to his erratic behavior. Furthermore, there are periods of time where he does not sleep for several days and redecorates the entire apartment. During those times he spends huge amounts of money on online shopping. These periods usually last for about 2 weeks and happen every other month. On physical exam, he appears unkept and irritated. He seems to respond to invisible stimuli, and he jumps from topic to topic without clear focus. Which of the following is most consistent with this patient's presentation?

Answer Choices:

(A) Brief psychotic disorder
(B) Schizoaffective disorder
(C) Schizophreniform disorder
(D) Schizotypal personality disorder

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/38fdbe67-66d8-42ee-ba01-28d7288cb29c

OpenEvidence Explanation

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The answer is **B. Schizoaffective disorder**.

This patient's presentation combines two key features that define schizoaffective disorder: **persistent psychotic symptoms** (auditory hallucinations for 7 months, disorganized speech, responding to internal stimuli) alongside **distinct manic episodes** (decreased need for sleep, excessive spending, increased goal-directed activity lasting ~2 weeks every other month).[1][2]

Why schizoaffective disorder fits:

- The patient meets **Criterion A for schizophrenia** — auditory hallucinations and disorganized speech (tangential, jumping between topics) have been present over a 7-month period.[1]
- Superimposed on this are **recurrent manic episodes** — periods of insomnia, excessive spending, and increased activity lasting ~2 weeks, consistent with a major mood episode (manic type).[2]
- Critically, the psychotic symptoms (voices, disorganized thinking) persist **between** the manic episodes, satisfying the DSM-5 requirement that hallucinations or delusions be present for at least 2 weeks in the absence of a major mood episode (Criterion B). This distinguishes schizoaffective disorder from bipolar disorder with psychotic features, where psychosis occurs only during mood episodes.[1]

Why the other options are incorrect:

- **A. Brief psychotic disorder** — requires psychotic symptoms lasting **less than 1 month** with full return to premorbid functioning. This patient has had symptoms for 7 months.[1][3]
- **C. Schizophreniform disorder** — involves schizophrenia-like symptoms lasting **1–6 months** without prominent mood episodes. This patient's illness exceeds 6 months and includes clear manic episodes, which rules out this diagnosis.[1]
- **D. Schizotypal personality disorder** — a personality disorder characterized by eccentric behavior, odd beliefs, and social deficits, but **not** frank

psychotic episodes (sustained hallucinations, delusions) or manic episodes. [1]

The typical age of onset for schizoaffective disorder is early adulthood, consistent with this 21-year-old's presentation.[1] Treatment typically involves a combination of antipsychotics with mood stabilizers and/or antidepressants, depending on the subtype (bipolar vs. depressive).[4][5]

Would you like to explore the evidence-based pharmacotherapy approach for schizoaffective disorder, bipolar type, including the role of specific antipsychotics and mood stabilizers?

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Question 509

An 81-year-old man is brought to the clinic by his son to be evaluated for memory issues. The patient's son says he has difficulty remembering recent events and names. He says the patient's symptoms have progressively worsened over the last several years but became acutely worse just recently. Also, yesterday, the patient complained that he could not see out of his right eye, but today he can. When asked about these concerns, the patient seems to have no insight into the problem and reports feeling well. His medical history is significant for diabetes mellitus type 2 and hypertension. He had a left basal ganglia hemorrhage 12 years ago and a right middle cerebral artery infarction 4 years ago. Current medications are amlodipine, aspirin, clopidogrel, metformin, sitagliptin, and valsartan. He lives with his son and can feed himself and change his clothes. There is no history of urinary or fecal incontinence. His vitals include: blood pressure 137/82 mm Hg, pulse 78/min, respiratory rate 16/min, temperature 37.0°C (98.6°F). On physical examination, the patient is alert and oriented. He is unable to perform simple arithmetic calculations and the mini-mental status exam is inconclusive. He can write his name and comprehend written instructions. Muscle strength is 4/5 on the right side. The tone is also slightly reduced on the right side with exaggerated reflexes. His gait is hemiparetic. Which of the following is the most likely diagnosis in this patient?

Answer Choices:

(A) Alzheimer's disease
(B) Lewy body dementia
(C) Normal-pressure hydrocephalus
(D) Vascular dementia

Correct Answer:

(D)

OpenEvidence Response:

> **(D)** ✓

OpenEvidence Link: https://openevidence.com/ask/073ef3ef-744f-440c-85e9-065ebc81f4ec

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OpenEvidence Explanation

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The most likely diagnosis is **D. Vascular dementia**.

This patient's presentation is classic for vascular dementia based on several converging features:

- **History of multiple cerebrovascular events**: A left basal ganglia hemorrhage (12 years ago) and a right MCA infarction (4 years ago), establishing significant cumulative vascular brain injury.[1][2]
- **Stepwise cognitive decline**: Progressive memory difficulties over years with an **acute recent worsening**, consistent with the characteristic stepwise pattern of vascular dementia where cognitive function declines abruptly after new vascular events, then plateaus.[3]
- **Transient monocular visual loss**: The episode of transient right eye vision loss lasting approximately one day is consistent with **amaurosis fugax** (a TIA), suggesting ongoing cerebrovascular disease and further supporting a vascular etiology.[4][5]
- **Focal neurological deficits on exam**: Right-sided hemiparesis (4/5 strength), reduced tone, exaggerated reflexes, and hemiparetic gait — all consistent with sequelae of prior left-sided cerebrovascular events. Focal neurologic signs on examination are characteristic of vascular dementia and argue against Alzheimer disease, where the neurologic exam is typically normal in early stages.[3]

- **Vascular risk factors**: Diabetes mellitus type 2 and hypertension are major risk factors for vascular dementia.[1][3]

- **Cognitive profile**: Difficulty with arithmetic (executive function) with preserved writing and comprehension is more consistent with vascular cognitive impairment, where executive dysfunction and processing speed deficits predominate, rather than the episodic memory loss typical of early Alzheimer disease.[1][2]

Why not the other options:

- **Alzheimer disease (A)**: Typically presents with insidious, gradually progressive episodic memory loss without stepwise decline, focal neurologic deficits, or TIA episodes. The normal neurologic exam in early AD contrasts sharply with this patient's hemiparesis and hyperreflexia.[3]

- **Lewy body dementia (B)**: Characterized by visual hallucinations, fluctuating cognition, REM sleep behavior disorder, and parkinsonian features (rigidity, bradykinesia, tremor) — none of which are described here.[3]

- **Normal-pressure hydrocephalus (C)**: Presents with the classic triad of gait disturbance, urinary incontinence, and dementia. This patient has no urinary incontinence, and his gait abnormality is hemiparetic (lateralized) rather than the magnetic/apraxic gait of NPH.[3]

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Question 510

A 46-year-old woman with a history of previously well-controlled HIV infection comes to the physician for follow-up after a health maintenance examination last week. She is currently unemployed and lives in a low-income neighborhood with her 3 children. For the past 3 years, her HIV RNA viral load was undetectable, but last week, her viral load was 8,391 copies/mL (N < 50). Current medications include dolutegravir, tenofovir, and emtricitabine. On questioning, she says that she misses her medications every other day. Which of the following responses by the physician is most appropriate?

Answer Choices:

(A) Let's talk about what makes it difficult for you to take your medications.
(B) Are you aware that it is essential to take your medications every day?
(C) The social worker can help subsidize next month's medications.
(D) We should go over the instructions on how to take your medications again.

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/ec5a7b2f-8dbb-4e8e-b097-13055a1de33b

OpenEvidence Explanation

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The correct answer is **A. "Let's talk about what makes it difficult for you to take your medications."**

This response exemplifies the **open-ended, nonjudgmental, barrier-eliciting approach** that is the cornerstone of effective adherence counseling in HIV care. The NIH/OARAC Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV explicitly recommend that clinicians "engage people struggling with adherence with a constructive, collaborative, nonjudgmental, and problem-solving approach rather than reprimanding them or lecturing them on the importance of adherence".[1] The guidelines further state that simply instructing adherence and warning about consequences "fails to acknowledge a person's barriers to adherence, fails to provide actionable information, erodes rather than builds the patient-provider relationship, and has been demonstrated to not improve adherence".[1]

Why the other options are inferior:

- **B ("Are you aware that it is essential to take your medications every day?")** — This is a closed-ended, lecturing approach that assumes a knowledge deficit. It is paternalistic and does not explore the patient's barriers. Guidelines specifically caution against this type of response.[1][2]
- **C ("The social worker can help subsidize next month's medications")** — While financial barriers are a recognized driver of nonadherence, this response assumes the reason for nonadherence without first asking the patient. The IDSA/HIVMA guidelines emphasize that barriers are heterogeneous and must be individually elicited before solutions are offered. Cost may not be this patient's primary barrier.[1][2]
- **D ("We should go over the instructions on how to take your medications again")** — This assumes the patient does not understand how to take the medications, which is unlikely given 3 years of previously successful therapy. It is also a didactic rather than collaborative approach.

The patient's social context (unemployment, low-income neighborhood, three children) suggests multiple potential barriers — financial, logistical, psychosocial — but the first step is always to **elicit the patient's own perspective** on what is making adherence difficult before proposing specific interventions.[1][2]

Would you like to explore evidence-based strategies for improving ART adherence once specific barriers have been identified, such as single-tablet regimens, long-acting injectables, or motivational interviewing?

References

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Question 511

A 67-year-old man comes to the physician for a routine medical check-up prior to a scheduled elective femoropopliteal bypass surgery of his left leg. He feels well but reports occasional episodes of weakness and numbness in his left hand. He has a history of peripheral arterial disease, type 2 diabetes mellitus, hypertension, hypercholesterolemia, and gout. The patient has smoked 1 pack of cigarettes daily for the past 50 years. He drinks 3 cans of beer daily. His current medications include aspirin, metformin, enalapril, simvastatin, and febuxostat. His temperature is 37.3°C (99.1°F), pulse is 86/min, and blood pressure is 122/76 mm Hg. The lungs are clear to auscultation. Cardiac examination shows no murmurs, rubs, or gallops. Auscultation of the right side of the neck shows a bruit. There is a right-sided reducible inguinal hernia. Neurological examination shows no abnormalities. A complete blood count and serum concentrations of electrolytes, creatinine, and glucose are within the reference ranges. An electrocardiogram shows signs of mild left ventricular hypertrophy. An x-ray of the chest shows no abnormalities. Which of the following is the most appropriate next step in management?

Answer Choices:

(A) Ultrasonography of the neck
(B) Echocardiography
(C) Warfarin therapy
(D) CT angiography of the head

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/47f6e0b8-13c4-48a2-bfdd-3b54c2e27279

OpenEvidence Explanation

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The most appropriate next step is **A. Ultrasonography of the neck** (carotid duplex ultrasound). This patient has a right-sided cervical bruit on auscultation combined with episodes of left-hand weakness and numbness — symptoms that lateralize to the right carotid territory — raising concern for right carotid artery stenosis with possible transient ischemic attacks (TIAs).

Why carotid duplex ultrasound is the correct answer:

This patient has multiple risk factors for carotid atherosclerosis: age >65, peripheral arterial disease, 50-pack-year smoking history, hypertension, diabetes, and hypercholesterolemia. The Society for Vascular Surgery guidelines identify **duplex ultrasound as the first-line imaging modality** for evaluating carotid occlusive disease, with high sensitivity and specificity.[1][2] The finding of a carotid bruit in a patient with additional atherosclerotic risk factors is considered an appropriate indication for directed screening with carotid duplex ultrasound.[3] Critically, this patient's left-hand weakness and numbness are ipsilateral to the right carotid bruit, suggesting these may represent TIA symptoms referable to right carotid stenosis.

Current AHA/ASA guidelines recommend that patients with high-grade carotid stenosis (>70%) and ipsilateral symptoms of TIA within the past 6 months should be strongly considered for revascularization.[4] Identifying significant stenosis before elective femoropopliteal bypass would be important for perioperative stroke risk management.

Why the other options are less appropriate:

- **Echocardiography (B):** The ECG shows LVH (expected with longstanding hypertension), but there is no dyspnea, heart failure symptoms, or murmur.

Routine preoperative LV function assessment is not recommended without clinical indication.[5]

- **Warfarin therapy (C):** There is no indication for anticoagulation — no atrial fibrillation, DVT/PE, or mechanical valve is identified.
- **CT angiography of the head (D):** CTA may be appropriate as a second-line study if duplex ultrasound confirms significant stenosis and further anatomic detail is needed, but it is not the initial diagnostic step.[1][2]

Would you like to explore the evidence on timing of carotid revascularization relative to other planned noncardiac surgeries in patients with symptomatic carotid stenosis?

Relevant images

(CONTENT OMITTED)

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Question 512

A 35-year-old woman presents to her primary care provider concerned that she may be pregnant. She has a history of regular menstruation every 4 weeks that lasts about 4 days with mild to moderate bleeding, but she missed her last period 2 weeks ago. A home pregnancy test was positive. She has a 6-year history of hyperthyroidism that is well-controlled with daily methimazole. She is currently asymptomatic and has no complaints or concerns. A blood specimen is taken and confirms the diagnosis. Additionally, her thyroid-stimulating hormone (TSH) is 2.0 µU/mL. Which of the following is the next best step in the management of this patient?

Answer Choices:

(A) Continue methimazole
(B) Discontinue methimazole, start propylthiouracil
(C) Add glucocorticoids
(D) Refer for radioiodine therapy

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/dd5fba1c-9143-427b-9b26-2375e0d9bf83

OpenEvidence Explanation

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The answer is **B. Discontinue methimazole, start propylthiouracil**.

This patient is in the **first trimester** of pregnancy (approximately 6 weeks gestation based on a missed period 2 weeks ago with a 4-week cycle). Methimazole is associated with a rare but well-characterized **embryopathy** during the first trimester, including aplasia cutis, esophageal atresia, choanal atresia, abdominal wall defects, and ventricular septal defects.[1] A meta-analysis of over 5 million pregnancies found a higher adjusted relative risk of congenital anomalies with methimazole (aRR 1.28) compared to propylthiouracil (aRR 1.16).[1] Another meta-analysis confirmed that methimazole-exposed pregnancies had significantly higher congenital anomaly risk than propylthiouracil-exposed pregnancies (OR 1.90; 95% CI 1.30–2.78).[2]

Per ACOG and ATA guidelines, **propylthiouracil is the preferred antithyroid drug during the first trimester** due to its lower teratogenic risk.[3] After the first trimester, consideration can be given to switching back to methimazole, as propylthiouracil carries a small risk of clinically significant hepatotoxicity.[4][5] A dose conversion ratio of approximately 20:1 (PTU:methimazole) is recommended when switching.[3]

Why the other options are incorrect:

- **A (Continue methimazole):** Methimazole should be avoided in the first trimester due to teratogenicity risk.
- **C (Add glucocorticoids):** Glucocorticoids are used in thyroid storm management, not routine hyperthyroidism in pregnancy.[1]
- **D (Radioiodine therapy):** Radioactive iodine is **absolutely contraindicated** in pregnancy, as it crosses the placenta and destroys the fetal thyroid gland.[4][6]

Would you like to explore the monitoring strategy and dose adjustment approach for propylthiouracil during pregnancy?

Relevant images

(CONTENT OMITTED)

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Question 513

A 65-year-old man presents to the emergency department with back pain. The patient states that he has gradually worsening back pain that seems to have worsened after moving furniture the other day. He also states that while he walks, he feels numbness and weakness in his legs. The only time the patient states his back pain is improved is when he is riding his bike or pushing a cart at the grocery store. The patient has a past medical history of osteoporosis, dyslipidemia, and diabetes. He drinks 3 alcoholic drinks every day and has a 44 pack-year smoking history. His temperature is 99.5°F (37.5°C), blood pressure is 157/108 mmHg, pulse is 90/min, respirations are 17/min, and oxygen saturation is 98% on room air. Physical exam is notable for a non-tender spine with normal mobility in all 4 directions. Radiography of the spine and basic labs are ordered. Which of the following is the most likely diagnosis?

Answer Choices:

(A) Compression fracture
(B) Herniated nucleus pulposus
(C) Musculoskeletal strain
(D) Spinal stenosis

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/35602d9f-cae6-41ef-b688-25e347b79883

OpenEvidence Explanation

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The most likely diagnosis is **D. Spinal stenosis** (lumbar spinal stenosis with neurogenic claudication).

This presentation is classic for lumbar spinal stenosis. The key distinguishing features include:

- **Neurogenic claudication**: Numbness and weakness in the legs provoked by walking (lumbar extension)[1][2]
- **Relief with spinal flexion**: Symptoms improve when riding a bike or pushing a grocery cart — both activities that flex the lumbar spine, increasing the cross-sectional area of the spinal canal and neural foramina. A JAMA review specifically notes that "some patients with spinal stenosis report that walking is more comfortable when leaning on a shopping cart, when the spine is flexed".[2]
- **Non-tender spine with normal mobility**: The spine in lumbar spinal stenosis is generally not tender on exam, in contrast to compression fractures (which typically cause point tenderness) or musculoskeletal strain.[2][3]
- **Age and risk profile**: Lumbar spinal stenosis is the most common reason for spine surgery in individuals older than 65 years, and advanced age is a primary risk factor.[1][4]

Why not the other choices:

- **A. Compression fracture** — While this patient has osteoporosis (a risk factor), compression fractures present with **midline tenderness** and **decreased range of motion**, neither of which is present here. The positional relief pattern (flexion-dependent improvement) is not characteristic of compression fractures.[1][3]
- **B. Herniated nucleus pulposus** — Disc herniations typically present with **unilateral** leg pain greater than back pain, a positive straight leg raise, and

peak incidence at age 30–50. Symptoms are often worsened by sitting and improved by extension — the opposite of this patient's pattern.[1][3]

- **C. Musculoskeletal strain** — Strain would not explain the bilateral neurogenic claudication (numbness and weakness with walking) or the characteristic positional relief with flexion. Strain typically causes localized pain without neurologic symptoms.[3]

Would you like to discuss the recommended workup (e.g., MRI indications) or initial management approach for this patient?

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Question 516

A 59-year-old man presents to general medical clinic for his yearly checkup. He has no complaints except for a dry cough. He has a past medical history of type II diabetes, hypertension, hyperlipidemia, asthma, and depression. His home medications are sitagliptin/metformin, lisinopril, atorvastatin, albuterol inhaler, and citalopram. His vitals signs are stable, with blood pressure 126/79 mmHg. Hemoglobin A1C is 6.3%, and creatinine is 1.3 g/dL. The remainder of his physical exam is unremarkable. If this patient's cough is due to one of the medications he is taking, what would be the next step in management?

Answer Choices:

(A) Change lisinopril to propanolol
(B) Change lisinopril to amlodipine
(C) Change atorvastatin to to lovastatin
(D) Change lisinopril to losartan

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/8940bcbf-43eb-44dc-a182-cc63646151f6

OpenEvidence Explanation

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The correct answer is **D. Change lisinopril to losartan**.

Lisinopril is an ACE inhibitor, and **dry cough** is a well-known side effect of this drug class, occurring in up to **20% of patients**.[1] The mechanism involves inhibition of kininase, which increases levels of **bradykinin and substance P**, leading to bronchoconstriction and cough.[2] The recommended management for ACE inhibitor-induced cough is to **switch to an angiotensin receptor blocker (ARB)** such as losartan, which does not inhibit kininase and is associated with a much lower incidence of cough.[1]

Why the other options are incorrect:

- **A. Change lisinopril to propranolol** — Propranolol is a non-selective beta-blocker, which is **contraindicated in this patient with asthma** due to the risk of bronchospasm. It would also not be an appropriate first-line antihypertensive replacement.
- **B. Change lisinopril to amlodipine** — While amlodipine (a calcium channel blocker) would resolve the cough and is a reasonable antihypertensive, it does not provide the same renin-angiotensin system blockade that is particularly beneficial in a patient with **type II diabetes** for renal protection. An ARB is the preferred switch to maintain RAAS inhibition.[3]
- **C. Change atorvastatin to lovastatin** — Cough is not a recognized side effect of statins, and switching between statins would not address the problem.

A network meta-analysis of 135 RCTs confirmed that ACEIs carry approximately **3.2 times the risk of cough compared with ARBs** (RR 3.2; 95% CI: 2.91–3.51).[4] ARBs and ACE inhibitors have comparable efficacy for blood pressure control and cardiovascular protection, making ARBs the ideal substitute when ACE inhibitor-induced cough occurs.[3]

Would you like to explore the specific renal protective benefits of RAAS inhibition in diabetic patients and how ARBs compare to ACE inhibitors in this regard?

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Question 517

A male newborn is evaluated 24 hours after delivery for high-pitched crying, poor feeding, rhinorrhea, and low-grade fever. He was born at 40 weeks' gestation at 2514 g (5.54 lb) to a 28-year-old woman, gravida 3, para 2, by an uncomplicated cesarean section. Apgar scores were 8 and 9 at 1 and 5 minutes, respectively. The mother did not receive prenatal care. The infant's temperature is 38.0°C (100.4°F), pulse is 170/min, and blood pressure is 71/39 mm Hg. Examination shows hyperreflexia, tremors, and an excessive startle response. These symptoms are mostly like due to maternal use of which of the following?

Answer Choices:

(A) Mu receptor agonist
(B) Nicotinic acetylcholine receptor agonist
(C) Monoamine reuptake antagonist
(D) Thyroperoxidase inhibitor

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/564b559b-cf24-40f7-baa2-f5d4b33c9d07

OpenEvidence Explanation

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The answer is **A. Mu receptor agonist**.

This presentation is classic for **neonatal opioid withdrawal syndrome (NOWS)**, previously termed neonatal abstinence syndrome (NAS), caused by maternal use of a **mu (μ) opioid receptor agonist** such as heroin, methadone, or prescription opioids during pregnancy.

Why mu receptor agonist is correct:

The constellation of findings — **high-pitched crying, poor feeding, rhinorrhea (nasal stuffiness), low-grade fever, hyperreflexia, tremors, and an exaggerated startle (Moro) reflex** — at 24 hours of life is the hallmark presentation of NOWS.[1][2] Chronic in utero opioid exposure causes fetal physiologic dependence; after delivery, the abrupt cessation of transplacental opioid supply triggers a withdrawal cascade involving increased noradrenergic signaling and CNS hyperexcitability.[3] The lack of prenatal care and low birth weight (2514 g, small for a term infant) further support maternal substance use.

Table 2. Clinical Manifestations and Outcomes of the Neonatal Abstinence Syndrome.*

Metabolic, vasomotor, and respiratory manifestations
Fever
Frequent yawning
Sneezing
Sweating
Nasal stuffiness
Respiratory rate >60 breaths per minute, with or without retractions
Mottling
Tachypnea
Gastrointestinal manifestations
Projectile vomiting
Regurgitation
Loose or watery stools
Weight loss
Poor feeding
Excessive sucking
Central nervous system manifestations
Tremors
High-pitched crying
Sleep disturbances
Increased muscle tone
Excoriation
Myoclonic jerks

Table 2. Clinical Manifestations and Outcomes of the Neonatal Abstinence Syndrome.

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Why the other options are less likely:

- **B. Nicotinic acetylcholine receptor agonist (nicotine/tobacco):** Prenatal nicotine exposure is associated with low birth weight and may potentiate NAS severity, but nicotine alone does not produce this full withdrawal syndrome with hyperreflexia, tremors, and high-pitched crying.[4][5]
- **C. Monoamine reuptake antagonist (e.g., SSRIs, cocaine):** SSRIs can cause a neonatal adaptation syndrome, but it is typically milder and self-limited. Cocaine exposure causes vasoconstriction-related effects (e.g., placental abruption, growth restriction) rather than this classic withdrawal pattern. [4]
- **D. Thyroperoxidase inhibitor (e.g., methimazole, propylthiouracil):** These antithyroid drugs can cause neonatal hypothyroidism, which presents with lethargy, poor feeding, and constipation — essentially the opposite of the hyperexcitable state seen here.

Would you like to explore the Finnegan scoring system and current evidence-based management protocols for neonatal opioid withdrawal syndrome?

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Question 520

Mutations in the ATP2A1 gene results in loss of function of the calcium ATPase pump, which is in the sarcoplasmic reticulum membranes of skeletal muscle in humans. This mutation results in a rare disease characterized by muscle cramping and stiffening that is usually most severe after exercise or strenuous activity and is typically relieved after affected individuals rest for a few minutes. Which of the following is expected in individuals with an ATP2A1 gene mutation?

Answer Choices:

(A) Muscle relaxation time: decreased, cytosolic calcium concentration: increased
(B) Muscle relaxation time: increased, cytosolic calcium concentration: increased
(C) Muscle relaxation time: increased, cytosolic calcium concentration: no change
(D) Muscle relaxation time: no change, cytosolic calcium concentration: decreased

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/bc61c35f-5936-485d-b563-bb5733c4604c

OpenEvidence Explanation

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The answer is **B. Muscle relaxation time: increased, cytosolic calcium concentration: increased**.

The ATP2A1 gene encodes **SERCA1 (sarco/endoplasmic reticulum Ca^{2+} -ATPase 1)**, the calcium pump responsible for actively transporting Ca^{2+} from the cytosol back into the sarcoplasmic reticulum (SR) after muscle contraction. Loss of function of this pump has two predictable physiological consequences:

- **Increased cytosolic calcium concentration:** Without functional SERCA1, Ca^{2+} cannot be efficiently sequestered back into the SR lumen after its release during excitation-contraction coupling. This leads to prolonged elevation of cytosolic [Ca^{2+}], which keeps Ca^{2+} bound to troponin C and maintains actin-myosin cross-bridge cycling.
- **Increased muscle relaxation time:** Because relaxation requires the removal of Ca^{2+} from the cytosol (lowering [Ca^{2+}] below the threshold for troponin C binding), impaired SERCA1 function directly delays this process. The sustained cross-bridge activity manifests clinically as the **muscle cramping and stiffening** described in the vignette — consistent with **Brody disease**, the rare autosomal recessive myopathy caused by ATP2A1 mutations.

The other options are incorrect because a loss-of-function mutation in the SR calcium pump cannot decrease cytosolic calcium or leave it unchanged — the pump's sole role is to clear cytosolic Ca^{2+} . Similarly, relaxation time cannot decrease or remain unchanged when the primary mechanism of relaxation is impaired.

Would you like to explore how Brody disease is distinguished from other causes of exercise-induced muscle stiffness, such as myotonia or McArdle disease?

Question 522

A 54-year-old man comes to the emergency department because of a 2-day history of increasingly severe abdominal pain, nausea, and bilious vomiting. His last bowel movement was yesterday and he has not passed flatus since then. He underwent appendectomy at the age of 39. He has psoriasis, hypertension, type 2 diabetes mellitus, and chronic back pain. He drinks two beers daily. He takes a topical corticosteroid, ramipril, metformin, and ibuprofen daily. He is 176 cm (5 ft 9 in) tall and weighs 108 kg (240 lb); BMI is 35.4 kg/m2. His temperature is 36.8°C (98.4°F), respirations are 15/min, pulse is 90/min, and blood pressure is 112/67 mm Hg. Examination shows thick, scaly, plaques over both elbows and knees. Abdominal examination shows three well-healed laparoscopic scars. The abdomen is distended and there are frequent, high-pitched bowel sounds on auscultation. Digital rectal examination shows an empty rectum. Laboratory studies show:
Hematocrit 44%
Leukocyte count 9,000/mm3
Platelet count 225,000/mm3
Serum
Na+ 139 mEq/L
K+ 4.1 mEq/L
Cl− 101 mEq/L
HCO3− 26 mEq/L
Glucose 95 mg/dL
Creatinine 1.1 mg/dL
Alkaline phosphatase 78 U/L
Aspartate aminotransferase (AST, GOT) 19 U/L
Alanine aminotransferase (ALT, GPT) 14 U/L
γ-Glutamyltransferase (GGT) 52 U/L (N=5–50 U/L)
Hemoglobin A1C 6.4%
Abdominal ultrasound shows nonpropulsive peristalsis of the small bowel.
Which of the following is the most likely cause of this patient's condition?

Answer Choices:

(A) Chronic inflammatory bowel disease
(B) Ibuprofen

(C) History of abdominal surgery
(D) Alcohol

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/bec7da27-9180-4d48-a437-98c26e9c7602

OpenEvidence Explanation

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The answer is **C. History of abdominal surgery**.

This patient presents with classic findings of **small bowel obstruction (SBO)** — progressive abdominal pain, bilious vomiting, obstipation (no flatus), abdominal distension, high-pitched bowel sounds, empty rectum on digital exam, and nonpropulsive peristalsis on ultrasound. The most likely cause is **adhesive SBO from his prior appendectomy**.

Intra-abdominal adhesions account for approximately 60–75% of all small bowel obstructions, and prior abdominal surgery is the dominant risk factor.[1][2][3] Appendectomy is specifically identified as a high-risk procedure for subsequent adhesive SBO.[4] Although this patient underwent laparoscopic appendectomy (evidenced by the three well-healed laparoscopic scars), adhesive SBO still occurs after laparoscopic procedures — the incidence is lower than after open surgery but not eliminated. A population-level study found a 5-year aSBO incidence of 0.35% after laparoscopic appendectomy versus 0.58% after open appendectomy.[5]

Why the other options are less likely:

- **A. Chronic inflammatory bowel disease** — There is no history of IBD, and the presentation is acute mechanical obstruction rather than a chronic inflammatory process. Labs show no anemia, leukocytosis, or elevated inflammatory markers.
- **B. Ibuprofen** — NSAIDs can cause NSAID diaphragm disease (thin mucosal strictures), but this is rare and typically presents with chronic partial obstruction rather than acute complete SBO.[6]
- **D. Alcohol** — Two beers daily is modest consumption. The mildly elevated GGT (52 U/L) may reflect enzyme induction from alcohol or medications, but alcohol does not cause mechanical SBO. Normal AST, ALT, and alkaline phosphatase argue against significant liver disease.

Would you like to explore the evidence-based approach to initial nonoperative management of adhesive SBO, including the role of water-soluble contrast (Gastrografin) as both a diagnostic and therapeutic tool?

References

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Question 523

A 28-year-old Caucasian woman presents to your office with recurrent abdominal cramping on her left side for 6 months. She additionally reports bloody diarrhea and tenesmus. You suspect ulcerative colitis. Which of the following findings would most strongly confirm your diagnosis?

Answer Choices:

(A) Involvement of terminal ileum
(B) Noncaseating granulomas
(C) Transmural inflammation
(D) Continuous mucosal damage

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/911d358d-ea50-4b8c-b551-fa6b4aa75264

OpenEvidence Explanation

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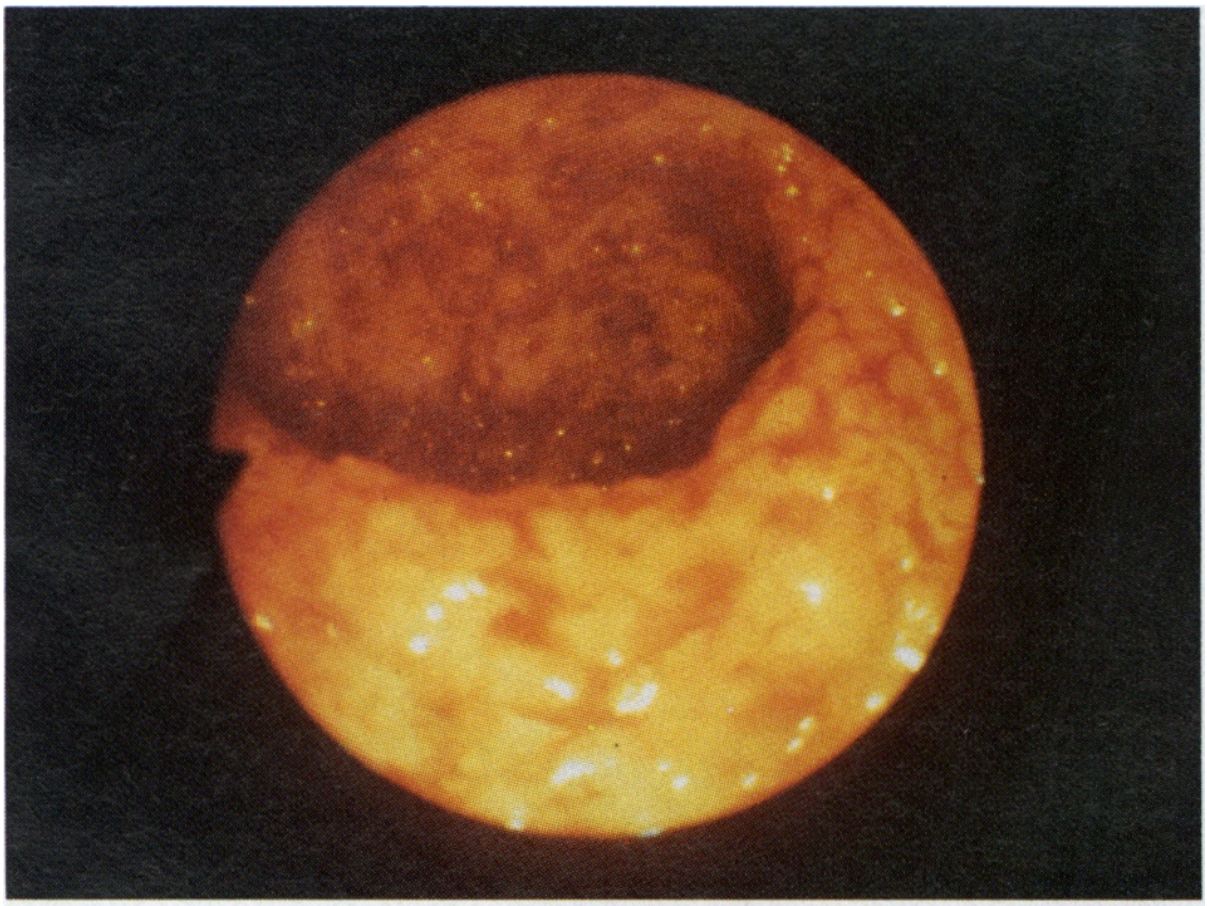
The answer is **D. Continuous mucosal damage**. Ulcerative colitis characteristically presents as **continuously inflamed mucosa** beginning at the anorectal junction and extending proximally in a circumferential pattern, with a clear transition zone between inflamed and healthy tissue.[1] This continuous, uninterrupted pattern of mucosal and submucosal inflammation is the hallmark

endoscopic and histologic finding that distinguishes UC from other forms of colitis.

The other options are features of **Crohn's disease**, not ulcerative colitis:

- **A. Terminal ileum involvement** — Classic for Crohn's disease. UC is confined to the colon and rectum; terminal ileum involvement in UC is limited to "backwash ileitis" in some pancolitis cases, which is not a defining feature.[2][3]
- **B. Noncaseating granulomas** — A hallmark histologic finding of Crohn's disease, not seen in UC.[3]
- **C. Transmural inflammation** — Crohn's disease involves the full thickness of the bowel wall, whereas UC inflammation is confined to the **mucosa and submucosa**.[2][3]

The following figure illustrates the characteristic endoscopic and histologic features of UC, including continuous mucosal ulceration with crypt abscesses and inflammation limited to the mucosa/submucosa:



A

Figure 2. Endoscopic and Histologic Features of Ulcerative Colitis.

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Would you like to explore how to differentiate ulcerative colitis from Crohn's disease when features overlap, such as in cases of IBD-unclassified?

References

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Question 524

A 6-month-old boy is brought to the physician by his parents for difficulty breathing and bluish discoloration of the lips for the past hour. During the past 3 months, the patient has had several upper respiratory tract infections and poor weight gain. Physical examination shows crackles over both lung fields and enlargement of the tonsils and cervical lymph nodes. His serum IgA, IgE, and IgG titers are decreased. An x-ray of the chest shows bilateral interstitial infiltrates. Methenamine silver staining of bronchial lavage fluid shows disc-shaped cysts. A defect in which of the following is the most likely underlying cause of this patient's condition?

Answer Choices:

(A) Actin filament assembly
(B) T-cell receptor signaling
(C) Microtubule polymerization
(D) B-cell maturation

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/28e4e401-30f0-4b93-8d02-e612b0acb60a

OpenEvidence Explanation

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The answer is **B. T-cell receptor signaling**.

This clinical vignette describes a 6-month-old boy with **X-linked hyper-IgM syndrome (XHIGM)**, caused by a defect in **CD40 ligand (CD40L)** expressed on activated T cells — a defect in T-cell signaling to B cells.

Key clinical clues pointing to this diagnosis:

- **Decreased IgA, IgE, and IgG** with presumably normal or elevated IgM — the hallmark immunoglobulin pattern of hyper-IgM syndrome[1][2][3]
- **Pneumocystis jirovecii pneumonia (PJP)** — identified by the disc-shaped cysts on methenamine silver staining of bronchoalveolar lavage fluid. PJP is frequently the initial presenting infection in XHIGM, reported in approximately 42% of patients[4][5][6]
- **Recurrent upper respiratory infections and failure to thrive** in a male infant — consistent with the X-linked inheritance pattern and early-onset immunodeficiency[3]

Pathophysiology: XHIGM results from mutations in the **CD40LG gene**, which encodes CD40 ligand on the surface of activated CD4+ T cells. Normally, CD40L on T cells engages CD40 on B cells, delivering a critical costimulatory signal required for immunoglobulin class-switch recombination (from IgM to IgG, IgA, and IgE).[1][7][8] Without functional CD40L, this T-cell-to-B-cell signaling fails, and B cells remain locked in IgM production. Importantly, the B cells themselves are intrinsically normal — the defect lies in the T-cell signal.[7][9]

The following figure illustrates the CD40-CD40L interaction required for immunoglobulin class switching:

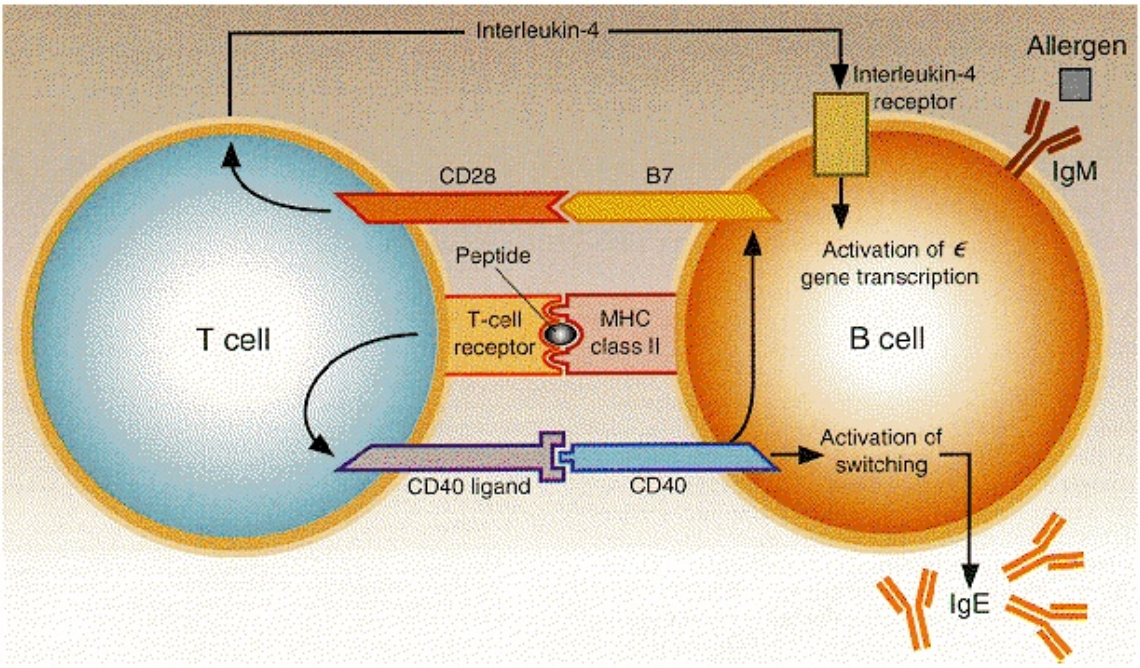


Figure 1. Collaboration of T and B Cells in the Process of Isotype Switching from the Synthesis of IgM to Allergen-Specific IgE Antibody.

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Why not the other options:

- **A (Actin filament assembly)** — would suggest Wiskott-Aldrich syndrome, which presents with thrombocytopenia, eczema, and recurrent infections
- **C (Microtubule polymerization)** — would suggest Chédiak-Higashi syndrome, characterized by partial albinism and giant granules in leukocytes
- **D (B-cell maturation)** — would suggest X-linked agammaglobulinemia (Bruton's), which features absent or very low levels of all immunoglobulin classes including IgM, due to a BTK defect

Would you like to explore the management approach for hyper-IgM syndrome, including the role of hematopoietic stem cell transplantation versus immunoglobulin replacement therapy?

References

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Question 526

A 81-year-old man is brought to the emergency department after he fell asleep at the dinner table and was not able to be roused by his family. His past medical history is significant for Alzheimer disease though he is still relatively functional at baseline. He has also been taking warfarin over the last 3 months after he suffered a deep venous thrombosis. After he was transported to the ED, his family found that the pills his grandson takes for seizures were missing. On presentation, he is found to be somnolent and physical exam reveals ataxia and nystagmus. After determining the cause of this patient's symptoms, his physicians begin monitoring his international normalized ratio, because they are concerned that it will start trending down. Which of the following treatments would most improve the urinary excretion of the substance likely responsible for these symptoms?

Answer Choices:

(A) Ammonium chloride
(B) Mannitol
(C) Sodium bicarbonate
(D) Thiazide diuretics

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/1205f22e-c455-4553-973a-c5a238be7b94

OpenEvidence Explanation

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Wait — let me reconsider this question more carefully. The clinical presentation (somnolence, ataxia, nystagmus from a grandson's seizure medication) and the concern about INR trending *down* are key clues. Valproic acid would cause INR to go *up* (it inhibits warfarin metabolism). A drug that causes INR to trend *down* would be a CYP450 inducer — this points to **phenytoin** or **phenobarbital**, both antiepileptic drugs that are CYP450 inducers and would increase warfarin clearance, causing INR to decrease.

Phenytoin classically presents with ataxia, nystagmus, and somnolence. Phenytoin is a weak acid (pKa ~8.3). Let me reconsider — actually, phenobarbital is also a weak acid and its urinary excretion is enhanced by alkalinization. Let me search for this.

(CONTENT OMITTED)

The answer is **C. Sodium bicarbonate**.

The clinical scenario describes **phenobarbital ingestion** — the grandson's seizure medication that causes somnolence, ataxia, and nystagmus. The key clue that the INR will trend *down* confirms the ingested drug is a **CYP450 inducer**: barbiturates (including phenobarbital) induce CYP2C9 and CYP1A2, which increases warfarin clearance and reduces INR.[1][2][3][4]

Urinary alkalinization with sodium bicarbonate enhances renal excretion of phenobarbital because phenobarbital is a **weak acid** (pKa ~7.24). Alkalinizing the urine ionizes the drug in the renal tubules, trapping it in the tubular lumen and preventing reabsorption.[5][6] This principle — "ion trapping" — is the same mechanism used for salicylate poisoning.[7]

Why the other options are incorrect:

- **Ammonium chloride** (urine acidifier) would *decrease* excretion of a weak acid like phenobarbital by promoting its non-ionized, reabsorbable form.
- **Mannitol** is an osmotic diuretic that increases urine volume but does not specifically enhance excretion of weak acids through ion trapping.
- **Thiazide diuretics** do not alkalinize the urine and would not improve phenobarbital clearance through this mechanism.

Notably, while urinary alkalinization does increase phenobarbital renal clearance, **multiple-dose activated charcoal (MDAC)** has been shown to be more effective than urinary alkalinization alone for phenobarbital overdose in clinical studies, and some systematic reviews have concluded there is limited clinical role for urinary alkalinization compared to MDAC.[6][8]

Would you like to explore the evidence comparing multiple-dose activated charcoal versus urinary alkalinization for phenobarbital overdose management?

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Question 527

A 10-year-old girl is brought to the physician because of high-grade fever, myalgia, and generalized fatigue for 3 days. She returned from a vacation to northern Brazil 4 days ago. She took the appropriate medications and immunizations prior to her visit. There is no family history of serious illness. She appears ill. Her temperature is 39.4°C (103°F), pulse is 110/min and blood pressure is 94/54 mm Hg. Examination shows jaundice of the conjunctivae and skin. The abdomen is soft and nontender; the spleen is palpated 2 to 3 cm below the left costal margin. Laboratory studies show:
Hemoglobin 10.1 g/dL
Leukocyte count 4,650/mm3
Platelet count 200,000/mm3
Serum
Glucose 56 mg/dL
Creatinine 0.8 mg/dL
Bilirubin
Total 4.7 mg/dL
Direct 0.9 mg/dL
Lactate dehydrogenase 212 U/L
Which of the following is the most likely to confirm the diagnosis?

Answer Choices:

(A) Thick and thin blood smear
(B) Direct antiglobulin test
(C) Sickle cell test
(D) Ultrasound of the abdomen

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/3f2b091e-f437-4029-b2c4-a5f5eb4ce02a

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OpenEvidence Explanation

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The answer is **A. Thick and thin blood smear**.

This presentation is classic for **malaria**: a child returning from an endemic region (northern Brazil) with high-grade fever, myalgia, fatigue, jaundice, splenomegaly, anemia, hypoglycemia, and predominantly **indirect hyperbilirubinemia** (total 4.7 mg/dL with direct only 0.9 mg/dL), indicating hemolysis. The elevated LDH further supports hemolytic anemia. Notably, she took appropriate prophylaxis, but no antimalarial chemoprophylaxis is 100% effective.

Thick and thin peripheral blood smears are the gold standard for confirming malaria. The thick smear is more sensitive for detecting parasites, while the thin smear allows species identification (e.g., *Plasmodium falciparum* vs. *P. vivax*) and quantification of parasitemia, which guides management decisions.

Why not the other options:

- **B. Direct antiglobulin test (Coombs test)** — Used to diagnose autoimmune hemolytic anemia. While hemolysis is present here, the travel history and clinical picture strongly favor an infectious etiology over autoimmune disease.
- **C. Sickle cell test** — Sickle cell disease can cause hemolytic crises and splenomegaly, but the acute onset temporally linked to travel to an endemic area makes malaria far more likely. Additionally, splenomegaly from sickle cell is typically seen in younger children before autosplenectomy.
- **D. Ultrasound of the abdomen** — Would confirm splenomegaly but is nonspecific and would not establish the underlying diagnosis.

Would you like to explore the criteria for severe versus uncomplicated malaria and how they guide treatment selection?

Question 528

A 56-year-old woman presents to a physician with severe pain and swelling of the left inguinal area for 3 days. She has a fever and malaise. Last week she noted several painless red papules on her left thigh when she was on a summer trip to Madagascar. She has no history of serious illnesses and is on no medications. There has been no recent contact with any animals or pets. The temperature is 38.6°C (101.5°F), the pulse is 78/min, the respiration rate is 12/min, and the blood pressure is 110/65 mm Hg. Swelling of the left inguinal area was noted; however, there were no skin changes. Several large, tense, and tender lymph nodes with a boggy consistency were palpated in the inguinal region. The right inguinal area is normal on physical exam. There was no lymphadenopathy in other areas. No abnormalities existed in the lungs, heart, and abdomen. Microscopic examination of pus from the inguinal lymph nodes revealed gram-negative Coccobacilli. Serum anti-F1 titers show a 4-fold rise. Which of the following is the most appropriate pharmacotherapy at this time?

Answer Choices:

(A) Azithromycin
(B) Imipenem
(C) Streptomycin
(D) No pharmacotherapy

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/e57e2f55-f311-446a-abc8-ad6a012077d4

OpenEvidence Explanation

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The correct answer is **C. Streptomycin**.

This clinical presentation is classic for **bubonic plague** caused by *Yersinia pestis*. The key diagnostic features include:

- Travel to **Madagascar** (the most plague-affected country globally)[1]
- Painless red papules at the inoculation site (flea bite) on the thigh, followed days later by painful inguinal lymphadenopathy (bubo) draining that region
- Fever and malaise
- **Gram-negative coccobacilli** on microscopy of bubo aspirate — characteristic of *Y. pestis*[2]
- A **4-fold rise in anti-F1 titers**, which is the WHO-defined serologic criterion for confirmed plague[3][4]

Streptomycin is the first-line treatment for bubonic plague. Per CDC guidelines, streptomycin and gentamicin remain first-line agents for all forms of plague based on their long history of successful use and robust clinical data.[5] Streptomycin is FDA-approved for plague treatment and has been the traditional drug of choice.[1][2] A systematic review of 762 published plague cases found a case fatality rate of only **13%** among those treated with aminoglycosides, compared to higher rates with other drug classes.[6]

Among the other options:

- **Azithromycin** has no established role in plague treatment and is not among recommended agents.[5]
- **Imipenem** is not recommended for plague; notably, penicillin-class agents were associated with a 75% case fatality rate in historical data.[7]
- **No pharmacotherapy** would be inappropriate — untreated bubonic plague has a mortality rate exceeding 50% and can progress to fatal septicemic or pneumonic plague.[5]

Would you like to explore the emerging evidence for oral fluoroquinolone monotherapy as an alternative to aminoglycosides for bubonic plague, based on the recent IMASOY trial from Madagascar?

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Question 532

A 38-year-old man is brought to the emergency room by his father because of altered mental status. According to the father, the patient was unable to get out of bed that morning and has become increasingly confused over the past several hours. The father also noticed it was “pretty cold” in his son's apartment because all of the windows were left open overnight. He has a history of hypothyroidism, schizoaffective disorder, type 2 diabetes mellitus, dyslipidemia, and hypertension for which he takes medication. Ten days ago, he was started on a new drug. He appears lethargic. His rectal temperature is 32°C (89.6°F), pulse is 54/min, respirations are 8/min, and blood pressure is 122/80 mm Hg. Examination shows weakness in the lower extremities with absent deep tendon reflexes. Deep tendon reflexes are 1+ in the upper extremities. The pupils are dilated and poorly reactive to light. Throughout the examination, the patient attempts to remove his clothing. Which of the following drugs is the most likely cause of these findings?

Answer Choices:

(A) Lisinopril
(B) Fluphenazine
(C) Levothyroxine
(D) Atorvastatin

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/6feffcf3-c024-4e8d-a1b3-2e84c7b7d7e9

OpenEvidence Explanation

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The answer is **B. Fluphenazine**.

This clinical presentation is best explained by **antipsychotic-induced hypothermia** from fluphenazine, a high-potency first-generation antipsychotic that would be prescribed for this patient's schizoaffective disorder. The key features pointing to this diagnosis include:

Hypothermia with environmental exposure: The rectal temperature of 32°C (89.6°F) represents moderate hypothermia. Antipsychotic drugs impair central thermoregulation by disrupting hypothalamic dopaminergic circuits, making patients vulnerable to environmental cold exposure (windows left open overnight).[1][2][3] The risk of antipsychotic-induced hypothermia is highest during the first 7–10 days after initiation — consistent with the drug being started 10 days ago.[4] Underlying **hypothyroidism** is an additional well-established risk factor for hypothermia, as it reduces basal metabolic rate.[2]

Paradoxical undressing: The patient's attempts to remove his clothing during the examination is a classic phenomenon of moderate-to-severe hypothermia, caused by sudden peripheral vasodilation that creates a paradoxical sensation of warmth.[5][6][7]

Neurological findings consistent with hypothermia: Bradycardia (54/min), respiratory depression (8/min), altered mental status, lower extremity weakness with absent deep tendon reflexes, and dilated poorly reactive pupils are all expected findings in moderate hypothermia as brain activity and peripheral nerve function decline with cooling.[2][8]

Why not the other options:

- **Lisinopril** (A) — ACE inhibitors do not cause hypothermia or these neurological findings.
- **Levothyroxine** (C) — Levothyroxine treats hypothyroidism and would not cause hypothermia; if anything, excess levothyroxine causes hyperthermia.

- **Atorvastatin** (D) — Statins can cause myopathy but do not cause hypothermia or this constellation of findings.

Notably, while fluphenazine can also cause neuroleptic malignant syndrome (NMS), NMS presents with **hyperthermia**, rigidity, and autonomic instability — the opposite thermal picture from what is seen here.[9][10]

Would you like to explore the specific monitoring protocols and risk factor assessment for antipsychotic-induced hypothermia in patients with multiple predisposing conditions?

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Question 536

A 63-year-old man with diverticular disease comes to the emergency department because of painless rectal bleeding, dizziness, and lightheadedness for 2 hours. His temperature is 37.6°C (99.6°F), pulse is 115/min, respirations are 24/min, and blood pressure is 86/60 mm Hg. He appears pale. Physical examination shows bright red rectal bleeding. Colonoscopy shows profuse diverticular bleeding; endoscopic hemostasis is performed. After initiating fluid resuscitation, the patient becomes hemodynamically stable. The following day, laboratory studies show:
Hemoglobin 8 g/dL
Leukocyte count 15,500/mm3
Platelet count 170,000/mm3
Serum
Urea nitrogen 60 mg/dL
Creatinine 2.1 mg/dL
Bilirubin
Total 1.2 mg/dL
Indirect 0.3 mg/dL
Alkaline phosphatase 96 U/L
Alanine aminotransferase (ALT, GPT) 2,674 U/L
Aspartate aminotransferase (AST, GOT) 2,254 U/L
Which of the following cells in the patient's liver were most likely damaged first?

Answer Choices:

(A) Periportal hepatocytes
(B) Hepatic sinusoidal endothelial cells
(C) Hepatic Kupffer cells
(D) Centrilobular hepatocytes

Correct Answer:

(D)

OpenEvidence Response:

> **(D)** ✓

OpenEvidence Link: https://openevidence.com/ask/b21e423c-ae7e-4ec9-8e36-b36355d0acb2

OpenEvidence Explanation

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The answer is **D. Centrilobular hepatocytes**.

This patient presented with hemorrhagic shock (BP 86/60, tachycardia to 115/min) from profuse diverticular bleeding, followed by markedly elevated transaminases (ALT 2,674 U/L, AST 2,254 U/L) with relatively normal bilirubin — a classic pattern of **ischemic hepatitis** ("shock liver"). The concurrent acute kidney injury (BUN 60, creatinine 2.1) further supports end-organ hypoperfusion.

Why centrilobular hepatocytes are damaged first:

Within the hepatic lobule, blood flows from the portal triad (zone 1, periportal) through the sinusoids toward the central vein (zone 3, centrilobular). Centrilobular hepatocytes in **zone 3** are the most distal from the oxygen-rich arterial supply and therefore exist in a relatively hypoxic microenvironment at baseline. During systemic hypoperfusion, these cells are the first to experience critical oxygen deprivation.[1]

The histopathological hallmark of ischemic hepatitis is **centrilobular (zone 3) coagulative necrosis**, which may extend to mid-zonal hepatocytes with prolonged ischemia but rarely affects the periportal region.[1][2][3] Perivenous hepatocytes (zone 3) accumulate intracellular reactive oxygen species in a mitochondrial-dependent manner during hypoxia, making them selectively vulnerable to ischemic injury.[4]

The clinical pattern here — massively elevated aminotransferases with near-normal bilirubin following a documented hypotensive episode — is characteristic. Aminotransferase concentrations >3,000 IU/L with bilirubin <5.0

mg/dL essentially narrow the differential to ischemia or acetaminophen toxicity. [5]

Would you like to explore the expected time course of transaminase recovery in ischemic hepatitis and when persistent elevation should prompt concern for ongoing hepatic injury?

Relevant images

(CONTENT OMITTED)

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Question 538

A 25-year-old female presents to urgent care with complaints of one day of burning and pain with urination, urgency, and frequency. She denies having a fever but has experienced intermittent chills. She is sexually active and inconsistently uses condoms. The patient has no past medical history. She is allergic to sulfa drugs. Physical examination of the genitalia is normal. Urinalysis shows positive leukocyte esterase and nitrites. The urine culture demonstrates gram-negative rods that form pink colonies on MacConkey agar. She is treated with an antibiotic and her symptoms quickly improve. The mechanism of the antibiotic she was most likely treated with is which of the following?

Answer Choices:

(A) Inhibits cell wall synthesis
(B) Binds D-ala D-ala in the cell wall
(C) Inhibits initiation complex
(D) Inhibits sterol synthesis

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/c1a92265-b051-438b-b325-a3588a3f9df0

OpenEvidence Explanation

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The answer is **A. Inhibits cell wall synthesis**.

This question presents a classic case of uncomplicated UTI caused by *E. coli* (gram-negative rods forming pink/lactose-fermenting colonies on MacConkey agar) in a patient with a **sulfa drug allergy**, which eliminates trimethoprim-sulfamethoxazole from consideration.

Why nitrofurantoin is the most likely antibiotic used — and why the answer requires careful interpretation:

Per IDSA guidelines, first-line agents for uncomplicated cystitis include nitrofurantoin, trimethoprim-sulfamethoxazole, fosfomycin, and pivmecillinam.[1] With a sulfa allergy, TMP-SMX is contraindicated, making **nitrofurantoin** the most likely empiric choice given its widespread availability and guideline-recommended first-line status.[1][2]

However, this is where the question becomes nuanced. Nitrofurantoin has a **unique, multi-target mechanism**: it is reduced by bacterial flavoproteins to reactive intermediates that inhibit protein synthesis, DNA synthesis, RNA synthesis, aerobic energy metabolism, and **cell wall synthesis** simultaneously.[3][4] Among the answer choices provided, "**inhibits cell wall synthesis**" (option A) is one of nitrofurantoin's documented mechanisms of action per the FDA label.[3]

The other options can be eliminated:

- **B (Binds D-ala D-ala)** — This is the mechanism of vancomycin, not a first-line UTI agent
- **C (Inhibits initiation complex)** — This describes aminoglycosides or linezolid
- **D (Inhibits sterol synthesis)** — This describes antifungals (e.g., azoles), not relevant here

While nitrofurantoin's mechanism is broader than simple cell wall synthesis inhibition, option A is the best fit among the choices provided.

Would you like to explore the comparative efficacy and resistance profiles of first-line antibiotics for uncomplicated UTI in more detail?

Relevant images

(CONTENT OMITTED)

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Question 539

A 70-year-old man with a history of hypertension and atrial fibrillation comes to the physician for shortness of breath with mild exertion, progressive weakness, and a dry cough that has persisted for 6 months. He has smoked a pack of cigarettes daily for 45 years. His medications include warfarin, enalapril, and amiodarone. His pulse is 85/min and irregularly irregular. Physical examination shows enlarged fingertips and markedly curved nails. A CT scan of the chest shows clustered air spaces and reticular opacities in the basal parts of the lung. Which of the following is the most likely underlying mechanism of this patient's dyspnea?

Answer Choices:

(A) Chronic airway inflammation
(B) Bronchial hyperresponsiveness and obstruction
(C) Pleural scarring
(D) Excess collagen deposition in the extracellular matrix of the lung

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/cd4cc003-ec0e-4da9-8905-348d392695ac

OpenEvidence Explanation

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The answer is **D. Excess collagen deposition in the extracellular matrix of the lung**.

This patient's presentation — progressive exertional dyspnea, dry cough, digital clubbing (enlarged fingertips with curved nails), and CT findings of **clustered air spaces (honeycombing) and reticular opacities in the basal lung** — is classic for **pulmonary fibrosis**, most likely idiopathic pulmonary fibrosis (IPF) or amiodarone-induced pulmonary fibrosis. Both amiodarone use and a 45-pack-year smoking history are recognized risk factors for pulmonary fibrosis.[1][2]

Why excess collagen deposition is the mechanism:

In pulmonary fibrosis, recurrent subclinical epithelial injury leads to aberrant wound healing, with activated myofibroblasts depositing excessive amounts of collagen and extracellular matrix. This destroys normal alveolar architecture, reduces lung compliance, and impairs gas exchange — ultimately causing dyspnea.[2][3][4] As described in a review of fibrosis mechanisms, "fibrosis of the interstitial spaces hinders gas exchange, culminating in abnormal oxygenation and clinical dyspnea".[5]

Why the other options are incorrect:

- **A. Chronic airway inflammation** — This describes COPD/chronic bronchitis. While this patient has a significant smoking history, the CT findings (basal reticular opacities, honeycombing) and clubbing point to a fibrotic rather than inflammatory airway process.
- **B. Bronchial hyperresponsiveness and obstruction** — This is the mechanism of asthma, which does not produce honeycombing or clubbing.
- **C. Pleural scarring** — Pleural disease (e.g., from asbestos exposure) would show pleural thickening or plaques, not the parenchymal reticular pattern and honeycombing described here.

The CT pattern described — subpleural, basal-predominant reticular opacities with clustered cystic airspaces — corresponds to the usual interstitial pneumonia (UIP) pattern, which is the radiologic hallmark of IPF.[2][6][7]

Would you like to explore how to differentiate amiodarone-induced pulmonary toxicity from idiopathic pulmonary fibrosis in this clinical scenario?

Relevant images

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Question 541

In a study to determine the risk factors for myocardial infarction (MI) at a young age (age < 30 years), 30 young patients with the condition are recruited into the study group. Sixty similar but healthy individuals are recruited into the control group. Educational status is considered to be an important variable, as it would affect the awareness of the disease and its risk factors among the participants. Based on the level of education, 2 groups are formed: low educational status and high educational status. A chi-square test is performed to test the significance of the relationship, and an odds ratio of 2.1 was computed for the association between low education and the risk of MI, with a confidence interval of 0.9–9.7. What inference can be made on the association between young age MI and educational status from this study?

Answer Choices:

(A) The association is not statistically significant, and low education is not a risk factor.
(B) The association is statistically significant, but low education is not a risk factor.
(C) The association is not statistically significant, but low education is a risk factor.
(D) One can not comment, as the p-value is not given.

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/53ef6cf3-513a-40bc-9927-5c0592de67c2

OpenEvidence Explanation

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The answer is **A. The association is not statistically significant, and low education is not a risk factor.**

The key to this question lies in interpreting the **confidence interval (CI) of the odds ratio (OR)**.

Odds Ratio and Confidence Interval Interpretation

The OR is 2.1 with a 95% CI of **0.9–9.7**. Because this confidence interval **crosses 1.0** (the null value for an odds ratio), the result is **not statistically significant** at the $\alpha = 0.05$ level. A p-value is not needed to make this determination — the CI provides equivalent information:

- If the 95% CI for an OR **excludes 1.0**, the association is statistically significant ($p < 0.05$).
- If the 95% CI for an OR **includes 1.0**, the association is **not** statistically significant ($p \geq 0.05$).

Since the lower bound of the CI is 0.9 (below 1.0), the null hypothesis — that there is no association between low educational status and young-age MI — cannot be rejected. This means the study fails to demonstrate that low education is a statistically significant risk factor for MI in this population.

Why not option C?

Although the point estimate of 2.1 might suggest a trend toward increased risk, the confidence interval spanning below 1.0 means this finding could be due to chance. Without statistical significance, the study does not provide sufficient evidence to label low education as a risk factor based on these data.

Why not option D?

The p-value and the 95% CI convey the same information regarding statistical significance. When the 95% CI for an OR includes 1.0, it is equivalent to a p-value ≥ 0.05 — no separate p-value is required to draw this conclusion.

Would you like to explore how sample size and study power may have contributed to the wide confidence interval in this case-control study?

Question 542

A 32-year-old primigravid woman at 16 weeks' gestation comes to the physician for a routine prenatal visit. She is asymptomatic and has no history of serious illness. Her only medication is a prenatal vitamin. Her temperature is 37.2°C (99°F) and blood pressure is 108/60 mm Hg. Pelvic examination shows a uterus consistent in size with a 16-week gestation. A quadruple screening test shows maternal serum AFP of 3 times the median and normal levels of serum β-hCG, estriol, and inhibin A. Which of the following is most likely to account for these findings?

Answer Choices:

(A) Partial molar pregnancy
(B) Neural tube defect
(C) Trisomy 18
(D) Trisomy 21

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/db8f1d7f-d584-438a-8481-b92f9448acc8

OpenEvidence Explanation

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The answer is **B. Neural tube defect**.

An **isolated elevation of maternal serum AFP (MSAFP) at 3 times the median**, with normal levels of β-hCG, estriol, and inhibin A, is the classic quadruple screen pattern associated with an **open neural tube defect** (NTD) such as anencephaly or open spina bifida. AFP is a glycoprotein produced by the fetal liver and yolk sac; open NTDs expose fetal membrane and blood vessel surfaces, allowing AFP to leak into the amniotic fluid and subsequently into the maternal circulation.[1] MSAFP ≥2.5 MoM has a detection rate of >95% for anencephaly and 65–80% for open spina bifida.[2]

The other answer choices are excluded by the marker pattern:

- **Trisomy 21 (Down syndrome)** — associated with **low** AFP, **high** hCG, low estriol, and **high** inhibin A. This is the opposite AFP pattern.[3]
- **Trisomy 18 (Edwards syndrome)** — associated with **low** AFP, **low** hCG, and **low** estriol. Again, AFP would be decreased, not elevated.[3]
- **Partial molar pregnancy** — associated with markedly **elevated β-hCG**, which is normal in this case.

The isolated, significantly elevated MSAFP with otherwise normal quad screen markers points squarely to an open neural tube defect as the most likely explanation.

Would you like to explore the recommended next steps after an elevated MSAFP, including the role of targeted ultrasound versus amniocentesis for confirmation?

Relevant images

(CONTENT OMITTED)

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Question 543

A 39-year-old man presents to the emergency department complaining of a sharp pain that radiates along his right hemithorax, which worsens with deep inspiration. He says this started abruptly about 6 hours ago. He says that he has not noticed that anything that makes his pain better or worse. He also denies any other symptoms. He works as a long-haul truck driver, and he informs you that he recently returned to the east coast from a trip to Utah. His medical history is significant for gout, hypertension, hypercholesterolemia, diabetes mellitus type 2, and acute lymphoblastic leukemia from when he was a child. He currently smokes 2 packs of cigarettes/day, drinks a 6-pack of beer/day, and he denies any illicit drug use. The vital signs include: temperature 36.7°C (98.0°F), blood pressure 126/74 mm Hg, heart rate 98/min, and respiratory rate 23/min. His physical examination shows minimal bibasilar rales, but otherwise clear lungs on auscultation, normal heart sounds, and a benign abdominal physical examination. Which of the following is the most reasonable 1st step towards ruling out the diagnosis of pulmonary embolism in a low-risk patient?

Answer Choices:

(A) ECG
(B) V/Q scan
(C) D-dimer
(D) CT pulmonary angiogram with IV contrast

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/cc1481da-ea18-4f1f-948b-faad113a61df

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OpenEvidence Explanation

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The answer is **C. D-dimer**.

In a **low-risk patient** with suspected pulmonary embolism, the standard diagnostic algorithm follows a stepwise approach: clinical probability assessment → D-dimer testing → imaging if indicated. A **D-dimer** is the most reasonable first step toward ruling out PE in this setting because of its high negative predictive value (97–100% at a threshold of 500 ng/mL), which can safely exclude PE without the need for imaging.[1]

Why D-dimer and not the other options:

- **ECG (A):** While commonly obtained in the ED, ECG findings in PE are nonspecific (e.g., sinus tachycardia, S1Q3T3) and cannot rule out PE. It is not part of the validated PE diagnostic algorithm.[2]
- **V/Q scan (B):** This is an imaging modality used when D-dimer is elevated or in patients who cannot receive IV contrast. It is not a first-line screening test in low-risk patients.[3]
- **CT pulmonary angiogram (D):** CTPA is the definitive imaging test for PE but should be reserved for patients with elevated D-dimer or high pretest probability. Proceeding directly to CTPA in a low-risk patient exposes the patient to unnecessary radiation and contrast without first using a simpler, less invasive test.[1][4]

The 2026 AHA/ACC guidelines and multiple international guidelines uniformly recommend that in patients with low or intermediate pretest probability, a normal D-dimer level can safely exclude PE, reducing unnecessary imaging.[2][5] The following figure from the 2026 AHA/ACC PE guideline illustrates this stepwise diagnostic algorithm:

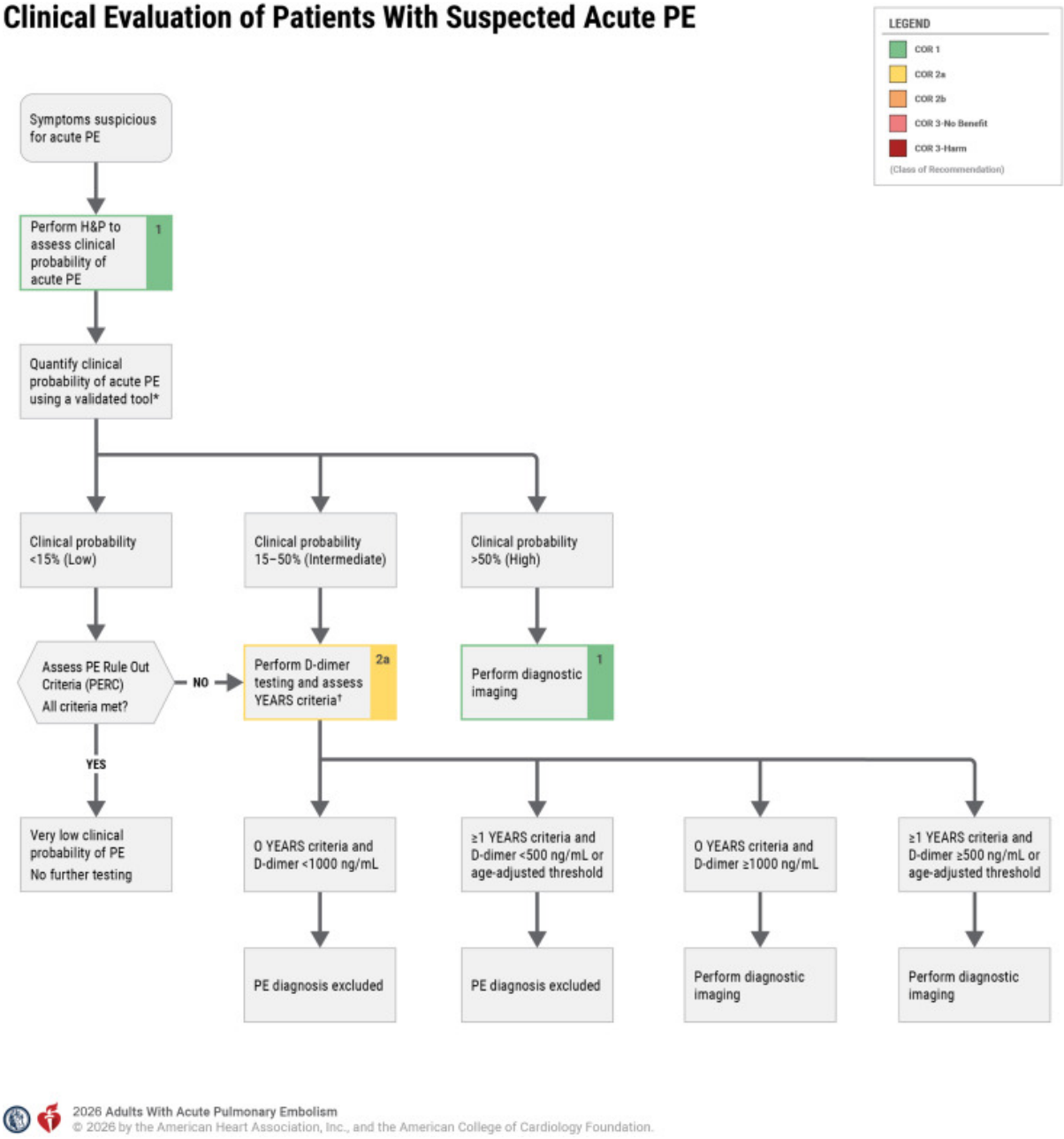


Figure 1. Clinical Evaluation of Patients With Suspected Acute PE

Notably, this patient does have some risk factors (prolonged immobilization as a truck driver, heart rate 98/min which is borderline), but the question stem specifies a "low-risk patient," making D-dimer the appropriate initial test. If the D-dimer is normal, PE can be excluded; if elevated, imaging (typically CTPA) would then be indicated.[1][7]

Would you like to explore how the PERC rule could be applied to this patient to determine whether even D-dimer testing could be safely avoided?

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Question 545

A 24-year-old woman presents to the emergency department with a severe headache. She states it is 10/10 in intensity and states that it is associated with chewing. She describes it as a dull pain over the sides of her head. The patient is otherwise healthy and is not currently taking any medications. Her temperature is 97.0°F (36.4°C), blood pressure is 111/74 mmHg, pulse is 83/min, respirations are 13/min, and oxygen saturation is 98% on room air. Physical exam is notable for pain and tenderness over the mandibular and temporal region that is worsened when the patient opens and closes their mouth. Which of the following is the most likely diagnosis?

Answer Choices:

(A) Migraine headache
(B) Temporal arteritis
(C) Temporomandibular joint dysfunction
(D) Tension headache

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/2a3ac99b-0fea-4c2d-8a8e-bbf2830cc702

OpenEvidence Explanation

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The most likely diagnosis is **C. Temporomandibular joint dysfunction (TMD)**.

This presentation is classic for TMD based on several key features:

- **Age and demographics**: A 24-year-old woman — TMD is most common in young women aged 20–40.
- **Pain location**: Dull pain over the **bilateral temporal and mandibular regions**, corresponding to the temporomandibular joint and associated musculature.
- **Aggravating factor**: Pain worsened with **jaw movement** (opening and closing the mouth, chewing) is the hallmark of TMD.
- **Physical exam**: Tenderness over the **mandibular and temporal region** reproduced by jaw motion is the characteristic finding.

Why not the other options?

- **A. Migraine headache** — Migraines are typically unilateral, pulsating/throbbing, associated with nausea, photophobia, or phonophobia, and are not specifically worsened by jaw movement.
- **B. Temporal arteritis (giant cell arteritis)** — While jaw claudication can occur, this condition overwhelmingly affects patients **>50 years old** and is associated with elevated ESR/CRP, visual symptoms, and systemic inflammation. A 24-year-old would be exceedingly unlikely to have this diagnosis.
- **D. Tension headache** — Tension-type headaches present as bilateral, band-like pressure around the head, but are not specifically localized to the mandibular region and are not worsened by jaw movement.

The combination of bilateral temporomandibular tenderness, pain exacerbated by jaw function, and a young female patient makes TMD the clear diagnosis.

Would you like to explore the evidence-based management approach for TMD, including conservative therapies and indications for specialist referral?

Question 550

A 65-year-old previously healthy man presents to the primary care physician with the chief complaint of red colored urine over the past month. He states that he does not experience dysuria. On physical exam there is no costovertebral angle tenderness. With this presentation which is the most likely cause of this patient's hematuria?

Answer Choices:

(A) Bladder tumor
(B) Renal cell carcinoma
(C) Beeturia
(D) Urinary tract infection

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/cb31e51e-7bc2-4772-a03e-e6ad2c175208

OpenEvidence Explanation

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The answer is **A. Bladder tumor**.

Painless gross hematuria in a 65-year-old male is the classic presentation of **bladder cancer**. Several key features of this case point to this diagnosis:

- **Painless gross hematuria** has a strong association with urologic malignancy, particularly bladder cancer. The American College of Physicians notes that painless gross hematuria has a stronger association with cancer than symptomatic hematuria, with a pretest probability of cancer consistently >10% and >25% in some referral series.[1]
- **Bladder cancer is the most common malignancy** found during hematuria evaluation. In the DETECT 1 study of 3,556 adults with hematuria (mean age 65.7 years), 8.0% had bladder cancer — far exceeding renal parenchymal cancer (1.0%), upper tract urothelial cancer (0.7%), or prostate cancer (0.3%).[2]
- **Risk factors present in this patient** — male sex, age >40 years — are well-established risk factors for bladder cancer in the setting of hematuria. The pooled incidence of urothelial bladder cancer is approximately **17%** for visible hematuria.[3][4]
- Hematuria is the presenting symptom in up to **85% of bladder cancer** patients, and the most common presentation is visible (gross) hematuria.[5][6]

Why not the other options?

- **B. Renal cell carcinoma** — While RCC can cause hematuria, it is far less common than bladder cancer in hematuria evaluations (pooled incidence ~2% for visible hematuria vs. 17% for bladder cancer). The classic triad of flank pain, hematuria, and palpable mass is present in only a minority of cases.[4]
- **C. Beeturia** — Beeturia causes red-colored urine but is not true hematuria; it would be excluded by urinalysis showing no red blood cells. The question describes "red colored urine" over a month, making a dietary cause far less likely.
- **D. Urinary tract infection** — UTI typically presents with dysuria, frequency, and urgency. This patient explicitly denies dysuria, making UTI unlikely as the cause.

Would you like to explore the recommended diagnostic workup algorithm for a patient presenting with gross hematuria, including the role of cystoscopy and upper tract imaging?

References

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Question 551

A 13-year-old boy is brought to the emergency room by his mother with confusion, abdominal pain, and vomiting for the previous day. The patient's mother says he started complaining of pain in his abdomen after he got back from school yesterday and vomited 3 times during the night. This morning, he seemed confused so she rushed him to the ER. She has also noticed that he has been urinating frequently and drinking a lot of water recently, and he has lost 6 kg (13.2 lb) over the past 20 days. His vital signs include: blood pressure 100/50 mm Hg, heart rate 110/min, respiratory rate 27/min, and temperature 35.6°C (96.0°F). His BMI is 18 kg/m2. On physical examination, he is disoriented to time and place and is taking deep and labored breaths. There is diffuse tenderness to palpation in the abdomen with guarding. Laboratory tests are significant for a pH of 7.19 and a blood glucose level of 754 mg/dL. The doctor explains to his mother that her son has developed a life-threatening complication of a disease characterized by decreased levels of a hormone. Which of the following would you most likely expect to see in this patient?

Answer Choices:

(A) Decreased glucose uptake by adipocytes
(B) Decreased activity of hormone sensitive lipase
(C) Decreased proteolysis
(D) Increased lipoprotein lipase activity

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/55d10b5f-dda8-4eab-9a0e-493dcbe99e51

OpenEvidence Explanation

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The correct answer is **A. Decreased glucose uptake by adipocytes**.

This patient presents with classic new-onset **type 1 diabetes mellitus** complicated by **diabetic ketoacidosis (DKA)** — polyuria, polydipsia, weight loss, abdominal pain, vomiting, confusion, Kussmaul breathing (deep and labored), pH 7.19, and blood glucose 754 mg/dL. The underlying disease is characterized by **absolute insulin deficiency** due to autoimmune destruction of pancreatic β cells. [1][2]

The question asks what metabolic consequence would be expected in the setting of insulin deficiency:

- **A. Decreased glucose uptake by adipocytes — CORRECT.** Without insulin, GLUT4 transporters cannot translocate to the cell surface of adipocytes and skeletal muscle, so glucose uptake is markedly impaired. This is a hallmark of insulin deficiency and directly contributes to hyperglycemia.[2][3]
- **B. Decreased activity of hormone-sensitive lipase — INCORRECT.** Insulin normally suppresses hormone-sensitive lipase (HSL). In insulin deficiency, HSL activity is **increased**, driving lipolysis and release of free fatty acids from adipose tissue, which fuels hepatic ketogenesis.[4][5]
- **C. Decreased proteolysis — INCORRECT.** Insulin is anabolic and inhibits protein breakdown. In insulin deficiency, proteolysis is **increased**, contributing to muscle wasting and weight loss.[6]
- **D. Increased lipoprotein lipase activity — INCORRECT.** Insulin stimulates lipoprotein lipase (LPL) in adipose tissue. In insulin-deficient states, adipose tissue LPL activity is **decreased**, contributing to hypertriglyceridemia.[7][8]

The following figure illustrates the metabolic pathways in DKA, showing how insulin deficiency drives lipolysis in adipose tissue and subsequent hepatic ketogenesis.

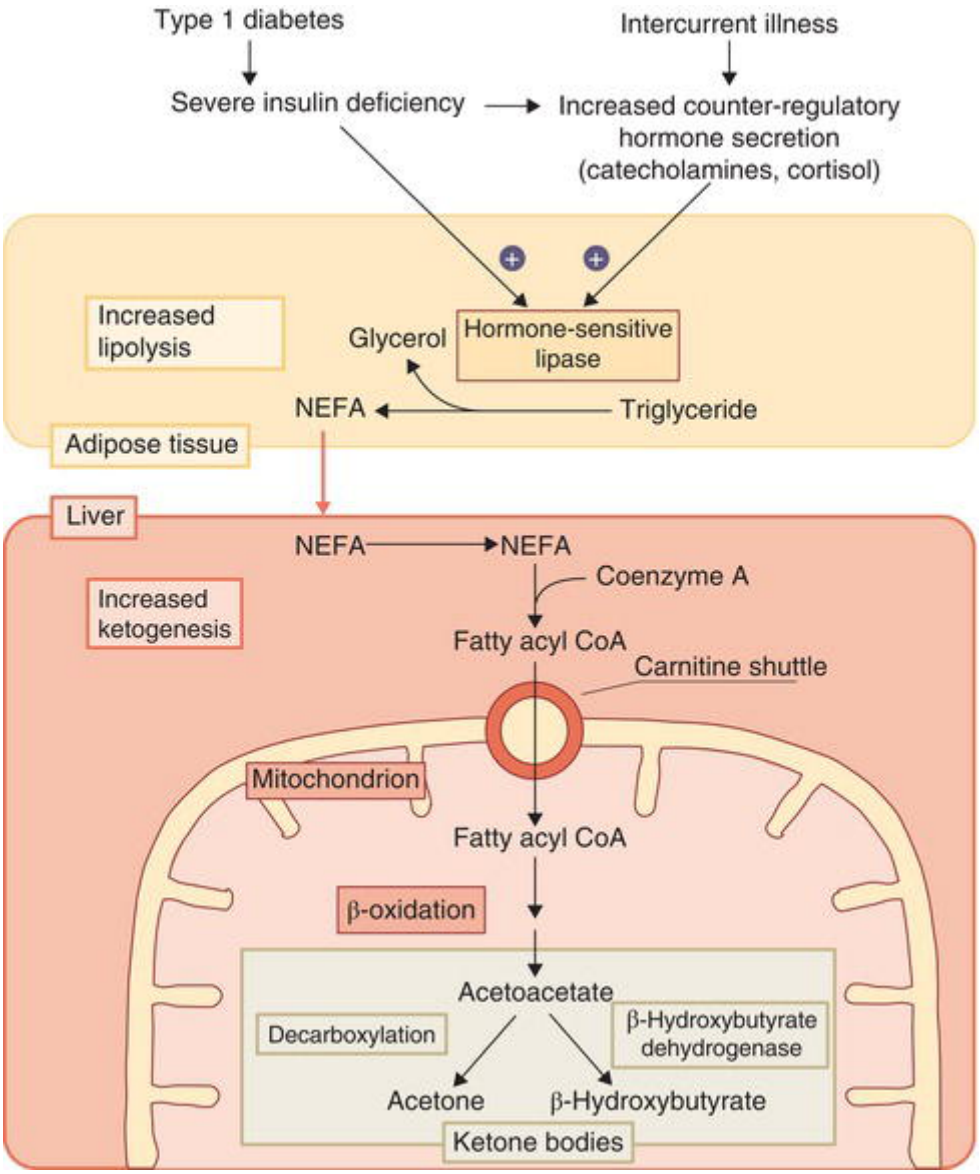


Figure 2. Mechanisms of ketacidosis. NEFA, non-esterified fatty acids.

Would you like to explore the specific management protocol for pediatric DKA, including fluid resuscitation, insulin infusion, and electrolyte monitoring?

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9. Diabetic ketoacidosis (DKA), hyperglycaemic hyperosmolar state (HHS) and lactic acidosis. Iskandar Idris, Rudy Bilous, Richard Donnelly. Chapter 12

Question 553

A 62-year-old man presents to his primary care doctor with continued hypertension despite adherence to multiple anti-hypertensive medications. The physician suspects that the patient may have elevated aldosterone levels and wants to initiate a trial of an aldosterone receptor antagonist. The patient is very concerned about side effects, particularly impotence and gynecomastia, as he had a friend who took a similar medication and had these side-effects. Which of the following is the best medication to initiate, given his concerns and the physician's diagnosis?

> **Answer Choices:**
>
> (A) Spironolactone
> (B) Eplerenone
> (C) Triamterene
> (D) Ethacrynic acid

> **Correct Answer:**
>
> **(B)**
>
> **OpenEvidence Response:**
>
> **(B)** ✓

OpenEvidence Link: https://openevidence.com/ask/812ba7c6-0eaf-44a5-85f4-5e6b1e36577e

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OpenEvidence Explanation

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The best answer is **B. Eplerenone**. Eplerenone is a selective aldosterone receptor antagonist that, unlike spironolactone, does not bind to androgen or

progesterone receptors, thereby largely avoiding the antiandrogenic side effects of gynecomastia and impotence that this patient is concerned about.

Why eplerenone over the other options:

- **Spironolactone** (choice A) is a first-generation steroidal MRA that also binds to androgen and progesterone receptors, leading to gynecomastia (incidence ~7.9% vs 0.6% with placebo) and sexual impotence (~9%). This is likely the medication the patient's friend was taking.[1][2][3]
- **Eplerenone** has higher selectivity for the mineralocorticoid receptor and has **no effect on androgen and progesterone receptors**, with gynecomastia occurring in only ~0.5% of patients. A meta-analysis comparing the two MRAs in heart failure patients found the relative odds of male gynecomastia was **8.44 for spironolactone vs 0.77 for eplerenone**. The AHA/ACC guidelines also note that gynecomastia is observed less often with eplerenone due to its higher receptor selectivity.[1][3][4]
- **Triamterene** (choice C) is a potassium-sparing diuretic but acts by blocking epithelial sodium channels (ENaC), not by antagonizing the mineralocorticoid receptor. It does not fulfill the physician's goal of initiating an aldosterone receptor antagonist.
- **Ethacrynic acid** (choice D) is a loop diuretic with no mineralocorticoid receptor antagonist activity.

It is worth noting that while eplerenone avoids antiandrogenic side effects, it is **less potent** than spironolactone and typically requires higher doses (50–100 mg daily) to achieve comparable antihypertensive effects.[3][5] Hyperkalemia remains a shared risk with both agents and requires monitoring.[4][6]

Would you like to explore the comparative efficacy of spironolactone versus eplerenone in resistant hypertension, including optimal dosing strategies?

Relevant images

(CONTENT OMITTED)

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Question 555

A previously healthy 14-year-old boy is brought to the physician for evaluation because of loss of appetite, sleeplessness, and extreme irritability for the past 3 weeks. He was recently kicked off of the school's football team after missing too many practices. He has also been avoiding his family and friends because he is not in the mood to see them, but he admits that he is lonely. He has not left his room for 2 days, which prompted his father to bring him to the physician. He has no medical conditions and does not take any medications. He does not drink alcohol or use recreational drugs. While the father is in the waiting room, a mental status examination is conducted, which shows a constricted affect. Cognition is intact. He says that he would be better off dead and refuses to be treated. He says he wants to use his father's licensed firearm to “end his misery” over the weekend when his parents are at church. Which of the following is the most appropriate next step in management?

Answer Choices:

(A) Agree to his wish for no further treatment
(B) Involuntary hospitalization after informing the parents
(C) Reassure the patient that he will feel better
(D) Start outpatient psychotherapy

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/d67d19ef-85c3-4f60-81ac-1dd883c9fc68

OpenEvidence Explanation

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The correct answer is **B. Involuntary hospitalization after informing the parents**.

This adolescent presents with multiple high-risk features for imminent suicide: **active suicidal ideation with a specific plan** (using his father's firearm), a **specific timeline** (this weekend), **access to lethal means** (a firearm in the home), **depressive symptoms** (anhedonia, insomnia, irritability, social withdrawal for 3 weeks), and **refusal of treatment**. This constellation constitutes an imminent danger to self, which is the standard criterion for involuntary psychiatric hospitalization.

Why the other options are incorrect:

- **A (Agree to no treatment):** A 14-year-old minor with active suicidal ideation, a concrete plan, and access to a firearm cannot be allowed to refuse treatment. Physicians have a duty to protect patients who are an imminent danger to themselves, and minors do not have the legal authority to refuse life-saving intervention in this context.[1][2]
- **C (Reassure the patient):** Simple reassurance is wholly inadequate for a patient expressing active suicidal intent with a specific plan and means. The AAP guidelines emphasize that when suicidal ideation with a plan is revealed, immediate intervention — including lethal means restriction and referral for acute evaluation — is imperative.[1][3]
- **D (Outpatient psychotherapy):** Outpatient treatment is appropriate for lower-risk patients. This patient has imminent risk factors (specific plan, timeline, access to a firearm, refusal of help) that necessitate inpatient-level care. The AAP guidelines note that outpatient management may be considered only for patients deemed safe for discharge, with safety planning and lethal means restriction in place.[1]

Key management principles: The AAP guidelines on suicide and suicide risk in adolescents recommend that when a patient is deemed to require inpatient psychiatric hospitalization for safety, the parents/guardians should be informed.

If guardians are not amenable, child protective services may need to be contacted as a last resort to facilitate hospitalization.[1] Confidentiality must be breached when there is concern for danger to self, as the duty to protect the minor patient supersedes confidentiality obligations.[2]

Would you like to explore the evidence on lethal means restriction counseling and its effectiveness in reducing adolescent suicide risk?

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Question 556

A previously healthy 6-year-old boy is brought to the physician because of generalized malaise and a palpable swelling in the left axilla. The parents report that 2 weeks ago, his daycare group visited an animal shelter, after which he developed a rash on the left hand. His temperature is 38.5°C (101.3°F). Physical examination shows three linear crusts on an erythematous background on the dorsum of the left hand. There is tender left-sided axillary and cervical lymphadenopathy. Histopathologic examination of an axillary lymph node shows necrotizing granulomas. The most likely causal organism of this patient's clinical findings is also involved in the pathogenesis of which of the following conditions?

Answer Choices:

(A) Bacillary angiomatosis
(B) Condylomata lata
(C) Brucellosis
(D) Bubonic plague

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/2d3b0392-66d1-43da-89b4-f1d6843369df

OpenEvidence Explanation

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The answer is **A. Bacillary angiomatosis**.

The clinical presentation — a 6-year-old child with a history of animal exposure (shelter visit), a papular/crusted lesion at the inoculation site on the hand, regional (axillary) lymphadenopathy, low-grade fever, and **necrotizing granulomas** on lymph node biopsy — is classic for **cat scratch disease (CSD)**, caused by **Bartonella henselae**.[1][2]

Bartonella henselae is also the causative organism of **bacillary angiomatosis**, a vasculoproliferative disorder seen almost exclusively in immunocompromised patients, particularly those with advanced HIV/AIDS (CD4 counts <50 cells/mm^3).[3][4] Bacillary angiomatosis presents as red papules or subcutaneous nodules and results from the unique ability of Bartonella species to trigger endothelial cell proliferation and angiogenesis.[4][5]

The other answer choices involve different organisms:

- **Condylomata lata** — caused by Treponema pallidum (secondary syphilis)
- **Brucellosis** — caused by Brucella species
- **Bubonic plague** — caused by Yersinia pestis

Would you like to explore the mechanisms by which Bartonella henselae uniquely induces vasculoproliferative lesions in immunocompromised hosts?

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Question 558

A 44-year-old man presents to the family medicine clinic for some small bumps on his left thigh. The lesions are non-pruritic and have been present for the last 3 weeks. He reports feeling fatigued and malaise for the past few months. The patient has no known medical problems and takes no medications. He smokes one pack of cigarettes per day and uses intravenous street drugs. His heart rate is 82/min, the respiratory rate is 14/min, the temperature is 36.7°C (98.1°F), and the blood pressure is 126/80 mm Hg. Auscultation of the heart is without murmurs. Lungs are clear to auscultation bilaterally. Three 2-3 mm, dome-shaped, hardened papules are noted on the left thigh. Central umbilication can be observed in each papule. There is a non-tender cervical lymphadenopathy present. Which of the following is the most likely diagnosis?

Answer Choices:

(A) Bed bug bite
(B) Molluscum contagiosum
(C) Atopic dermatitis
(D) Acute urticaria

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/08e2c127-4b90-4df7-b5f7-753cfd76a853

OpenEvidence Explanation

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The most likely diagnosis is **B. Molluscum contagiosum**.

The clinical presentation is classic for molluscum contagiosum: **small (2–3 mm), dome-shaped, hardened papules with central umbilication** that are non-pruritic.[1][2][3] These are the hallmark features of molluscum contagiosum, a cutaneous infection caused by the molluscum contagiosum virus (a poxvirus).[4]

Several key features support this diagnosis:

- **Morphology**: Molluscum contagiosum typically presents as 2–5 mm flesh-colored, dome-shaped, shiny, waxy papules with central umbilication — precisely matching this patient's lesions.[2][3]
- **Non-pruritic nature**: While molluscum lesions may occasionally itch, they are often painless and asymptomatic, consistent with this presentation.[4]
- **Risk factors**: This patient's IV drug use places him at risk for **HIV infection**, and molluscum contagiosum has a prevalence of 5–18% in HIV-positive individuals. The combination of fatigue, malaise, and cervical lymphadenopathy further raises concern for underlying immunosuppression.[3][4]

The other options are less consistent:

- **Bed bug bites** typically present as pruritic, erythematous papules or wheals, often in a linear pattern, without central umbilication.
- **Atopic dermatitis** presents with pruritic, erythematous, eczematous patches/plaques, not discrete dome-shaped umbilicated papules.
- **Acute urticaria** presents with pruritic, transient, erythematous wheals (hives), not persistent hardened papules with umbilication.

Given this patient's IV drug use, constitutional symptoms (fatigue, malaise), and cervical lymphadenopathy, **HIV testing should be strongly considered**, as molluscum contagiosum can be an early cutaneous manifestation of HIV infection.[3]

Would you like to explore the workup and management of molluscum contagiosum in the setting of suspected HIV infection?

Relevant images

(CONTENT OMITTED)

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Question 559

A prominent male politician has secret homosexual desires. However, rather than engaging in homosexual behavior, he holds rallies against gay rights and regularly criticizes gay people. The politician is displaying which of the following defense mechanisms?

Answer Choices:

(A) Repression
(B) Reaction formation
(C) Denial
(D) Displacement

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/4b0079f9-5916-4f8c-8543-51e90b8b785c

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OpenEvidence Explanation

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The answer is **B. Reaction formation**.

Reaction formation is a defense mechanism in which an individual unconsciously transforms an unacceptable impulse, thought, or feeling into its opposite. In this scenario, the politician harbors homosexual desires that he finds unacceptable, and rather than acknowledging them, he adopts an

exaggerated stance against homosexuality — holding rallies and publicly criticizing gay people. This outward behavior is the direct opposite of the underlying impulse, which is the hallmark of reaction formation.

Distinguishing from the other options:

- **Repression (A):** Involves unconsciously blocking unacceptable thoughts or desires from awareness entirely. While repression may be occurring here as well, it does not account for the active, exaggerated opposite behavior.
- **Denial (C):** Involves refusing to accept reality or facts. Denial would mean the politician simply refuses to acknowledge his desires, without necessarily adopting the opposite behavior publicly.
- **Displacement (D):** Involves redirecting emotions from a threatening target to a less threatening one (e.g., a person angry at their boss who instead yells at their spouse). The politician's behavior is not redirected toward a substitute target — it is directed against the very impulse he is defending against, in an opposite manner.

The key distinguishing feature of reaction formation is the **conversion of an unacceptable impulse into its exaggerated opposite**, which precisely describes this clinical vignette.

Would you like to explore other commonly tested defense mechanisms and how to differentiate them in clinical scenarios?

Question 560

A 55-year-old man presents to his primary care physician for a general checkup. The patient has a past medical history of diabetes, hypertension, and atrial fibrillation and is currently taking warfarin, insulin, lisinopril, and metoprolol. The patient's brother recently died from a heart attack and he has switched to an all vegetarian diet in order to improve his health. His temperature is 98.6°F (37.0°C), blood pressure is 167/108 mmHg, pulse is 90/min, respirations are 17/min, and oxygen saturation is 98% on room air. The patient's physical exam is unremarkable. His laboratory values are ordered as seen below.

Hemoglobin: 12 g/dL
Hematocrit: 36%
Leukocyte count: 7,550/mm^3 with normal differential
Platelet count: 197,000/mm^3
INR: 1.0

Serum:
Na+: 139 mEq/L
Cl-: 100 mEq/L
K+: 4.3 mEq/L
HCO3-: 25 mEq/L
BUN: 20 mg/dL
Glucose: 99 mg/dL
Creatinine: 1.1 mg/dL
Ca2+: 10.2 mg/dL

Which of the following is the best explanation for this patient's laboratory values?

> **Answer Choices:**
>
> (A) Dietary changes
> (B) Increased hepatic metabolism

(C) Increased renal clearance
(D) Medication noncompliance

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/a1f9f2fa-979d-451a-bc11-4228c68731d9

OpenEvidence Explanation

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The best explanation is **A. Dietary changes**. The key abnormality in this patient's labs is an **INR of 1.0**, which is subtherapeutic for a patient on warfarin for atrial fibrillation (target INR 2.0–3.0). This patient recently switched to an all-vegetarian diet, which likely includes significantly increased consumption of **green leafy vegetables rich in vitamin K**.

Vitamin K is a cofactor for the synthesis of clotting factors II, VII, IX, and X. Warfarin works by inhibiting vitamin K epoxide reductase, thereby reducing the regeneration of active vitamin K. When dietary vitamin K intake increases substantially — as occurs with a drastic shift to a vegetarian diet heavy in green leafy vegetables — it overwhelms warfarin's inhibitory effect, restoring clotting factor synthesis and driving the INR down toward normal.[1][2][3]

The FDA warfarin label specifically warns that patients should "avoid drastic changes in dietary habits, such as eating large amounts of green leafy vegetables," and the ACCP guidelines note that "an increased intake of dietary vitamin K sufficient to reduce the anticoagulant response to warfarin occurs in

patients consuming green vegetables".[1][2] Each 100 µg increase in daily vitamin K intake has been estimated to reduce INR by approximately 0.2.[4]

Why the other options are less likely:

- **B. Increased hepatic metabolism** — While CYP450 inducers (e.g., rifampin, St. John's wort) can increase warfarin metabolism, there is no indication of such an exposure here. Hepatic dysfunction would actually potentiate warfarin's effect, not reduce it.[2]
- **C. Increased renal clearance** — Warfarin is primarily hepatically metabolized, not renally cleared. The patient's creatinine is normal, and renal function changes would not meaningfully alter warfarin's effect.[2]
- **D. Medication noncompliance** — While noncompliance could produce an INR of 1.0, the clinical vignette provides a clear dietary explanation. The question stem specifically highlights the dietary change, making this the intended answer. Noncompliance would also not explain why the question emphasizes the vegetarian diet.

Would you like to explore strategies for counseling patients on warfarin about maintaining consistent vitamin K intake while following a vegetarian diet?

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Question 562

A 60-year-old man with a long-standing history of chronic hepatitis C infection comes to the emergency department because of abdominal distention and scleral icterus for the past month. His heart rate is 76/min, respiratory rate is 14/min, temperature is 36.0°C (96.8°F), and blood pressure is 110/86 mm Hg. Physical examination show signs suggestive of liver cirrhosis. Which of the following signs is a direct result of hyperestrinism in cirrhotic patients?

Answer Choices:

(A) Coagulopathy
(B) Gynecomastia
(C) Jaundice
(D) Caput medusae

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/62b4dcce-9b6d-41a7-a53c-41440a1d7a2b

OpenEvidence Explanation

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The answer is **B. Gynecomastia**. Gynecomastia is a direct result of **hyperestrogenism** in cirrhotic patients, caused by decreased hepatic metabolism and clearance of androstenedione, which allows increased peripheral conversion

to estrogen (estrone and estradiol).[1][2] Elevated circulating estrogen levels promote benign proliferation of male breast glandular tissue.[3]

The other options have different pathophysiologic mechanisms in cirrhosis:

- **Coagulopathy** results from reduced hepatic synthesis of coagulation factors (I, II, V, VII, IX, X), thrombocytopenia from hypersplenism, and vitamin K deficiency due to cholestasis — not from hyperestrogenism.[1][4]
- **Jaundice** results from loss of functioning hepatocellular mass and impaired bilirubin clearance — a consequence of hepatocellular insufficiency.[1][5]
- **Caput medusae** results from **portal hypertension**, which causes collateral venous channels to develop around the umbilicus as blood is shunted from the portal to systemic circulation.[6]

> "Palmar erythema, spider nevi, gynecomastia, decreased body hair, and testicular atrophy are thought to result from decreased hepatic metabolism and clearance of androstenedione, allowing increased peripheral conversion to estrogen."
>
> None
>
> Used under license from JAMA Network.

Other signs of hyperestrogenism in cirrhosis include spider angiomas, palmar erythema, testicular atrophy, and loss of male hair pattern.[2][7]

Would you like to explore the hormonal management strategies for hypogonadism and feminization in men with cirrhosis?

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Question 563

A 47-year-old woman seeks evaluation at your office because she has had postcoital vaginal bleeding for the past 8 months with occasional intermenstrual watery, blood-tinged vaginal discharge. Her family history is negative for malignancies and inherited disorders. She is the result of a pregnancy complicated by numerous miscarriages in the 1960s, for which her mother received diethylstilbestrol. During a pelvic examination, you notice a polypoid mass on the anterior wall of the vagina. The bimanual examination is negative for adnexal masses. You suspect the presence of carcinoma and, therefore, send tissue samples to pathology, which confirmed the presence of malignant cells. Which of the following is the most likely malignant tumor in this patient?

Answer Choices:

(A) Clear cell adenocarcinoma
(B) Melanoma
(C) Botryoid sarcoma
(D) Verrucous carcinoma

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/6b08a846-070a-4fd2-b2af-946539b104ee

OpenEvidence Explanation

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The answer is **A. Clear cell adenocarcinoma**.

This patient's history of **in utero diethylstilbestrol (DES) exposure** — evidenced by her mother receiving DES in the 1960s for recurrent miscarriages — combined with a polypoid vaginal mass and postcoital bleeding is classic for **clear cell adenocarcinoma (CCA)** of the vagina. The association between prenatal DES exposure and vaginal/cervical CCA was first described by Herbst and Scully in 1970 and is one of the most well-established examples of transplacental carcinogenesis.[1]

Key supporting points:

- DES-exposed women have a **40- to 110-fold increased risk** of developing vaginal and cervical CCA compared with unexposed individuals (SIR = 40.9–109.9 depending on the cohort). While 80% of cases are diagnosed between ages 15 and 31, a second smaller peak occurs around age 42, and risk persists into the 40s and beyond.[2][3][4][5]
- CCA lesions are typically **papillary or nodular**, involving the upper or middle third of the vagina, and present with vaginal bleeding or discharge — consistent with this patient's anterior vaginal wall polypoid mass and postcoital bleeding.[2]
- The cumulative risk of CCA by age 50 in DES-exposed women is approximately **1 per 750**.[2][4]

The other answer choices are less likely in this clinical context:

- **Melanoma** (B): Vaginal melanoma is rare and not associated with DES exposure.
- **Botryoid sarcoma** (C): Sarcoma botryoides (embryonal rhabdomyosarcoma) typically presents in young children, not in a 47-year-old woman.
- **Verrucous carcinoma** (D): A variant of squamous cell carcinoma, not specifically linked to DES exposure.

Would you like to explore the current ASCCP screening recommendations for DES-exposed women, including the recommended surveillance intervals and examination techniques?

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Question 566

A 61-year-old man is brought to the emergency room with chest pain. He developed severe, crushing, substernal chest pain 10 hours ago while he was hiking in the Adirondack mountains. He was with 2 friends at the time who gave him aspirin before carrying him 5 miles to a town to get phone service, where they then called emergency medical services. His past medical history is notable for hypertension, diabetes mellitus, and hyperlipidemia. He takes enalapril, metformin, and atorvastatin. He has a 20-pack-year smoking history and is an avid hiker. His temperature is 100°F (37.8°C), blood pressure is 102/60 mmHg, pulse is 130/min, and respirations are 28/min. He is diaphoretic and intermittently conscious. Bilateral rales are heard on pulmonary auscultation. An electrocardiogram demonstrates ST elevations in leads I and aVL. Despite appropriate management, the patient expires. An autopsy is performed demonstrating ischemia in the left atrium and posterior left ventricle. Which of the following vessels was most likely affected in this patient?

Answer Choices:

(A) Left anterior descending artery
(B) Left circumflex artery
(C) Left coronary artery
(D) Right marginal artery

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/6a318da0-1a23-4194-bc30-bf1970a30591

OpenEvidence Explanation

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The answer is **B. Left circumflex artery**.

The key to this question lies in integrating the **autopsy findings** (ischemia of the **left atrium and posterior left ventricle**) with the ECG findings (ST elevations in leads I and aVL). The left circumflex artery (LCx) courses through the atrioventricular groove between the left atrium and left ventricle, and its branches — including the left atrial circumflex artery and obtuse marginal branches — are the primary blood supply to the **left atrium** and the **lateral and posterior walls of the left ventricle**.[1][2]

The following figure illustrates the coronary artery anatomy and corresponding ECG lead territories:

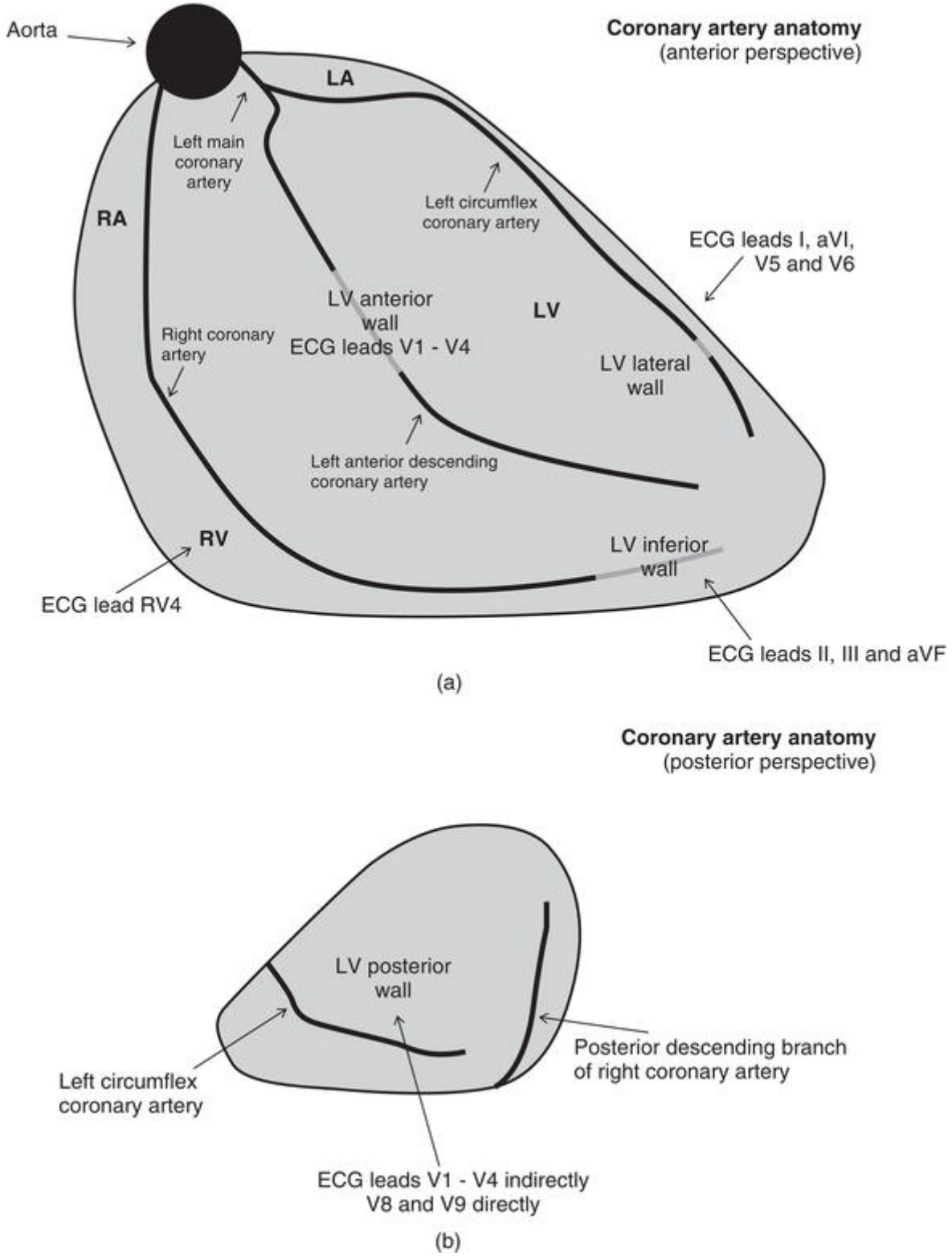


Figure 3. Cardiac and coronary anatomy with corresponding coronary artery, ECG lead, and cardiac segment. (a) Anterior perspective and (b) posterior perspective (LA, left atrium; RA, right atrium; RV, right ventricle; LV, left ventricle).

Why the other options are incorrect:

- **A. Left anterior descending artery (LAD):** Supplies the anterior wall, anterior septum, and apex. Occlusion produces ST elevation in V1–V4 (± I,

aVL if proximal), and autopsy would show anterior wall ischemia, not posterior LV or left atrial ischemia.[4][5]

- **C. Left coronary artery (left main):** While the left main gives rise to both the LAD and LCx, occlusion of the left main would cause massive ischemia involving the anterior wall, septum, and lateral wall — far more extensive than what is described. Left main occlusion is typically rapidly fatal with diffuse ST changes, not isolated I/aVL elevations.

- **D. Right marginal artery:** A branch of the right coronary artery that supplies the right ventricular free wall, not the left atrium or posterior left ventricle.

The left atrium is perfused primarily by branches of the **proximal left circumflex coronary artery**, and depression of left atrial mechanical performance has been demonstrated during LCx occlusion.[2] ST elevation in leads I and aVL is consistent with lateral wall involvement, which is part of the LCx territory.[6] The combination of lateral ECG changes with posterior LV and left atrial ischemia on autopsy is most consistent with LCx occlusion.

Would you like to explore how left circumflex occlusions are frequently missed on standard 12-lead ECG and the role of posterior leads (V7–V9) in improving diagnostic sensitivity?

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Question 567

A 61-year-old man comes to the physician with several months of sharp, shooting pain in both legs. Twenty years ago, he had a painless ulcer on his penis that resolved without treatment. He has no history of serious illness. Examination shows small pupils that constrict with accommodation but do not react to light. Sensation to pinprick and light touch is decreased over the distal lower extremities. Patellar reflexes are absent bilaterally. His gait is unsteady and broad-based. This patient is at increased risk for which of the following complications?

Answer Choices:

(A) Atrioventricular block
(B) Mitral valve regurgitation
(C) Penile squamous cell carcinoma
(D) Thoracic aortic aneurysm

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/7c7abeed-1ee7-4209-8602-1d8e6c149a09

OpenEvidence Explanation

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The correct answer is **D. Thoracic aortic aneurysm**.

This patient presents with classic **tabes dorsalis**, a manifestation of late (tertiary) neurosyphilis, occurring 20 years after an untreated primary syphilitic chancre. The key findings — **Argyll Robertson pupils** (accommodate but do not react to light), lancinating (sharp, shooting) leg pain, decreased sensation distally, absent patellar reflexes, and a broad-based ataxic gait — are hallmarks of posterior column and dorsal root degeneration caused by chronic *Treponema pallidum* infection.[1][2]

Patients with tertiary syphilis are at increased risk for **cardiovascular syphilis**, which classically manifests as **syphilitic aortitis** leading to **thoracic aortic aneurysm**. Cardiovascular lesions of tertiary syphilis include aortitis, aortic aneurysm, aortic valve disease, and coronary ostial occlusion.[3] Syphilitic aortitis typically involves the ascending aorta and aortic arch, with thoracic aortic aneurysm appearing **10 to 25 years** after the initial spirochetal infection.[4] The 2022 ACC/AHA Guidelines on Aortic Disease list syphilitic infectious aortitis as a recognized cause of thoracic aortic aneurysm.[5][6]

Why the other options are incorrect:

- **A. Atrioventricular block** — Not a classic cardiovascular complication of syphilis. Syphilitic aortitis affects the aorta and aortic valve, not the conduction system.
- **B. Mitral valve regurgitation** — Syphilitic cardiovascular disease involves the aortic valve (aortic regurgitation from aortic root dilation), not the mitral valve.
- **C. Penile squamous cell carcinoma** — A healed syphilitic chancre does not predispose to squamous cell carcinoma. This is not a recognized complication of syphilis.

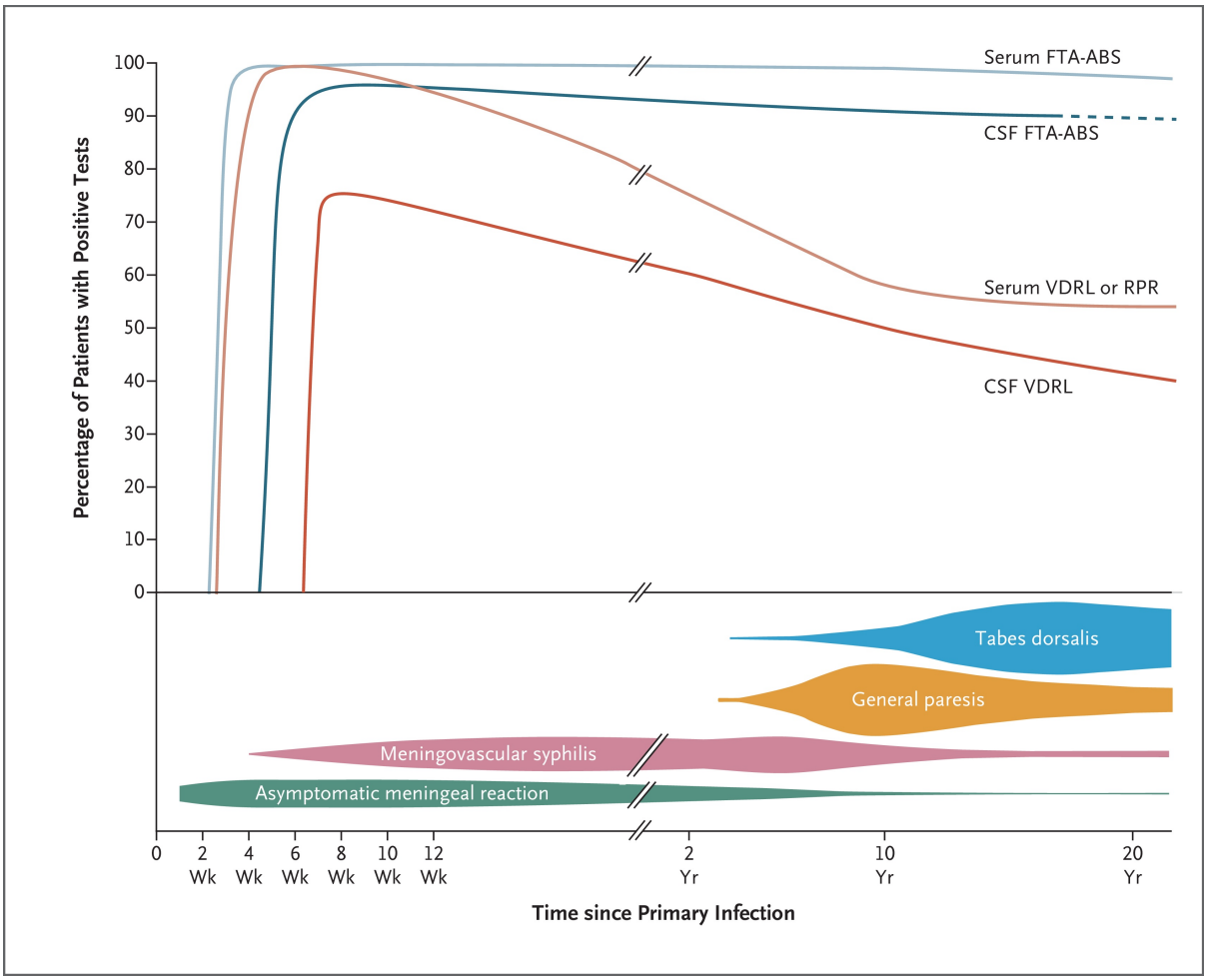


Figure 1. Serologic and Clinical Features of Early and Late Established Neurosyphilis.

Used under license from The New England Journal of Medicine.

Would you like to explore the diagnostic workup and treatment approach for late neurosyphilis, including CSF analysis interpretation and penicillin regimens?

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Question 568

A 55-year-old woman presents with severe pruritus and fatigue. She denies any similar symptoms in the past. No significant past medical history. Upon physical examination, scleral icterus is present, and significant hepatosplenomegaly is noted. Mild peripheral edema is also present. Laboratory findings are significant for elevated serum levels of bilirubin, aminotransferases, alkaline phosphatase (ALP), γ-glutamyl transpeptidase (GGTP), immunoglobulins, as well as cholesterol (especially HDL fraction). Antiviral antibodies are not present. The erythrocyte sedimentation rate is also elevated. Anti-mitochondrial antibodies are found. A liver biopsy is performed, and the histopathologic examination shows bile duct injury, cholestasis, and granuloma formation. Which of the following is the most likely diagnosis in this patient?

Answer Choices:

(A) Primary biliary cirrhosis
(B) Hemolytic anemia
(C) Hepatitis A
(D) Gilbert syndrome

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/e694a678-3d59-4556-9268-1477649760fb

OpenEvidence Explanation

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The correct answer is **A. Primary biliary cirrhosis** (now termed primary biliary cholangitis, PBC).

This presentation is classic for PBC: a **middle-aged woman** with **pruritus, fatigue, hepatosplenomegaly, cholestatic liver enzymes (elevated ALP and GGTP), positive anti-mitochondrial antibodies (AMA)**, and liver biopsy showing **bile duct injury, cholestasis, and granuloma formation** — the so-called "florid duct lesion," which is pathognomonic for PBC.[1][2]

Key diagnostic features supporting PBC:

- **Anti-mitochondrial antibodies** are present in ~95% of PBC patients and are highly disease-specific. Their presence alongside elevated ALP is essentially diagnostic.[3][4]
- **Histology** showing chronic non-suppurative destructive cholangitis with epithelioid cell granulomas adjacent to damaged bile ducts is pathognomonic.[1]
- **Elevated immunoglobulins** (particularly IgM), **hyperlipidemia** (especially elevated HDL cholesterol), and **elevated ESR** are all characteristic laboratory findings.[3][5]
- PBC predominantly affects **women aged 40–70 years**.[1]

Per the AASLD 2018 Practice Guidance, diagnosis requires at least 2 of 3 criteria: (1) biochemical cholestasis with ALP elevation, (2) positive AMA, and (3) histologic evidence of nonsuppurative destructive cholangitis.[4] This patient meets all three.

Why the other options are incorrect:

- **B. Hemolytic anemia** — would present with unconjugated hyperbilirubinemia, reticulocytosis, and anemia, not cholestatic liver enzymes or AMA.
- **C. Hepatitis A** — excluded by the absence of antiviral antibodies and the chronic cholestatic pattern with AMA positivity.

- **D. Gilbert syndrome** — a benign condition with isolated unconjugated hyperbilirubinemia, no hepatosplenomegaly, and normal liver enzymes.

Would you like to explore the current treatment algorithm for PBC, including first-line ursodeoxycholic acid and newer second-line agents like elafibranor and seladelpar?

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Question 569

A 25-year-old man is brought to the emergency department after being found unconscious. He was at a college party exhibiting belligerent behavior when he suddenly passed out and fell to the ground. His past medical history is not known. His temperature is 100°F (37.8°C), blood pressure is 107/48 mmHg, pulse is 125/min, respirations are 19/min, and oxygen saturation is 99% on room air. The patient is covered with emesis and responds incoherently to questions. As the patient begins to wake up he continues vomiting. The patient is started on IV fluids, analgesics, and anti-emetics and begins to feel better. Thirty minutes later the patient presents with muscle rigidity and is no longer responding coherently to questions. His temperature is 103°F (39.4°C), blood pressure is 127/68 mmHg, pulse is 125/min, respirations are 18/min, and oxygen saturation is 98% on room air. The patient's basic laboratory studies are drawn and he is started on IV fluids, given lorazepam, and placed under a cooling blanket. Despite these initial measures, his symptoms persist. Which of the following is the best next step in management?

Answer Choices:

(A) Acetaminophen
(B) Dantrolene
(C) Intubation
(D) Supportive therapy

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/49cd591a-0265-4e2a-9fc9-92e64afa6464

OpenEvidence Explanation

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The best next step in management is **B. Dantrolene**.

This clinical scenario is consistent with **neuroleptic malignant syndrome (NMS)** or a similar hyperthermia-rigidity syndrome (potentially from a recreational drug with dopaminergic or serotonergic effects at a college party). The cardinal features are present: **hyperthermia** (103°F), **muscle rigidity**, **altered mental status**, and **autonomic instability** (tachycardia, blood pressure changes). The patient has already received appropriate initial measures — IV fluids, lorazepam, and cooling — but symptoms persist.

The treatment of NMS follows a **tiered approach**. Lorazepam provides muscle relaxation in mild cases, but when muscular signs persist or worsen despite benzodiazepines, **dantrolene** is the recommended next step.[1] Dantrolene is a direct-acting skeletal muscle relaxant that inhibits calcium release from the sarcoplasmic reticulum, thereby reducing rigidity and mitigating hyperthermia.[1][2]

> "Lorazepam causes muscle relaxation in mild cases. However, if muscular signs of neuroleptic malignant syndrome persist or worsen, dantrolene, a direct-acting skeletal-muscle relaxant that inhibits the release of calcium at the sarcoplasmic reticulum, can be administered."
>
> —Eelco F.M. Wijdicks, M.D., Ph.D. et al., Mayo Clinic Hospital. Neuroleptic Malignant Syndrome. N Engl J Med. September 26, 2024.
>
> Used under license from The New England Journal of Medicine.

Why the other options are incorrect:

- **A. Acetaminophen** — Antipyretics are largely ineffective in NMS because the hyperthermia is not prostaglandin-mediated; it results from excessive muscle contraction and central thermoregulatory dysfunction. While acetaminophen may be used adjunctively, it does not address the underlying rigidity driving the hyperthermia.[3]

- **C. Intubation** — There is no indication for intubation at this time. The patient's oxygen saturation is 98%, and respirations are 18/min. Intubation would be warranted if there were respiratory compromise from chest wall rigidity or aspiration, but that is not described here.[1]

- **D. Supportive therapy** — Supportive measures (IV fluids, cooling, benzodiazepines) have already been initiated and have failed to control symptoms. Continuing supportive therapy alone without escalation is insufficient in this scenario. In severe NMS cases, specific therapies such as dantrolene are associated with lower mortality compared to symptomatic therapy alone (10% vs. 30%).[3]

Would you like to explore the differentiation between NMS and serotonin syndrome, given the party setting where recreational drug exposure is possible?

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Question 570

A 13-year-old boy is brought to the emergency department because of pain in his right knee for the past week. The pain is exacerbated by jogging and climbing up stairs. He has no history of trauma to the knee. He is otherwise healthy. He is an active member of his school's gymnastics team. His vital signs are within normal limits. Examination of the right knee shows a tender swelling at the proximal tibia; range of motion is full. Knee extension against resistance causes pain in the anterior proximal tibia. The remainder of the examinations shows no abnormalities. X-ray of the right knee shows anterior tibial soft tissue swelling with fragmentation of the tibial tuberosity. Which of the following is the most appropriate next step?

Answer Choices:

(A) Administration of oral ketorolac
(B) Perform joint aspiration
(C) Open reduction of the tuberosity
(D) Application of a lower leg cast

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/daa3fc70-f339-4b6b-ad00-9ba80732502c

OpenEvidence Explanation

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However, it is important to carefully re-read this question. The clinical presentation here — a 13-year-old gymnast with gradual onset anterior knee pain over a week, no acute trauma, tibial tuberosity tenderness, and X-ray showing fragmentation of the tibial tuberosity — is most consistent with **Osgood-Schlatter disease** (tibial tuberosity apophysitis), not an acute tibial tubercle avulsion fracture. Let me search further to confirm.

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The answer is **A. Administration of oral ketorolac** (an NSAID), though this is a nuanced question worth discussing.

The clinical presentation — a 13-year-old male gymnast with insidious onset anterior knee pain over one week, no acute trauma, tenderness and swelling at the tibial tuberosity, pain with resisted knee extension, and X-ray showing soft tissue swelling with fragmentation of the tibial tuberosity — is classic for **Osgood-Schlatter disease** (OSD), a traction apophysitis of the tibial tubercle.[1][2][3]

Why answer A is correct: OSD is managed conservatively with activity modification, icing, **NSAIDs**, and physical therapy. Over 90% of patients respond well to nonoperative treatment.[1][3][4] Ketorolac is an NSAID, and while it carries a boxed warning stating it is "not indicated for use in pediatric patients" per the FDA label, the question is testing the principle that NSAIDs are the appropriate pharmacologic intervention for OSD — and ketorolac is the only NSAID option listed.[5][6]

Why the other options are incorrect:

- **B. Joint aspiration** — There is no effusion or signs of septic arthritis/inflammatory arthropathy. OSD does not produce a joint effusion requiring aspiration.
- **C. Open reduction** — Surgery is reserved for displaced tibial tubercle avulsion fractures or for refractory OSD after physeal closure with symptomatic ossicle excision. The fragmentation seen here is characteristic of OSD, not a displaced fracture requiring ORIF.[3][7]

- **D. Lower leg cast** — Cast immobilization is used for nondisplaced tibial tubercle avulsion fractures, but this presentation lacks an acute injury mechanism and is consistent with OSD, which does not require casting.[8]

The key distinguishing feature is the **absence of acute trauma** and the **gradual onset** of symptoms in an active adolescent athlete, which points to OSD rather than an acute avulsion fracture. Radiographic fragmentation of the tibial tuberosity is a well-described finding in OSD and does not indicate a surgical fracture.[2][3][9]

Would you like to explore the indications for surgical intervention in Osgood-Schlatter disease versus tibial tubercle avulsion fractures?

Relevant images

(CONTENT OMITTED)

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Question 571

Three days after undergoing an open cholecystectomy, an obese 57-year-old woman has fever, chills, and a headache. She has right-sided chest pain that increases on inspiration and has had a productive cough for the last 12 hours. She had an episode of hypotension after the operation that resolved with intravenous fluid therapy. She underwent an abdominal hysterectomy 16 years ago for multiple fibroids of the uterus. She has smoked one pack of cigarettes daily for 17 years. She appears uncomfortable. Her temperature is 39°C (102.2°F), pulse is 98/min, respirations are 18/min, and blood pressure is 128/82 mm Hg. Inspiratory crackles are heard at the right lung base. The abdomen is soft and nontender. There is a healing surgical incision below the right ribcage. The remainder of the examination shows no abnormalities. Which of the following is the most likely diagnosis?

Answer Choices:

(A) Pulmonary embolism
(B) Subphrenic abscess
(C) Pneumonia
(D) Pneumothorax

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/f5ab318c-6d49-48c2-91c3-cefbfd951b90

OpenEvidence Explanation

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The most likely diagnosis is **C. Pneumonia**.

This presentation is classic for **postoperative pneumonia** following open cholecystectomy. Several features strongly support this diagnosis:

- **Timing**: Onset on postoperative day 3 is typical for hospital-acquired pneumonia, which commonly develops 2–5 days after upper abdominal surgery.[1]
- **Risk factors**: Open cholecystectomy (OR 1.60 vs. laparoscopic), obesity, smoking history, and upper abdominal incision all significantly increase the risk of postoperative pneumonia. The subcostal incision causes splinting, reduced diaphragmatic excursion, and atelectasis — a well-recognized precursor to pneumonia.[2][3]
- **Clinical features**: Fever (39°C), productive cough, pleuritic right-sided chest pain, and **inspiratory crackles at the right lung base** are consistent with a consolidative process. The productive cough is particularly important, as it points toward an infectious pulmonary parenchymal process rather than PE or subphrenic abscess.[4]

Why not the other options?

- **Pulmonary embolism (A)**: While this patient has risk factors for PE (obesity, recent surgery, postoperative hypotension/immobility), PE typically presents with sudden-onset dyspnea, tachycardia, and pleuritic chest pain — but a **productive cough with crackles** is not characteristic. PE more commonly has a clear lung exam or decreased breath sounds rather than focal crackles.[5]
- **Subphrenic abscess (B)**: This typically presents **later** (5–10+ days postoperatively) and is associated with abdominal tenderness, referred shoulder pain, or an elevated hemidiaphragm. The abdomen here is soft and nontender, making this less likely at day 3.
- **Pneumothorax (D)**: Would present with decreased or absent breath sounds and hyperresonance on the affected side, not inspiratory crackles. There is no precipitating event described (e.g., central line placement, mechanical ventilation).

The combination of productive cough, fever, and focal inspiratory crackles at the right lung base in a patient with multiple risk factors for postoperative pulmonary complications makes pneumonia the most likely diagnosis.[2][3]

Is there a specific aspect of postoperative pulmonary complications or the workup of postoperative fever you'd like to explore further?

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Question 574

An 11-year-old boy presents to your office with pitting edema and proteinuria exceeding 3.5g in 24 hours. You suspect that this patient has experienced a loss of polyanions in his glomerular basement membranes. Which of the following findings would confirm your diagnosis?

Answer Choices:

(A) WBC casts in the urine
(B) Selective albuminuria
(C) Negatively birefringent crystals in the urine
(D) Bence-Jones proteinuria

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/6ec19391-c91c-4627-86f1-d74380e20fc9

OpenEvidence Explanation

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The correct answer is **B. Selective albuminuria**.

This clinical scenario describes **minimal change disease (MCD)**, the most common cause of nephrotic syndrome in children, accounting for 70–90% of cases in those older than 1 year.[1][2] The key pathophysiologic clue is the **loss of polyanions (glycosaminoglycans such as heparan sulfate) in the glomerular**

basement membrane (GBM), which constitutes the charge-selective barrier.[3][4]

Why selective albuminuria confirms the diagnosis:

The glomerular filtration barrier normally has two components: a **charge-selective barrier** (polyanionic glycosaminoglycans) and a **size-selective barrier** (pore structure). In MCD, the primary defect is loss of charge selectivity, not size selectivity.[3] Albumin (~69 kDa) is a polyanionic protein that is normally repelled by the negatively charged GBM. When these polyanions are lost, albumin preferentially leaks through while larger proteins (e.g., immunoglobulins >150 kDa) remain restricted by the intact size-selective barrier.[3][5] This produces **selective proteinuria** — predominantly albumin with minimal excretion of higher-molecular-weight proteins.[5][6]

In contrast, diseases like membranous nephropathy cause loss of size selectivity, resulting in **nonselective proteinuria** with excretion of both albumin and larger proteins.[3]

Why the other options are incorrect:

- **A. WBC casts** — Indicate pyelonephritis or interstitial nephritis, not a podocytopathy.
- **C. Negatively birefringent crystals** — Indicate monosodium urate (gout), unrelated to nephrotic syndrome.
- **D. Bence-Jones proteinuria** — Indicates light chain excretion seen in multiple myeloma, not a primary glomerular disease.

Would you like to explore the pathophysiologic differences between charge-selective and size-selective barrier defects across different glomerular diseases?

Relevant images

(CONTENT OMITTED)

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Question 576

A 32-year-old female is brought to the emergency room by her friend for acute onset abdominal pain. She states that she was in a kickboxing class when she suddenly developed left-sided abdominal pain. Her past medical history is significant for chlamydia. She is currently sexually active and does not use contraception. Her menstrual periods occur regularly every 30 days. Her last menstrual period ended 2 days ago. The patient's temperature is 99°F (37.2°C), blood pressure is 110/68 mmHg, pulse is 88/min, and respirations are 14/min with an oxygen saturation of 98% on room air. On physical exam, there is left-sided, lower abdominal tenderness and guarding. Pelvic examination is notable for clear mucous in the vaginal introitus and tenderness of the left adnexa. A pelvic ultrasound with Doppler reveals a large amount of fluid in the rectouterine pouch. Which of the following is the most likely diagnosis?

Answer Choices:

(A) Ectopic pregnancy
(B) Ovarian torsion
(C) Pelvic inflammatory disease
(D) Ruptured ovarian cyst

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/5185ce35-6cbf-45ed-af58-4f9c2924aaba

OpenEvidence Explanation

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The most likely diagnosis is **D. Ruptured ovarian cyst**.

Several clinical features point toward this diagnosis and away from the alternatives:

Timing and menstrual cycle: The patient's last menstrual period ended 2 days ago, placing her in the early follicular phase (approximately cycle day 7 of a 30-day cycle). Ovarian cysts — particularly follicular cysts from a prior cycle — can rupture, especially with physical trauma or vigorous activity such as kickboxing.[1][2] Ruptured ovarian cysts are among the most common gynecologic causes of acute pelvic pain in reproductive-age women, and haemorrhagic or ruptured corpus luteum cysts are the most frequently identified subtypes.[1]

Free fluid in the rectouterine pouch (pouch of Douglas) is a hallmark finding of cyst rupture, representing hemorrhagic fluid from the ruptured cyst accumulating in the dependent pelvis.[1][3] The acute onset during vigorous physical activity is a classic precipitant for cyst rupture.[2]

Why not the other options:

- **Ectopic pregnancy (A):** Ectopic pregnancy requires a positive pregnancy test. With her last menstrual period ending just 2 days ago, she is very early in her cycle and essentially cannot be pregnant from this cycle. While prior chlamydia is a risk factor for ectopic pregnancy, the timing makes this diagnosis extremely unlikely.[4][5]
- **Ovarian torsion (B):** Torsion typically presents with severe, intermittent pain often accompanied by nausea and vomiting. Doppler ultrasound was performed and would be expected to show abnormal or absent ovarian blood flow in torsion — the question does not mention this finding, making torsion less likely.[2][6]
- **Pelvic inflammatory disease (C):** PID typically presents with bilateral lower abdominal pain, cervical motion tenderness, vaginal discharge (often purulent), and fever. This patient has clear mucous (normal), unilateral pain,

only a low-grade temperature, and an acute onset triggered by physical activity — all inconsistent with the more indolent presentation of PID.[7][8]

Would you like to explore the management algorithm for ruptured ovarian cysts, including indications for surgical versus conservative management?

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Question 578

A 36-year-old woman comes to the physician because of difficulty discarding items in her home. She says that the accumulation of things in her kitchen and dining room makes regular use of these spaces incredibly difficult. Her behavior started when she was in high school. She feels anxious when she tries to discard her possessions and her husband tries to clean and organize the home. This behavior frustrates her because most of the items she saves have little emotional or monetary value. She reports that there has been no improvement despite attending cognitive behavioral therapy sessions for the past 6 months. She now feels that her behavior is "taking over" her life. She does not drink, smoke, or use illicit drugs. She takes no medications. Her temperature is 36°C (96.8°F), pulse is 90/min, respirations are 12/min, and blood pressure is 116/80 mm Hg. On mental status examination, she is calm, alert, and oriented to person, place, and time. Her mood is depressed; her speech is organized, logical, and coherent; and there are no psychotic symptoms. Which of the following is the most appropriate next step in management?

Answer Choices:

(A) Fluoxetine
(B) Lamotrigine
(C) Buspirone
(D) Methylphenidate

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/5ed84ed9-3377-4e22-90e2-d6063856f18e

OpenEvidence Explanation

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The correct answer is **A. Fluoxetine**.

This patient presents with classic **hoarding disorder** — difficulty discarding possessions, resulting clutter that impairs use of living spaces, anxiety when attempting to discard items, and significant functional impairment — with onset in adolescence and a chronic course. She has had an inadequate response to 6 months of cognitive behavioral therapy (CBT), which is the first-line treatment for hoarding disorder.[1][2] The most appropriate next step is to add an **SSRI such as fluoxetine** as pharmacologic augmentation.

Rationale for fluoxetine over the other options:

- **SSRIs** are the most commonly recommended pharmacotherapy for hoarding disorder. Although large-scale controlled trials are lacking, an NEJM clinical practice review notes that SSRIs "may also be helpful" and are the primary pharmacologic agents suggested for this condition. A meta-analysis of pharmacotherapy for pathological hoarding found that over half of participants treated with serotonin-reuptake inhibitors responded (estimated response rate 0.58). SSRIs also address the comorbid depressed mood present in this patient.[1][3]
- **Lamotrigine** (B) is a mood stabilizer used primarily for bipolar disorder and seizure disorders; it has no established role in hoarding disorder.
- **Buspirone** (C) is an anxiolytic used for generalized anxiety disorder. While this patient has anxiety related to discarding, buspirone does not target the core pathology of hoarding disorder.
- **Methylphenidate** (D) has been explored in very small, uncontrolled studies based on a hypothesized overlap between hoarding disorder and ADHD neurobiology, but the evidence level is low and it is not a standard recommendation.[4]

Given the inadequate response to CBT alone, adding an SSRI is the most evidence-supported pharmacologic intervention. The combination of

pharmacotherapy and CBT is likely more effective than either treatment alone. [5]

Would you like to explore the specific CBT modifications (e.g., cognitive rehabilitation techniques, therapist-guided exposure) that may improve outcomes in patients with hoarding disorder who have had a suboptimal response to standard CBT?

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Question 580

A 20-year-old woman is brought in for a psychiatric consultation by her mother who is concerned because of her daughter's recent bizarre behavior. The patient's father died from lung cancer 1 week ago. Though this has been stressful for the whole family, the daughter has been hearing voices and having intrusive thoughts ever since. These voices have conversations about her and how she should have been the one to die and they encourage her to kill herself. She has not been able to concentrate at work or at school. She has no other history of medical or psychiatric illness. She denies recent use of any medication. Today, her heart rate is 90/min, respiratory rate is 17/min, blood pressure is 110/65 mm Hg, and temperature is 36.9°C (98.4°F). On physical exam, she appears gaunt and anxious. Her heart has a regular rate and rhythm and her lungs are clear to auscultation bilaterally. CMP, CBC, and TSH are normal. A urine toxicology test is negative. What is the patient's most likely diagnosis?

Answer Choices:

(A) Brief psychotic disorder
(B) Adjustment disorder
(C) Schizophrenia
(D) Bereavement

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/5e1fbd09-5b26-4b6e-807e-5eb2a80cac22

OpenEvidence Explanation

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The most likely diagnosis is **A. Brief psychotic disorder**.

This presentation is classic for **brief psychotic disorder with marked stressor** (formerly called "brief reactive psychosis"). The key features supporting this diagnosis include:

- **Acute onset of psychotic symptoms** (auditory hallucinations with command features) directly following a clearly identifiable stressor (father's death 1 week ago)
- **Duration less than 1 month** (symptoms present for ~1 week)
- **No prior psychiatric history**
- **Negative medical workup** (normal CMP, CBC, TSH, and urine toxicology), ruling out substance-induced or medical causes of psychosis

Why not the other options:

- **Adjustment disorder (B):** Adjustment disorder can involve depressed mood, anxiety, or behavioral disturbance, but by definition it does **not** include frank psychotic symptoms such as auditory hallucinations with conversational quality and command features.[1]
- **Schizophrenia (C):** Requires symptoms lasting **≥6 months** (including prodromal/residual phases), with active-phase symptoms for at least 1 month. This patient has had symptoms for only 1 week with no prior history.[1]
- **Bereavement (D):** Normal grief can include transient illusions or brief hallucinations of the deceased (e.g., hearing the deceased's voice), but this patient's hallucinations are elaborate — third-person voices conversing about her and commanding self-harm — which goes well beyond typical bereavement phenomena.[2]

Per DSM-5, brief psychotic disorder is defined by at least one positive psychotic symptom (delusions, hallucinations, disorganized speech, or grossly disorganized behavior) lasting at least 1 day but less than 1 month, with eventual full return to premorbid functioning.[1] The specifier "with marked stressor" applies when symptoms occur in response to events that would be markedly stressful to almost anyone in similar circumstances.[3]

Immediate priorities in this case include a thorough **suicide risk assessment** given the command auditory hallucinations encouraging self-harm — first-episode psychosis carries the highest suicide risk in the first 3 months, particularly in younger patients with depressive symptoms and perceived stress.[4][5] Ensuring safety (including potential psychiatric hospitalization) and initiating short-term antipsychotic treatment should be considered while monitoring for symptom resolution within the expected timeframe.

Is there additional information about this patient's mental status exam findings or whether she has expressed any intent or plan to act on the command hallucinations?

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Question 584

A 33-year-old man presents to the emergency department after a motor vehicle collision. He was the front seat unrestrained driver in a head-on collision. The patient has a Glasgow Coma Scale of 5 and is subsequently intubated. Physical exam is notable for subcutaneous emphysema in the clavicular area. Needle decompression and chest tube placement are performed, and the patient is stabilized after receiving 2 units of blood and 2 liters of fluid. Chest radiography demonstrates proper tube location and resolution of the pneumothorax. The patient is transferred to the trauma intensive care unit. On the unit, a repeat chest radiograph is notable for a recurrent pneumothorax with the chest tube in place. Which of the following is the most likely diagnosis?

Answer Choices:

(A) Inappropriate chest tube placement
(B) Spontaneous pneumothorax
(C) Tension pneumothorax
(D) Tracheobronchial rupture

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/57375210-6cb2-48b2-bc36-438bf55c9099

OpenEvidence Explanation

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The answer is **D. Tracheobronchial rupture**.

The combination of a high-energy blunt chest trauma (unrestrained driver in a head-on collision), **subcutaneous emphysema**, and a **recurrent pneumothorax despite a properly positioned chest tube** is the classic presentation of tracheobronchial injury. The key clinical clue is that the initial chest radiograph confirmed proper tube location and resolution of the pneumothorax, yet the pneumothorax recurred — indicating a persistent air leak from an airway disruption that the chest tube alone cannot manage.

Why tracheobronchial rupture fits best:

- Post-traumatic tracheobronchial injuries typically present with massive subcutaneous emphysema and **intractable pneumothorax** — a pneumothorax that persists or recurs despite adequate chest tube drainage.[1]
- These injuries occur after high-energy impact mechanisms and are commonly associated with other severe injuries.[2][3]
- The WSES-AAST Thoracic Trauma Guidelines specifically identify **persistent pneumothorax despite chest tube drainage** as an indication for surgical repair of tracheobronchial injury.[4]

Why the other options are less likely:

- **A. Inappropriate chest tube placement** — The post-procedure radiograph confirmed proper tube position and initial resolution of the pneumothorax, effectively ruling this out.
- **B. Spontaneous pneumothorax** — This is a diagnosis of exclusion in a young patient without known lung disease and would not explain recurrence in the setting of high-energy trauma with subcutaneous emphysema.
- **C. Tension pneumothorax** — While possible as a complication, it does not explain the underlying etiology of the recurrent air collection; the question asks for the diagnosis, not the complication. A functioning chest tube should prevent tension physiology.

Bronchoscopy is the gold standard for confirming the diagnosis, with fiberoptic bronchoscopy achieving approximately 90% sensitivity.[4]

Would you like to explore the surgical management approach and timing of repair for tracheobronchial injuries in the setting of polytrauma?

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Question 585

A 55-year-old man is brought to the emergency department 12 hours after the sudden onset of shortness of breath and substernal chest pain at rest; the pain is increased by inspiration. He has also had a nonproductive cough, fever, and malaise for the past 5 days. He does not smoke or use illicit drugs. His temperature is 38°C (100.4°F), pulse is 125/min, respirations are 32/min, and blood pressure is 85/45 mm Hg. Physical examination shows distended neck veins. Auscultation of the chest discloses bilateral basilar rales and muffled heart sounds. An ECG shows sinus tachycardia, diffuse ST segment elevation, low voltage QRS complexes, and fluctuating R wave amplitude. Which of the following is the most likely diagnosis?

Answer Choices:

(A) Kawasaki disease
(B) Rheumatic fever
(C) Infective endocarditis
(D) Cardiac tamponade

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/2b676390-7490-47e0-8463-4cef33c4f77b

OpenEvidence Explanation

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The answer is **D. Cardiac tamponade**.

This presentation is classic for **acute pericarditis complicated by cardiac tamponade**. The key findings align precisely with this diagnosis:

Clinical features supporting pericarditis:

- Substernal chest pain worsened by inspiration (pleuritic quality)
- Preceding viral prodrome (5 days of cough, fever, malaise)
- Diffuse ST-segment elevation on ECG[1]

Clinical features supporting tamponade (Beck's triad and ECG findings):

- **Hypotension** (BP 85/45 mmHg)
- **Distended neck veins** (elevated jugular venous pressure)
- **Muffled heart sounds**

These three findings constitute **Beck's triad**, the hallmark of cardiac tamponade.[2][3] Sinus tachycardia (pulse 125/min) is the most sensitive clinical sign of tamponade, representing a compensatory mechanism to maintain cardiac output.[2][4]

ECG findings are particularly diagnostic:

- **Low-voltage QRS complexes** result from the insulating effect of pericardial fluid and are a feature of tamponade rather than pericardial effusion alone[5]
- **Fluctuating R-wave amplitude** represents **electrical alternans**, caused by the swinging motion of the heart within a fluid-filled pericardium — this finding is highly specific for cardiac tamponade[6]
- Diffuse ST elevation reflects the underlying acute pericarditis[1][7]

Why the other options are incorrect:

- **Kawasaki disease** (A) — occurs in children, typically under age 5

- **Rheumatic fever** (B) — follows group A streptococcal pharyngitis, presents with migratory polyarthritis, carditis, and other Jones criteria; does not produce this ECG pattern
- **Infective endocarditis** (C) — presents with valvular vegetations, embolic phenomena, and new murmurs; does not cause diffuse ST elevation or electrical alternans

Would you like to explore the emergency management of cardiac tamponade, including indications and techniques for pericardiocentesis?

Relevant images

(CONTENT OMITTED)

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Question 588

A 45-year-old G3P3 presents complaining of the feeling of a foreign body in her vagina that worsens on standing. She does not have urinary or fecal incontinence or any other genitourinary symptoms. She has no known gynecologic diseases. There were no complications with her pregnancies, all of which were full-term vaginal deliveries. She is sexually active with her husband and no longer uses oral contraceptives. She has an 11 pack-year history of smoking. Her weight is 79 kg (174 lb) and her height is 155 cm (5 ft). Her vital signs are within normal limits. The physical examination is unremarkable. The gynecologic examination reveals descent of the cervix halfway towards the introitus. On Valsalva and standing, the cervix descents to the plane of the hymen. The uterus is not enlarged and the ovaries are non-palpable. Which of the following treatments is most reasonable to offer this patient?

Answer Choices:

(A) Support pessary
(B) Space-filling pessary
(C) Posterior colporrhaphy
(D) Sacral colpopexy

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/8f453586-5345-44e9-8f62-12e27932dabf

OpenEvidence Explanation

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The correct answer is **A. Support pessary**.

This patient presents with **stage II uterine prolapse** (cervix descends to the hymenal plane on Valsalva), which is symptomatic (foreign body sensation worsening on standing). The most reasonable initial treatment is a **support pessary (e.g., ring pessary)**, which is the recommended first-line nonsurgical intervention for symptomatic pelvic organ prolapse.

Why a support pessary is correct:

The ACOG Practice Bulletin on Pelvic Organ Prolapse recommends that all symptomatic women be **offered a vaginal pessary as an alternative to surgery**, and that nonsurgical treatment should be offered first before considering surgical options.[1][2] Ring pessaries (a type of support pessary) are used most successfully with **stage II prolapse (100% success rate)** and stage III prolapse (71%), making them ideal for this patient's degree of prolapse.[1] Pessaries are a low-risk intervention that can be offered to all women considering treatment of POP.[1] This patient is sexually active, which further favors a ring (support) pessary, as it allows for intercourse.

Why the other options are less appropriate:

- **B. Space-filling pessary** (e.g., Gellhorn): These are typically reserved for more advanced prolapse (stage III–IV) or when a support pessary fails to stay in place. Ring pessaries are tried first, and Gellhorn pessaries are used if the ring does not stay in place. Additionally, space-filling pessaries generally must be removed for intercourse.[1]
- **C. Posterior colporrhaphy**: This is a surgical repair of the posterior vaginal wall, which is not indicated here — the patient has apical (uterine) prolapse, not posterior compartment prolapse.
- **D. Sacral colpopexy**: This is an abdominal surgical procedure typically reserved for vault prolapse after hysterectomy or for patients who have

failed conservative management. Surgery is indicated only after nonsurgical treatments have been tried or declined.[1][2]

Would you like to explore the differences between types of pessaries and their indications based on prolapse stage and patient characteristics?

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Question 589

A 36-year-old woman, gravida 2, para 2, comes to the emergency department because of sudden-onset, severe right flank pain. She was in her aerobics class when the pain started but denies any trauma to the region. She has a history of recurrent ovarian cysts. Menses occur regularly at 28-day intervals. Her temperature is 37.1°C (99.3°F). Abdominal examination shows tenderness in the right lower quadrant with guarding. Pelvic ultrasound shows a large simple cyst on the right ovary. Right ovarian artery flow is detectable on Doppler, but there is no flow detected in the right ovarian vein. Which of the following ligaments is most likely to have been involved?

Answer Choices:

(A) Broad ligament
(B) Ovarian ligament
(C) Cardinal ligament
(D) Infundibulopelvic ligament

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/d53d20bd-697c-458b-b462-ae33dd0b0484

OpenEvidence Explanation

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The answer is **D. Infundibulopelvic ligament** (also called the suspensory ligament of the ovary).

This clinical scenario describes **ovarian torsion** — sudden-onset severe pelvic pain in a woman with a known ovarian cyst, with Doppler showing preserved arterial flow but absent venous flow. The **infundibulopelvic ligament** is the structure most directly involved because it contains the **ovarian artery and ovarian vein** as they course from the retroperitoneum to the ovary.[1] When the ovary torsions, it twists on its vascular pedicle — the infundibulopelvic ligament — compressing these vessels.

Why venous flow is lost first with preserved arterial flow:

In early or partial torsion, the thin-walled, low-pressure ovarian vein is compressed before the thick-walled, high-pressure ovarian artery. This explains the Doppler findings of detectable arterial flow but absent venous flow.[2][3] This pattern corresponds to a Class 2 torsion in the Doppler classification proposed by Auslender et al., which indicates surgical intervention is required.[4] Nizar et al. demonstrated that absent or abnormal ovarian venous flow had **100% sensitivity** for adnexal torsion and may be the only abnormal ultrasound sign in early torsion.[5]

Why not the other ligaments:

- The **ovarian ligament** (utero-ovarian ligament) connects the ovary to the uterus but does not carry the primary ovarian vessels.
- The **broad ligament** is a peritoneal fold that supports the uterus, tubes, and ovaries but is not the vascular pedicle.
- The **cardinal ligament** (transverse cervical ligament) supports the cervix/upper vagina and contains the uterine artery — it is unrelated to ovarian vascular supply.

The following figure illustrates the relevant anatomy, including the infundibulopelvic ligament transmitting the ovarian artery and veins to the ovary.

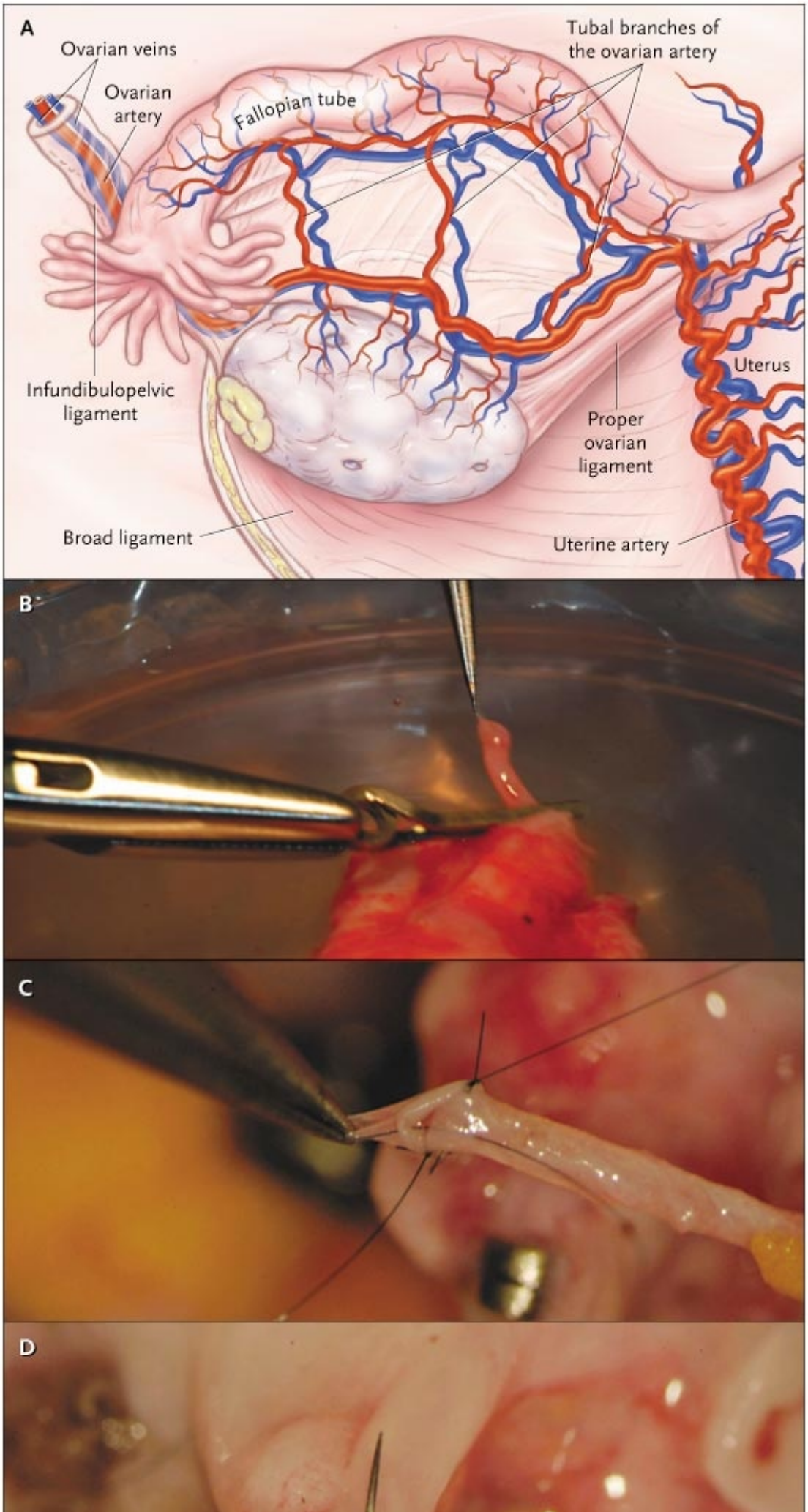

A
Ovarian veins
Ovarian artery
Fallopian tube
Tubal branches of the ovarian artery
Uterus
Infundibulopelvic ligament
Proper ovarian ligament
Broad ligament
Uterine artery
B
C
D

Figure 1. Whole-Ovary Transplantation between Monozygotic Twins.

Used under license from The New England Journal of Medicine.

Would you like to explore the Doppler ultrasound classification system for grading severity of ovarian torsion and how it guides surgical decision-making?

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Question 590

A 69-year-old woman comes to the physician for a routine health maintenance examination. She feels well. Physical examination shows nontender cervical and axillary lymphadenopathy. The spleen is palpated 5 cm below the costal margin. Her leukocyte count is 12,000/mm3 and platelet count is 217,000/mm3. Further evaluation is most likely to show which of the following findings?

Answer Choices:

(A) Ringed sideroblasts
(B) Teardrop cells
(C) Smudge cells
(D) Hypergammaglobulinemia

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/4501a499-0375-49c8-a51f-6ca706182f72

OpenEvidence Explanation

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The answer is **C. Smudge cells**.

This clinical presentation — an older adult with painless cervical and axillary **lymphadenopathy**, **splenomegaly**, and **leukocytosis** with a normal platelet count

— is classic for **chronic lymphocytic leukemia (CLL)** or its tissue counterpart, small lymphocytic lymphoma (SLL). CLL is the most common leukemia in adults in Western countries, with an average age at diagnosis of 72 years.[1] Approximately 70% of patients are diagnosed incidentally, and among symptomatic patients, ~50% present with lymphadenopathy and 20–50% with hepatosplenomegaly.[2]

Smudge cells (also called Gumprecht nuclear shadows) are a hallmark morphologic finding on peripheral blood smear in CLL. They represent fragile CLL lymphocytes that rupture during smear preparation, leaving behind disrupted nuclear remnants.[3] The percentage of smudge cells is an independent prognostic factor in CLL, with higher percentages (>30%) associated with more favorable outcomes, including longer time to treatment and improved overall survival.[4][5]

Why the other options are incorrect:

- **A. Ringed sideroblasts** — Characteristic of myelodysplastic syndromes (specifically MDS with ring sideroblasts), not CLL.
- **B. Teardrop cells** (dacrocytes) — Associated with myelofibrosis and other myeloproliferative neoplasms with marrow fibrosis, not CLL.
- **D. Hypergammaglobulinemia** — CLL is actually associated with **hypogammaglobulinemia** due to immunologically dysfunctional B cells, leading to increased susceptibility to infections. Up to 10% of patients present with hypogammaglobulinemia-related frequent infections.[2][6]

Would you like to explore the current staging systems and treatment indications for CLL, including when to initiate therapy versus observation?

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Question 591

A 24-year-old married woman presents to the emergency department with severe abdominal pain since last night. She also complains of scant vaginal bleeding. She says she visited a physician last year who said she had a pelvic infection, but she was never treated because of insurance issues. She also says her period has been delayed this month. She is afebrile. The pulse is 124/min and the blood pressure is 100/70 mm Hg. On examination, her abdomen is distended and tender. A pregnancy test was positive. A complication of infection with which of the following organisms most likely led to this patient's condition?

Answer Choices:

(A) Candida albicans
(B) Neisseria gonorrhoeae
(C) Chlamydia trachomatis
(D) Haemophilus influenzae

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/7176676a-14b7-46d6-9f44-7c5cf2c244ad

OpenEvidence Explanation

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The answer is **C. Chlamydia trachomatis**.

This patient presents with a classic **ruptured ectopic pregnancy**: delayed menstrual period, positive pregnancy test, severe abdominal pain, vaginal bleeding, abdominal distension, tachycardia, and hypotension — all consistent with hemoperitoneum from tubal rupture. The key historical detail is her **untreated pelvic infection**, which most likely caused fallopian tube scarring (salpingitis) leading to ectopic implantation.

Chlamydia trachomatis is the most common cause of pelvic inflammatory disease (PID) and the organism most strongly linked to tubal factor pathology and ectopic pregnancy.[1][2][3] While *Neisseria gonorrhoeae* also causes PID, chlamydial infection is more frequently implicated for several reasons:

- **Chlamydia is the most common sexually transmitted pathogen** identified in PID, found in approximately 23% of women with the disease in clinical trials.[3]
- Chlamydial infections are characteristically **asymptomatic and insidious**, making them more likely to go undiagnosed and untreated — exactly as in this patient's scenario.[3][4]
- Approximately **10% of untreated chlamydial infections** progress to clinically diagnosed PID, and nearly **10% of first pregnancies after PID are ectopic**.[3]
- Women with tubal factor infertility (from fallopian tube damage) are significantly more likely to be **seropositive for C. trachomatis** than fertile women, even without a known history of PID.[3]

The other options are less likely: *Candida albicans* causes vulvovaginal candidiasis but does not cause PID or tubal scarring. *Haemophilus influenzae* is primarily a respiratory pathogen and not a typical cause of PID. *Neisseria gonorrhoeae* does cause PID but tends to produce more symptomatic, acute infections and is less commonly the underlying etiology of subclinical tubal damage leading to ectopic pregnancy.

Would you like to explore the current evidence-based management of ruptured ectopic pregnancy, including surgical versus medical approaches?

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Question 593

A 42-year-old male presents to his primary care physician complaining of fatigue. He has not been to the doctor since he was 22 years of age. He reports that over the past three months, he has felt tired and weak despite no changes in diet or exercise. He is otherwise healthy and takes no medications. Family history is notable for colorectal cancer in his father and paternal uncle, ovarian cancer in his paternal grandmother, and pancreatic cancer in his paternal uncle. Physical examination is notable for conjunctival pallor. A complete blood count reveals a hemoglobin of 9.1 g/dL and hematocrit of 31%. A stool sample is hemoccult positive and a colonoscopy reveals a fungating hemorrhagic mass in the ascending colon. Which of the following processes is most likely impaired in this patient?

Answer Choices:

(A) Base excision repair
(B) Nucleotide excision repair
(C) Mismatch repair
(D) Non-homologous end joining

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/79b0d4e3-6372-40f1-9f58-3c3e66a631b1

OpenEvidence Explanation

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The answer is **C. Mismatch repair**.

This clinical presentation — a young man (age 42) with colon cancer and a striking family history of **colorectal cancer** (father, paternal uncle), **ovarian cancer** (paternal grandmother), and **pancreatic cancer** (paternal uncle) on the same side of the family — is classic for **Lynch syndrome** (hereditary nonpolyposis colorectal cancer, HNPCC). Lynch syndrome is caused by germline mutations in **DNA mismatch repair (MMR) genes**, most commonly MLH1 and MSH2, with MSH6 and PMS2 less frequently involved.[1][2][3]

Why mismatch repair?

MMR genes encode proteins that function as heterodimers (MLH1/PMS2 and MSH2/MSH6) to recognize and correct base-base mismatches and insertion/deletion loops that arise during DNA replication.[2][4] Loss of MMR function leads to microsatellite instability (MSI), a hallmark of Lynch syndrome tumors, and dramatically accelerates cancer development.[2][5] Germline defects in MMR genes confer a lifetime colorectal cancer risk of approximately 46%–80%, with cancers presenting at an average age of 44 years.[2][6] Lynch syndrome also increases risk for ovarian cancer (4%–38%) and pancreatic cancer — both present in this patient's family.[6]

The following figure illustrates the normal MMR process, showing how MutSα/MutSβ complexes recognize mismatches and recruit MutLα for repair:

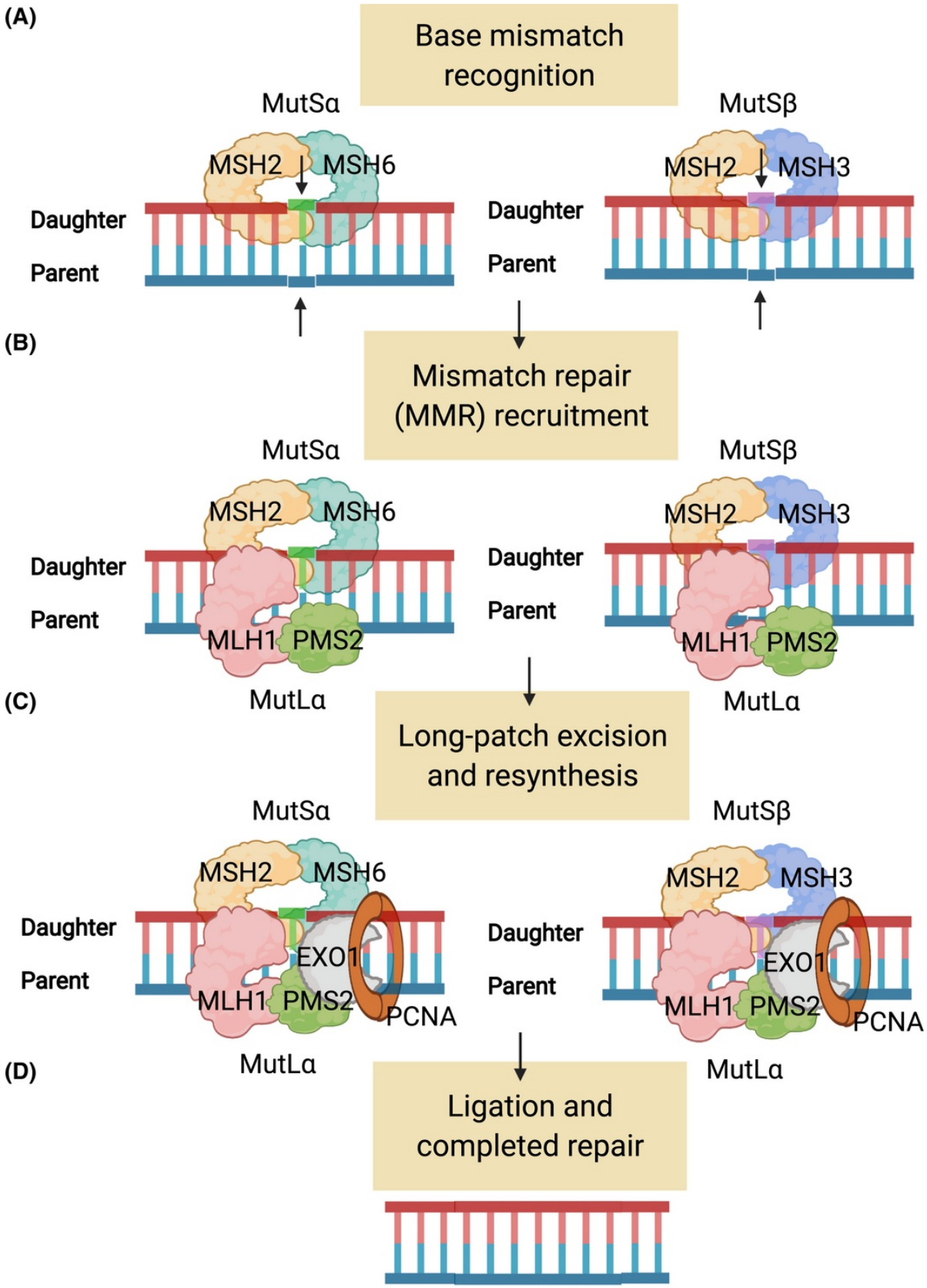


Figure 1. The DNA mismatch repair (MMR) system. A, The MutS MMR proteins recognise DNA errors (mispairs and loop-outs) made during S phase. They are only stable as heterodimers (MSH2 + MSH6 [MutSα] or MSH2 + MSH3 [MutSβ]). B, MutL (MutLα here) heterodimers bind to the MutS proteins and act as recruitment proteins for the DNA repair process. C, Enzymes such as exonuclease 1 (EXO1), DNA polymerase and proliferating cell nuclear antigen (PCNA) serving as a sliding clamp, perform

long patch excision to remove the error, and then enable resynthesis and ligation. D, The daughter strand is resynthesized, which results in correction of the DNA error

Why not the other options?

- **Base excision repair (A)** corrects small, non-helix-distorting base lesions (e.g., oxidative damage, deamination). Defects are associated with MUTYH-associated polyposis, not this family history pattern.
- **Nucleotide excision repair (B)** repairs bulky, helix-distorting lesions (e.g., UV-induced pyrimidine dimers). Defects cause xeroderma pigmentosum, not hereditary colorectal cancer syndromes.
- **Non-homologous end joining (D)** repairs double-strand DNA breaks. Defects are not associated with hereditary colorectal cancer syndromes.

Would you like to explore the recommended surveillance and management strategies for patients with confirmed Lynch syndrome?

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Question 595

A 19-year-old female college soccer player presents to a sports medicine clinic with right knee pain. One day prior she twisted her right knee and felt a “pop” while chasing after a ball. She has since felt severe throbbing knee pain and noticed a rapid increase in swelling around her knee. She is able to bear weight but feels “unstable” on her right leg. On exam, anterior drawer and Lachman’s tests are positive. The physician informs her that she has likely injured an important structure in her knee. What is the function of the structure that she has most likely injured?

Answer Choices:

(A) Prevent excess posterior translation of the tibia relative to the femur
(B) Prevent excess anterior translation of the tibia relative to the femur
(C) Resist excess valgus force on the knee
(D) Provide a cushion between the lateral tibial and femoral condyles

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/2468c89a-b034-4322-a080-c3e43f240b61

OpenEvidence Explanation

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The answer is **B. Prevent excess anterior translation of the tibia relative to the femur**.

The clinical presentation — a twisting mechanism with an audible "pop," rapid knee effusion (hemarthrosis), instability, and positive **anterior drawer** and **Lachman's tests** — is classic for an **anterior cruciate ligament (ACL) tear**. The primary function of the ACL is to **prevent excess anterior translation of the tibia relative to the femur**. Both the anterior drawer test and Lachman's test specifically assess this function by applying an anteriorly directed force on the tibia; increased laxity compared to the contralateral knee indicates ACL insufficiency.

Why the other options are incorrect:

- **A (posterior tibial translation)** — This is the function of the **posterior cruciate ligament (PCL)**, assessed by the posterior drawer test.
- **C (resist valgus force)** — This is the function of the **medial collateral ligament (MCL)**, assessed by valgus stress testing.
- **D (cushion between lateral condyles)** — This describes the **lateral meniscus**, not a ligament.

Would you like to explore the evidence on ACL reconstruction timing and outcomes in young athletes returning to sport?

Question 597

A study is conducted to determine the most effective ways to prevent transmission of various infective agents. One of the agents studied is a picornavirus that preferentially infects hepatocytes. The investigator determines that inactivating this virus can prevent its spread. Which of the following disinfectants is most likely to inactivate this virus?

Answer Choices:

(A) Chlorhexidine
(B) Sodium hypochlorite
(C) Sulfuric acid
(D) Ethyl alcohol

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/1244dc43-6f3e-4853-9f64-f6d716b02ecf

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OpenEvidence Explanation

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B. Sodium hypochlorite is the best answer. The hepatotropic picornavirus is **hepatitis A virus (HAV)**, a **nonenveloped** virus; nonenveloped viruses are relatively resistant to many common disinfectants, and **bleach (sodium hypochlorite)** is a well-established agent that inactivates HAV on surfaces.[1][2]

ACIP specifically notes that a **1:100 dilution of sodium hypochlorite** in tap water inactivates HAV.[3]

Why the other choices are less likely:

- **Chlorhexidine**: limited activity against many nonenveloped viruses; not a standard agent for HAV inactivation.
- **Sulfuric acid**: not a routine disinfectant used for environmental viral decontamination.
- **Ethyl alcohol**: alcohols are generally less reliable against nonenveloped viruses; although some HAV studies show efficacy under specific concentrations/contact times, bleach is the classic and most consistently recommended answer for HAV.[4][5]

High-yield test logic: **HAV = picornavirus + hepatocytes + fecal-oral + nonenveloped → resistant to alcohol/lipid solvents, susceptible to sodium hypochlorite**.[1][2][3]

Would you like to explore a rapid high-yield table of which disinfectants work best for enveloped vs nonenveloped viruses for board-style questions?

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Question 598

A 34-year-old woman comes to the physician requesting prenatal care. For the past 2 months, she has had increasing breast tenderness, nausea, 3-kg (6.6-lb) weight gain, and urinary frequency. She is not sure about the date of her last menstrual period. She has been trying to conceive with her husband since she stopped taking oral contraceptives 6 months ago; she was happy to tell him last week that she is pregnant. Her temperature is 37.2°C (99°F), pulse is 100/min, and blood pressure is 110/60 mm Hg. Physical examination shows mild, nontender abdominal enlargement. The cervical os is closed. Urine β-hCG is negative. Transvaginal ultrasonography shows no abnormalities. Which of the following is the most likely diagnosis?

Answer Choices:

(A) Delusion of pregnancy
(B) Pseudocyesis
(C) Pregnancy
(D) Incomplete abortion

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/b28230bf-6ca7-4bb2-a2dd-c7447235ff8b

OpenEvidence Explanation

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The most likely diagnosis is **B. Pseudocyesis**.

Pseudocyesis (false pregnancy) is defined as the belief of being pregnant accompanied by **objective physical signs and symptoms of pregnancy** — such as breast tenderness, nausea, weight gain, abdominal enlargement, and urinary frequency — in the absence of a confirmed pregnancy.[1][2] This patient's presentation is classic: she has been actively trying to conceive (a strong psychological motivator), exhibits multiple physical signs mimicking pregnancy, yet has a **negative urine β-hCG** and **normal transvaginal ultrasound**, definitively ruling out actual pregnancy.

Why the other options are incorrect:

- **A. Delusion of pregnancy** — This is a fixed false belief of being pregnant **without** accompanying physical signs or symptoms. It is typically associated with psychotic disorders (e.g., schizophrenia). Pseudocyesis, by contrast, features actual somatic manifestations (abdominal distension, breast changes, amenorrhea), which this patient demonstrates.[1][3]

- **C. Pregnancy** — Ruled out by the negative β-hCG and normal transvaginal ultrasound. Even very early pregnancies produce detectable hCG, and the 2-month duration of symptoms makes a false-negative β-hCG essentially impossible.[4][5]

- **D. Incomplete abortion** — This requires a prior confirmed pregnancy with retained products of conception, typically presenting with vaginal bleeding and an open cervical os. This patient has a **closed cervical os**, no bleeding, and a negative β-hCG.[6]

The neuroendocrine basis of pseudocyesis involves increased sympathetic nervous system activity, catecholaminergic pathway dysfunction, and hormonal changes (including elevated LH, estradiol, and sometimes prolactin) that can produce genuine physical symptoms mimicking pregnancy.[2][7] The condition is strongly associated with an intense desire to conceive, as seen in this patient who recently stopped contraception to try for pregnancy.[1]

Would you like to discuss the management approach for pseudocyesis, including how to sensitively communicate the diagnosis?

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Question 599

A 60-year-old man comes to the physician for a routine physical examination. He lives in a group home and takes no medications. During the appointment, he frequently repeats the same information and needs to be reminded why he is at the doctor's office. He says that he is a famous poet and recently had a poem published in a national magazine. His vital signs are within normal limits. He has a constricted affect. Neurological examination shows no focal deficits. On mental status examination, he has no long-term memory deficits and is able to count in serial sevens without error. An MRI of the brain shows atrophy of the anterior thalami and small mamillary bodies. Which of the following is the most likely predisposing factor for this patient's condition?

Answer Choices:

(A) Consumption of undercooked meat
(B) Chronic hypertension
(C) Alcohol use disorder
(D) Spirochete infection

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/d6a54f3f-15dd-4654-9d75-69377be3eca1

OpenEvidence Explanation

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The answer is **C. Alcohol use disorder**.

This clinical presentation is classic for **Korsakoff syndrome**, the chronic sequela of Wernicke encephalopathy caused by thiamine (vitamin B1) deficiency. The key features pointing to this diagnosis include:

- **Short-term memory impairment** (repeating information, needing reminders) with **preserved long-term memory** and intact arithmetic ability (serial sevens) — the hallmark disproportionate amnesia of Korsakoff syndrome[1][2]
- **Confabulation** — claiming to be a famous poet with a published poem, which represents the characteristic "false or erroneous memories arising involuntarily in the context of neurological amnesia"[1]
- **Constricted affect** — emotional blunting/apathy is a recognized feature[2]
- **MRI showing atrophy of the anterior thalami and small mammillary bodies** — the signature neuroanatomical findings of Korsakoff syndrome, reflecting damage to the diencephalic-hippocampal (Papez) circuit[3][4][5]

Alcohol use disorder is by far the most common predisposing factor for Wernicke-Korsakoff syndrome. Chronic alcohol use leads to thiamine deficiency through multiple mechanisms: poor nutritional intake, impaired gastrointestinal absorption, increased renal losses, reduced hepatic storage, and inhibition of thiamine-dependent enzymes.[6] Approximately 80% of patients with untreated Wernicke encephalopathy progress to Korsakoff syndrome.[7] The patient's residence in a group home is consistent with the level of functional impairment and need for supervised care typical of chronic Korsakoff syndrome.[1]

The other options are incorrect: undercooked meat (toxoplasmosis/tapeworm) and spirochete infection (neurosyphilis) would present with different neuroimaging and clinical findings, and chronic hypertension causes vascular dementia with a different pattern of cognitive deficits and brain changes.

Would you like to explore the evidence on thiamine replacement dosing strategies for prevention and treatment of Wernicke-Korsakoff syndrome?

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Question 604

A previously healthy 3-year-old boy is brought to the physician by his parents because of fever and a rash for 6 days. His temperature is 38.9°C (102°F). Examination shows right-sided anterior cervical lymphadenopathy, bilateral conjunctival injection, erythema of the tongue and lips, and a maculopapular rash involving the hands, feet, perineum, and trunk. Which of the following is the most common complication of this patient's condition?

Answer Choices:

(A) Coronary artery aneurysm
(B) Rapidly progressive glomerulonephritis
(C) Hearing loss
(D) Retinopathy

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/da411ab2-7dea-4717-84da-0c29af99c52b

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OpenEvidence Explanation

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The answer is **A. Coronary artery aneurysm**.

This presentation — a 3-year-old with ≥5 days of fever, cervical lymphadenopathy, bilateral conjunctival injection, oral mucosal changes (erythema of tongue and lips), and a polymorphous rash involving the hands, feet, perineum, and trunk — is classic for **Kawasaki disease** (KD). The most common and most serious complication of KD is **coronary artery aneurysm**.

Approximately **20–25% of untreated children** with KD develop coronary artery aneurysms, which can lead to thrombotic occlusion, myocardial infarction, and sudden death.[1][2][3] With timely treatment using high-dose **intravenous immunoglobulin (IVIG)** within 10 days of fever onset, this risk is reduced to less than 5%.[4][5] KD has replaced rheumatic fever as the **leading cause of acquired heart disease in children** in the developed world.[3]

The other answer choices are not associated with KD:

- **Rapidly progressive glomerulonephritis** is associated with conditions such as post-streptococcal glomerulonephritis, ANCA-associated vasculitis, or anti-GBM disease.
- **Hearing loss** is a complication of conditions such as meningitis or congenital infections.
- **Retinopathy** is not a recognized complication of KD.

Would you like to explore the risk stratification models used to predict IVIG resistance and coronary artery aneurysm development in Kawasaki disease?

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Question 606

A 75-year-old with hypertension and atrial fibrillation comes to the emergency department because of a 2-hour history of severe abdominal pain and nausea. He has smoked 1 pack of cigarettes daily for the past 45 years. The patient undergoes emergency laparotomy and is found to have dusky discoloration of the hepatic colonic flexure and an adjacent segment of the transverse colon. The most likely cause of his condition is occlusion of a branch of which of the following arteries?

Answer Choices:

(A) Median sacral artery
(B) Inferior mesenteric artery
(C) Celiac artery
(D) Superior mesenteric artery

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/73106949-ce55-4496-883c-dd9f229fb8f4

OpenEvidence Explanation

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The answer is **D. Superior mesenteric artery**.

The hepatic flexure and adjacent transverse colon receive their blood supply from branches of the **superior mesenteric artery (SMA)**, specifically the right colic artery and the middle colic artery.[1][2][3] The SMA supplies the midgut derivatives, which include the small intestine, ascending colon, hepatic flexure, and transverse colon.[3]

This clinical scenario — a 75-year-old with atrial fibrillation, hypertension, and a heavy smoking history presenting with acute severe abdominal pain and intraoperative findings of dusky (ischemic) bowel at the hepatic flexure and transverse colon — is classic for **acute mesenteric ischemia** due to arterial embolism or thrombosis of the SMA. Atrial fibrillation is a major risk factor for arterial thromboembolism, and the SMA is the most common site of mesenteric embolic occlusion, accounting for 40–50% of acute mesenteric ischemia cases.[4]

The following figure illustrates the arterial blood supply of the colon, showing the SMA branches (middle colic, right colic, and ileocolic arteries) supplying the right colon and transverse colon:

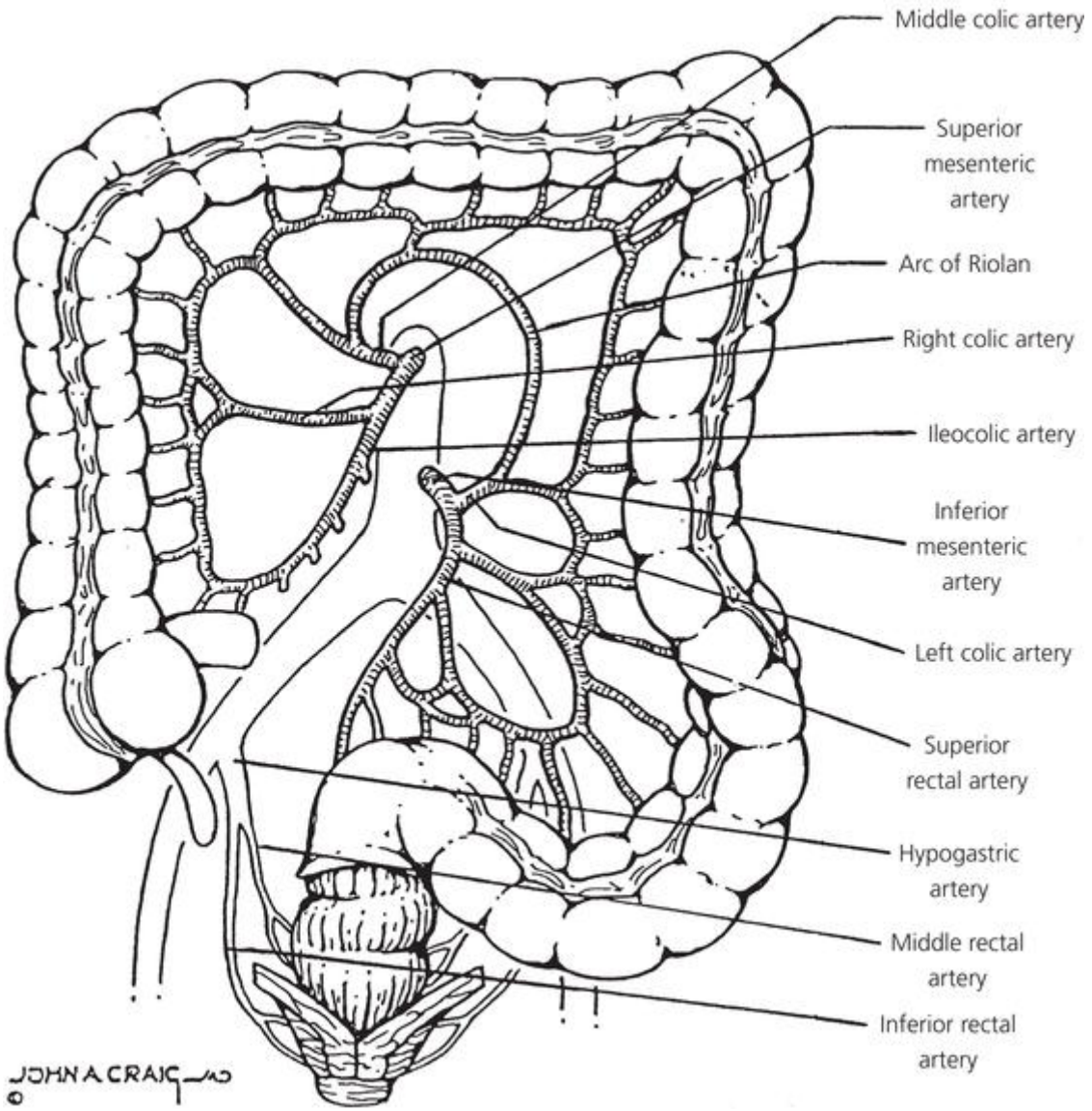


Figure 29. Arterial blood supply of the colon and rectum. Source: Kodner et al. 1993 [31]. Reproduced with permission of McGraw-Hill.

Why the other options are incorrect:

- **A. Median sacral artery** — supplies the sacrum and coccyx, with minor contribution to the anal canal; not relevant to the hepatic flexure[1]
- **B. Inferior mesenteric artery** — supplies the descending colon, sigmoid, and upper rectum (hindgut); occlusion would affect the left colon, not the hepatic flexure[3][6]
- **C. Celiac artery** — supplies foregut structures (stomach, liver, spleen, duodenum, pancreas); does not supply the colon[3]

Would you like to explore the distinction between embolic and thrombotic SMA occlusion in terms of the pattern and extent of bowel ischemia?

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Question 608

A 10-year-old boy is brought to the emergency room by his grandparents. He is in a wheelchair with soft restraints because he has been violent and had been trying to hurt himself that day. The child's parents died in a car accident 1 month ago. His grandparents also brought the medications he stopped taking after his parents' death, including multivitamins, allopurinol, and diazepam. They say that their grandson has been using these medications for many years; however, they are unable to provide any medical history and claim that their grandson has been behaving strangely, exhibiting facial grimacing, irregular involuntary contractions, and writhing movements for the past few days. They also note that he has had no teeth since the time they first met him at the age of 2. An intramuscular medication is administered to calm the boy down prior to drawing blood from him for laboratory tests. Which of the following biochemical pathway abnormalities is the most likely cause of this patient's condition?

Answer Choices:

(A) Hypoxanthine-guanine phosphoribosyl transferase of the pyrimidine metabolism pathway
(B) Aminolevulinic acid synthetase of the heme metabolism pathway
(C) Hypoxanthine-guanine phosphoribosyl transferase of the purine metabolism pathway
(D) Thymidylate synthetase of the pyrimidine metabolism pathway

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/ce4c67c6-e195-4b0b-ba90-057365b59d5f

OpenEvidence Explanation

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The correct answer is **C. Hypoxanthine-guanine phosphoribosyl transferase of the purine metabolism pathway**.

This clinical presentation is classic for **Lesch-Nyhan syndrome (LNS)**, an X-linked recessive disorder caused by deficiency of the enzyme **hypoxanthine-guanine phosphoribosyltransferase (HPRT)**, which is a key enzyme in the **purine salvage pathway**.[1][2] The enzyme catalyzes the recycling of hypoxanthine to inosine monophosphate (IMP) and guanine to guanine monophosphate (GMP), preventing excessive degradation of purines to uric acid.[2][3]

Key clinical features in this vignette pointing to LNS:

- **Self-injurious behavior** — the hallmark of LNS, including biting of fingers, hands, lips, and cheeks. This explains why the child has had no teeth since age 2; tooth extraction is the most common intervention to prevent oral self-mutilation (71% of cases in one study).[2][4]
- **Involuntary movements** — facial grimacing, irregular involuntary contractions, and writhing movements correspond to the **dystonia, chorea, and choreoathetosis** characteristic of LNS.[1][2]
- **Allopurinol use** — a xanthine oxidase inhibitor used to manage the **hyperuricemia** caused by excessive purine degradation to uric acid in HPRT deficiency.[5][6]
- **Diazepam use** — a benzodiazepine likely prescribed for spasticity/dystonia management.
- **Wheelchair-bound male child** — consistent with the severe motor disability seen in LNS, where affected boys cannot walk and require wheelchair assistance.[1][2]

The following figure illustrates the central role of HPRT in purine metabolism and why its deficiency leads to uric acid overproduction:

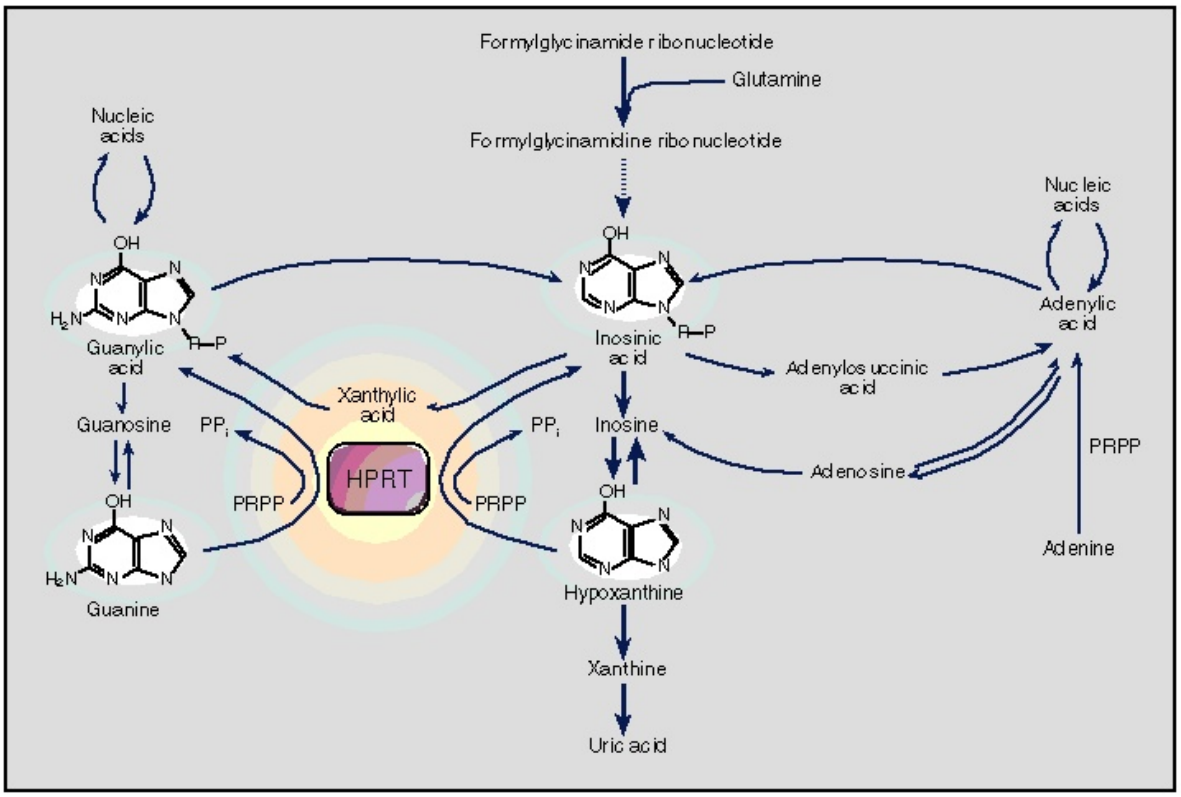


Figure 1. Reactions Catalyzed by Hypoxanthine–Guanine Phosphoribosyltransferase (HPRT).

Used under license from The New England Journal of Medicine.

Why the other options are incorrect:

- **A** — HPRT is part of the purine (not pyrimidine) salvage pathway, making this answer biochemically incorrect despite naming the correct enzyme.
- **B** — Aminolevulinic acid synthetase deficiency relates to porphyria/heme metabolism, not this presentation.
- **D** — Thymidylate synthetase is involved in pyrimidine synthesis and is unrelated to this clinical syndrome.

Would you like to explore the current management strategies for the neurobehavioral manifestations of Lesch-Nyhan syndrome, including emerging therapies beyond allopurinol?

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Question 609

A 34-year-old woman with poorly controlled Crohn disease comes to the physician because of a 2-week history of hair loss and a rash on her face. She has also noticed that food has recently tasted bland to her. She had to undergo segmental small bowel resection several times because of intestinal obstruction and fistula formation. Examination shows several bullous, erythematous perioral plaques. There are two well-circumscribed circular patches of hair loss on the scalp. A deficiency of which of the following is the most likely cause of this patient's condition?

Answer Choices:

(A) Niacin
(B) Cobalamin
(C) Iron
(D) Zinc

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/dcbf06a5-4cb6-49f3-af16-5c636b3f4641

OpenEvidence Explanation

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The answer is **D. Zinc**.

This patient's presentation — **perioral bullous erythematous plaques, alopecia, and dysgeusia (taste disturbance)** — is the classic triad of **zinc deficiency**, a condition known as **acrodermatitis enteropathica** when inherited, or acquired zinc deficiency when secondary to malabsorption. The clinical triad consists of **dermatitis** (characteristically periorificial and acral), **alopecia**, and **diarrhea**, though taste abnormalities are also a well-recognized feature.[1][2][3]

Why zinc deficiency fits this case:

- Poorly controlled Crohn disease with multiple segmental small bowel resections places this patient at high risk for zinc malabsorption. Zinc deficiency occurs in 40–50% of patients with IBD worldwide, driven by inadequate intake, impaired absorption, and chronic diarrhea.[4]
- The **bullous, erythematous perioral plaques** are characteristic of the dermatitis seen in zinc deficiency, which classically affects periorificial (perioral, perinasal, perianal) and acral areas.[1][2][5]
- **Alopecia** and **taste abnormalities** (dysgeusia/hypogeusia) are well-established manifestations of moderate-to-severe zinc deficiency.[3][6]

Why the other options are less likely:

- **Niacin (A):** Deficiency causes pellagra (dermatitis, diarrhea, dementia), but the dermatitis is photosensitive and affects sun-exposed areas (Casal necklace), not periorificial regions.
- **Cobalamin (B):** Deficiency causes megaloblastic anemia and neurologic symptoms (subacute combined degeneration), not the described dermatologic findings.[7][8]
- **Iron (C):** Deficiency causes anemia, angular cheilitis, koilonychia, and glossitis — not bullous periorificial plaques or patchy alopecia.[9]

Would you like to explore the recommended zinc supplementation strategies and monitoring parameters in patients with Crohn disease and short bowel syndrome?

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Question 610

A 23-year-old woman, gravida 2, para 1, at 20 weeks of gestation comes to the physician for a routine prenatal exam. Her last pregnancy was unremarkable and she gave birth to a healthy rhesus (RhD) positive girl. Her past medical history is notable for a blood transfusion after a car accident with a complex femur fracture about 3 years ago. Her temperature is 37.2°C (99°F), pulse is 92/min, and blood pressure is 138/82 mm Hg. Examination shows that the uterus is at the umbilicus. Ultrasound examination reveals normal fetal heart rate, movement, and anatomy. Routine prenatal labs show the following:
Blood type A Rh-
Leukocyte count 11,000/mm3
Hemoglobin 12.5 g/dL
Platelet count 345,000/mm3
Serum
Anti-D antibody screen Negative
Rubella IgM Negative
Rubella IgG Negative
Varicella IgM Negative
Varicella IgG Positive
STD panel Negative
Urine
Protein Trace
Culture No growth
Cervical cytology Normal
Which of the following is the best next step in management of this patient?

Answer Choices:

(A) Repeat antibody screening at 28 weeks. Administer anti-D immunoglobulin at 28 weeks and after delivery if the newborn is Rh(D) positive.
(B) Repeat antibody screening at 28 weeks and administer anti-D immunoglobulin at 28 weeks. No further management is needed.
(C) No further screening is needed. Administer anti-D immunoglobulin shortly after delivery

(D) No further management is needed

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/88b81e0f-814c-4716-b063-daa0ad62f8f2

OpenEvidence Explanation

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The correct answer is **A. Repeat antibody screening at 28 weeks. Administer anti-D immunoglobulin at 28 weeks and after delivery if the newborn is Rh(D) positive.**

Practice Guideline

The **American College of Obstetricians and Gynecologists (ACOG)** recommends the following for unsensitized Rh D-negative pregnant women:[1]

- **Prophylactic anti-D immune globulin (300 mcg) should be administered at 28 weeks of gestation** to all unsensitized Rh D-negative women (Level A recommendation).
- **Following birth, if the infant is confirmed to be Rh D positive**, all Rh D-negative women who are not known to be sensitized should receive anti-D immune globulin **within 72 hours of delivery** (Level A recommendation).
- **Repeat antibody screening at 28 weeks** before administration of anti-D immune globulin is advised. The USPSTF recommends repeated Rh D

antibody testing for all unsensitized Rh D-negative women at 24–28 weeks of gestation, unless the biological father is known to be Rh D negative. The primary rationale is to identify women who have become alloimmunized before 28 weeks in order to manage their pregnancies properly.[1]

The current standard practice of administering a single antenatal dose at 28 weeks followed by a second dose after birth (when newborn Rh D typing confirms the infant is Rh positive) is associated with less than a **0.2% rate of Rh alloimmunization**, compared to 2% without antenatal prophylaxis.[1]

This patient is an **Rh D-negative, unsensitized** (anti-D antibody screen negative) woman at 20 weeks of gestation. Despite her history of a prior Rh-positive child and a blood transfusion, her current antibody screen is negative, confirming she has not yet been sensitized. The standard management is:

1. **Repeat antibody screening at 28 weeks** to confirm she remains unsensitized before administering prophylaxis.[1][2]
2. **Administer anti-D immunoglobulin at 28 weeks** to prevent third-trimester alloimmunization from occult fetomaternal hemorrhage.[1][3]
3. **Administer anti-D immunoglobulin postpartum** (within 72 hours) if the newborn is confirmed Rh D positive.[1][4]

Why the other options are incorrect:

- **Option B** omits the critical postpartum dose if the newborn is Rh D positive, which would leave the mother at risk for sensitization from delivery-related fetomaternal hemorrhage.
- **Option C** omits the antenatal dose at 28 weeks, which reduces third-trimester alloimmunization from 2% to <0.2%.[1]
- **Option D** is incorrect because this Rh D-negative unsensitized patient requires both antenatal and postpartum prophylaxis.

The history of a prior blood transfusion is a notable risk factor for prior Rh D exposure, but since the antibody screen is currently negative, standard prophylaxis protocols apply.[3]

Would you like to explore the management approach when an Rh D-negative woman is found to have a positive antibody screen (i.e., already sensitized) during pregnancy?

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Question 611

A 52-year-old man presents to the physician because of ongoing shortness of breath, which is more prominent when he lies down. Occasionally, he experiences palpitations, especially during strenuous activities. In addition to this, he has been experiencing difficulty in digestion and often experiences regurgitation and dysphagia. He reports that he emigrated from Mexico 20 years ago and visits his hometown twice a year. The vital signs include: blood pressure 120/75 mm Hg, respiratory rate 19/min, and pulse 100/min. The physical examination shows jugular vein distention along with pitting edema in the ankles. Bilateral basilar crackles and an S3 gallop are heard on auscultation of the chest. A chest X-ray is taken. An electrocardiogram (ECG) shows no significant findings. What is the most likely explanation for this patient's physical and diagnostic findings?

Answer Choices:

(A) Alcohol abuse
(B) Hypertensive changes
(C) Parasitic infection
(D) Bacterial infection

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/a30ec5db-ce7d-44fc-9330-95185e4f689a

OpenEvidence Explanation

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The correct answer is **C. Parasitic infection** — specifically, chronic Chagas disease caused by **Trypanosoma cruzi**.

This patient's presentation is classic for **chronic Chagas cardiomyopathy with gastrointestinal involvement**. The key features that point to this diagnosis include:

Cardiac findings: Orthopnea, exertional palpitations, JVD, bilateral ankle edema, basilar crackles, S3 gallop, and tachycardia all indicate **dilated cardiomyopathy with decompensated heart failure**. Chagas cardiomyopathy is the most severe manifestation of chronic T. cruzi infection, developing in approximately one-third of infected individuals at a progression rate of 1–2% per year.[1]

Gastrointestinal findings: Dysphagia and regurgitation are hallmarks of **Chagas-related esophageal disease (megaesophagus)**, which results from destruction of the myenteric plexus by T. cruzi, producing a secondary achalasia with impaired peristalsis and failure of lower esophageal sphincter relaxation.[2][3] The combined cardiac and GI involvement is a well-recognized pattern in chronic Chagas disease.[4][5]

Epidemiologic link: Mexico is endemic for Chagas disease, and the patient emigrated 20 years ago with ongoing travel — ample time for chronic infection to progress from the indeterminate phase to symptomatic cardiomyopathy and megaesophagus.[6] Among Latin America–born patients with newly diagnosed nonischemic cardiomyopathy in Los Angeles, **19% had Chagas disease**.[6]

Why not the other options:

- **A. Alcohol abuse** — Can cause dilated cardiomyopathy but would not explain the esophageal dysmotility (dysphagia and regurgitation) or the epidemiologic context.
- **B. Hypertensive changes** — Blood pressure is normal (120/75), making hypertensive cardiomyopathy unlikely. Hypertension also does not cause esophageal symptoms.
- **D. Bacterial infection** — Rheumatic heart disease (from streptococcal infection) causes valvular disease, not dilated cardiomyopathy with

esophageal involvement. Infective endocarditis does not fit this chronic presentation.

The diagnosis of chronic Chagas disease is confirmed by **serology (IgG detection)** in the chronic phase, as parasitemia is too low for direct microscopy.[4][7] Cardiac evaluation should include echocardiography and Holter monitoring, and GI assessment should include barium swallow and esophageal manometry.[4][8]

Would you like to explore the management of Chagas cardiomyopathy or the specific antitrypanosomal treatment options in more detail?

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Question 612

A 33-year-old woman presents to her primary care physician with bilateral joint pain. She says that the pain has been slowly worsening over the past 3 days. Otherwise, she complains of fatigue, a subjective fever, and a sunburn on her face which she attributes to gardening. The patient is an immigrant from Spain and works as an office assistant. She is not aware of any chronic medical conditions and takes a multivitamin daily. Her temperature is 98.7°F (37.1°C), blood pressure is 125/64 mmHg, pulse is 80/min, respirations are 13/min, and oxygen saturation is 98% on room air. Physical exam reveals bilateral redness over the maxillary prominences. Which of the following is most likely to be seen in this patient?

Answer Choices:

(A) Decreased complement levels
(B) Increased anti-centromere antibodies
(C) Increased anti-cyclic citrullinated peptide antibodies
(D) Increased anti-topoisomerase antibodies

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/44a805e1-4699-4dd4-8bb2-12c82d05dee7

OpenEvidence Explanation

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The answer is **A. Decreased complement levels**.

This clinical vignette describes a young woman with classic features of **systemic lupus erythematosus (SLE)**: bilateral joint pain, fatigue, subjective fever, and bilateral erythema over the malar eminences (malar/butterfly rash) — which the patient misattributes to sunburn from gardening. The demographic (young woman of childbearing age) and the constellation of symptoms are highly characteristic of SLE.

Hypocomplementemia (decreased C3 and/or C4 levels) is a hallmark laboratory finding in SLE. Complement is consumed through immune complex–mediated activation of the classical pathway. Low complement levels are included in the 2019 EULAR/ACR classification criteria for SLE, with low C3 or C4 weighted at 3 points and low C3 and C4 together weighted at 4 points.[1] Complement levels are also routinely used to monitor disease activity, as decreases in C3 and C4 may indicate a disease flare.[2][3]

The other answer choices correspond to different autoimmune conditions:

- **Anti-centromere antibodies** (B) — associated with limited cutaneous systemic sclerosis (CREST syndrome)[2]
- **Anti-cyclic citrullinated peptide (anti-CCP) antibodies** (C) — highly specific for rheumatoid arthritis
- **Anti-topoisomerase (anti-Scl-70) antibodies** (D) — associated with diffuse cutaneous systemic sclerosis[2]

None of these conditions present with the malar rash, fatigue, fever, and polyarthralgia pattern seen here.

Would you like to explore the initial workup and serologic testing strategy for a patient with suspected new-onset SLE?

Relevant images

(CONTENT OMITTED)

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Question 617

A microbiologist has isolated several colonies of Escherichia coli on an agar plate. The microbiologist exposes the agar plate to ciprofloxacin, which destroys all of the bacteria except for one surviving colony. Which of the following is the most likely mechanism of antibiotic resistance in the surviving colony?

Answer Choices:

(A) Replacement of D-alanine
(B) Mutation of DNA gyrase
(C) Inactivation by bacterial transferase
(D) Modification of surface binding proteins

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/9645a05b-aa34-400f-8e04-9b85e80227b2

OpenEvidence Explanation

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The correct answer is **B. Mutation of DNA gyrase**.

Ciprofloxacin is a fluoroquinolone antibiotic that exerts its bactericidal effect by **inhibiting DNA gyrase (topoisomerase II) and topoisomerase IV**, enzymes essential for bacterial DNA replication, transcription, repair, and recombination.

[1][2] The primary mechanism of resistance to ciprofloxacin in *E. coli* is through **point mutations in the quinolone resistance-determining region* (QRDR) *of the* gyrA *gene, which encodes the* A *subunit of* DNA *gyrase.*[3][4][5] These mutations — most commonly at codons Ser-83 and Asp-87 — reduce the binding affinity of ciprofloxacin to the gyrase-DNA complex.[6][7]

Studies consistently demonstrate that **all fluoroquinolone-resistant* E. coli *isolates carry* gyrA *mutations, and these target enzyme alterations contribute the largest fold-changes in ciprofloxacin MIC compared to wild-type strains. Additional mutations in* [5][8]parC *(topoisomerase* IV*) and efflux pump upregulation can further augment resistance, but* gyrA *mutations are the foundational and most prevalent mechanism.*[9][10]

Why the other options are incorrect:

- **A. Replacement of D-alanine** — This mechanism relates to vancomycin resistance (e.g., *vanA/vanB* gene clusters replacing D-Ala-D-Ala with D-Ala-D-Lac), not fluoroquinolone resistance.
- **C. Inactivation by bacterial transferase** — While the aminoglycoside acetyltransferase variant aac(6')-Ib-cr can modify certain fluoroquinolones, this is a plasmid-mediated mechanism that confers only low-level resistance and is far less common than *gyrA* mutations.[3][7]
- **D. Modification of surface binding proteins** — Fluoroquinolones do not act on surface binding proteins (e.g., penicillin-binding proteins); this mechanism is irrelevant to ciprofloxacin resistance.

Would you like to explore how stepwise accumulation of resistance mutations in *gyrA* and *parC* progressively increases fluoroquinolone MICs in clinical isolates?

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Question 618

A 48-year-old man is brought to the emergency department by his son with a fever over the past day. The patient's son adds that his father has been having some behavioral problems, as well, and that he was complaining about bugs crawling over his skin this morning even though there were no insects. Past medical history is unremarkable. No current medications. The patient was an alcoholic for several years but abruptly quit drinking 5 days ago. The patient's temperature is 40.0°C (104.0°F), pulse is 130/min, blood pressure is 146/88 mm Hg, and respiratory rate is 24/min. On physical examination, he is confused, restless, agitated, and lacks orientation to time, place or person. Which of the following the most appropriate initial course of treatment of this patient?

Answer Choices:

(A) Chlorpromazine
(B) Clonidine
(C) Diazepam
(D) Haloperidol

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/8bf707c5-8f61-48bc-b5af-166bddfa72ad

OpenEvidence Explanation

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The correct answer is **C. Diazepam**. This patient presents with classic **delirium tremens** (DT) — the most severe manifestation of alcohol withdrawal syndrome — occurring 5 days after abrupt cessation of alcohol use, with high fever (40°C), tachycardia, hypertension, confusion, agitation, disorientation, and tactile hallucinations (formication). **Benzodiazepines are the first-line treatment** for alcohol withdrawal delirium.

Why diazepam? The American Society of Addiction Medicine (ASAM) and VA/DoD guidelines recommend benzodiazepines as first-line agents for managing alcohol withdrawal delirium, with the goal of achieving light somnolence.[1][2] Diazepam, a long-acting benzodiazepine, has a rapid onset of action when administered intravenously and effectively controls symptoms of DT.[3] Withdrawal is managed with benzodiazepines along with IV fluids and nutritional support, including parenteral thiamine for Wernicke's encephalopathy prophylaxis.[4]

Why not the other options?

- **A. Chlorpromazine** — A first-generation antipsychotic that lowers the seizure threshold, which is particularly dangerous in alcohol withdrawal where seizure risk is already elevated. It is not recommended.
- **B. Clonidine** — An alpha-2 adrenergic agonist. The ASAM guideline explicitly states that alpha-2 adrenergic agonists **should not be used** to treat alcohol withdrawal delirium.[1]
- **D. Haloperidol** — While haloperidol can be used as an adjunct to benzodiazepines for refractory hallucinations and agitation, antipsychotics are **not recommended as monotherapy** for alcohol withdrawal delirium. They do not prevent seizures or address the underlying GABAergic deficit.[1]

Would you like to explore the specific benzodiazepine dosing protocols (symptom-triggered vs. front-loading) used in the ICU management of delirium tremens?

Relevant images

(CONTENT OMITTED)

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Question 619

Eight weeks after starting a new weight-loss medication, a 43-year-old woman with obesity comes to the physician because of greasy diarrhea, excessive belching, and flatulence. She also complains of progressively worsening night-time vision. She has had no fever, chills, or vomiting. Physical examination shows dry, scaly skin on her extremities and face. Which of the following is the most likely mechanism of action of the drug she is taking?

Answer Choices:

(A) Stimulation of monoamine neurotransmitter release
(B) Inhibition of serotonin reuptake
(C) Stimulation of norepinephrine release
(D) Inhibition of lipase

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/b996dbc5-869e-4074-a645-152cb1934946

OpenEvidence Explanation

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The answer is **D. Inhibition of lipase**.

This clinical vignette describes a patient taking **orlistat**, a pancreatic and gastric lipase inhibitor used for weight loss. The mechanism of action — **inhibition of lipase** — prevents the hydrolysis and absorption of dietary triglycerides, leading to approximately 30% of ingested fat being excreted unabsorbed in the stool.

Key clinical clues in this case:

- **Greasy diarrhea (steatorrhea), excessive belching, and flatulence** are the hallmark gastrointestinal side effects of orlistat, resulting directly from undigested fat passing through the GI tract.
- **Progressively worsening night vision** points to **vitamin A deficiency**. Because orlistat impairs fat absorption, it also reduces absorption of fat-soluble vitamins (A, D, E, K). Vitamin A (retinol) is essential for rhodopsin synthesis in rod photoreceptors, and its deficiency causes **nyctalopia** (night blindness).
- **Dry, scaly skin (xerosis)** is another classic manifestation of vitamin A deficiency, as retinol is critical for normal epithelial cell differentiation and maintenance.

Why not the other options?

- **A (Stimulation of monoamine neurotransmitter release)** and **C (Stimulation of norepinephrine release)** describe sympathomimetic agents (e.g., phentermine), which cause anorexia centrally but do not produce steatorrhea or fat-soluble vitamin deficiency.
- **B (Inhibition of serotonin reuptake)** describes agents like fluoxetine or sibutramine (withdrawn), which also act centrally and would not cause fat malabsorption.

Patients on orlistat should receive supplementation with fat-soluble vitamins (A, D, E, K), taken at least 2 hours before or after the drug to ensure adequate absorption.

Would you like to explore the comparative efficacy and side effect profiles of currently approved anti-obesity medications?

Question 624

A 41-year-old man is brought to the emergency department after a suicide attempt. His wife found him on the bathroom floor with an empty bottle of medication next to him. He has a history of major depressive disorder. His only medication is nortriptyline. His pulse is 127/min and blood pressure is 90/61 mm Hg. Examination shows dilated pupils and dry skin. The abdomen is distended and there is dullness on percussion in the suprapubic region. An ECG shows tachycardia and a QRS complex width of 130 ms. In addition to intravenous fluid resuscitation, which of the following is the most appropriate pharmacotherapy?

Answer Choices:

(A) Naloxone
(B) Cyproheptadine
(C) Ammonium chloride
(D) Sodium bicarbonate

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/bce4870a-57af-482b-8b9f-7106d6ebfaf7

OpenEvidence Explanation

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The correct answer is **D. Sodium bicarbonate**.

This patient presents with classic findings of **tricyclic antidepressant (TCA) overdose** from nortriptyline ingestion, including:

- **Anticholinergic toxidrome**: tachycardia, dilated pupils, dry skin, and urinary retention (suprapubic distension/dullness)
- **Cardiovascular toxicity**: hypotension (90/61 mmHg) and **QRS prolongation to 130 ms** (≥100 ms indicates significant sodium channel blockade)

Intravenous sodium bicarbonate is the cornerstone pharmacotherapy for TCA-induced cardiotoxicity. It works through two complementary mechanisms: sodium loading, which overcomes sodium channel blockade and improves cardiac conduction, and serum alkalinization, which increases protein binding of the TCA and reduces free drug availability.[1][2][3] The FDA labeling for nortriptyline specifically states that intravenous sodium bicarbonate should be used to maintain serum pH in the range of 7.45–7.55.[1][4] The AHA guidelines recommend sodium bicarbonate boluses (1–2 mmol/kg) titrated to resolution of hypotension and QRS prolongation, with a target pH of approximately 7.50 and a maximum dose of 6 mmol/kg.[2][5][6]

Why the other options are incorrect:

- **A. Naloxone** – This is the antidote for opioid overdose, not TCA toxicity.
- **B. Cyproheptadine** – This is used for serotonin syndrome, which presents with clonus, hyperreflexia, diaphoresis, and hyperthermia — the opposite of the dry, anticholinergic picture seen here.
- **C. Ammonium chloride** – This would acidify the urine/serum, which would worsen TCA toxicity by increasing free drug levels and exacerbating sodium channel blockade. Acidosis is a known aggravating factor in TCA cardiotoxicity.[7]

Would you like to explore the specific indications for adjunctive lidocaine therapy in TCA overdose refractory to sodium bicarbonate?

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Question 626

A 21-year-old man is brought to the emergency department 30 minutes after being found unconscious in his apartment by his mother. On arrival, he is unable to provide history. The mother reports that there is no history of serious illness in the family. The patient appears drowsy and dehydrated. His temperature is 38.5°C (101.3°F), pulse is 110/min, and blood pressure is 170/100 mm Hg. Examination shows several track marks on his forearms and large contusions over his forehead, legs, and back. There is blood coming from the mouth. The patient is catheterized and tea-colored urine is drained. Urinalysis shows:
Urine
pH 5.8
Specific gravity 1.045
Blood 3+
Glucose 3+
Proteins 1+
Ketones 1+
RBC none
WBC 0-1/hpf
Urine toxicology is positive for opiates and cocaine. Intravenous fluids and sodium nitroprusside drip are started. The patient is most likely to have which of the following?

Answer Choices:

(A) Low serum potassium
(B) Low blood urea nitrogen
(C) Elevated serum calcium
(D) Elevated serum creatine kinase

Correct Answer:

(D)

OpenEvidence Response:

> **(D)** ✓

OpenEvidence Link: https://openevidence.com/ask/de318914-4c11-4152-8639-c7322c1ca86c

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OpenEvidence Explanation

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The answer is **D. Elevated serum creatine kinase**. This patient's presentation is classic for **rhabdomyolysis**, which causes markedly elevated CK levels due to skeletal muscle breakdown.

Key clinical features pointing to rhabdomyolysis:

- **Tea-colored (reddish-brown) urine** — caused by myoglobinuria. Myoglobin appears in the urine as grossly visible discoloration when serum myoglobin levels reach ~100 mg/dL.[1]
- **Urine dipstick positive for blood (3+) with no RBCs on microscopy** — the dipstick detects the pseudoperoxidase activity of myoglobin (and hemoglobin) but cannot distinguish between them. The absence of red cells on microscopy confirms this is myoglobinuria, not hematuria.[1][2]
- **Cocaine and opiate use** with prolonged immobilization (found unconscious) — both direct drug toxicity and compression/ischemia from immobility contribute to muscle necrosis. Cocaine-associated rhabdomyolysis has been well characterized, with mean CK levels of ~12,187 U/L (range 1,756–85,000) in one landmark series.[3]
- **Large contusions**, fever, dehydration, and hypertension are all consistent with this diagnosis.

Why the other options are incorrect:

- **A. Low serum potassium** — Rhabdomyolysis causes **hyperkalemia**, not hypokalemia, due to release of intracellular potassium from damaged myocytes.[4][5]
- **B. Low BUN** — BUN is typically **elevated** in rhabdomyolysis due to both muscle breakdown products and associated acute kidney injury.[6]
- **C. Elevated serum calcium** — Rhabdomyolysis characteristically causes **hypocalcemia** (not hypercalcemia) due to calcium deposition in damaged muscle and hyperphosphatemia.[4][5]

Would you like to explore the management of rhabdomyolysis-associated acute kidney injury, including fluid resuscitation targets and the role of urine alkalinization?

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Question 628

A 42-year-old man comes to the physician to establish care. He recently moved to the area and has not been to a primary care physician for over 5 years. He has no history of serious illness, but has intermittent bilateral knee pain for which he takes 650 mg acetaminophen every other day. He is married with three children and is sexually active with his wife. During the past 10 years, he has unsuccessfully tried to lose weight. He has smoked one half pack of cigarettes daily for 15 years. About 2–3 times per week he has 1–2 glasses of wine with dinner. He is 160 cm (5 ft 3 in) tall and weighs 93 kg (205 lb); BMI is 36.3 kg/m2. Vital signs are within normal limits. On abdominal examination, the liver is palpated 2 to 3 cm below the right costal margin. Laboratory studies show:
Hemoglobin 12.6 g/dL
Platelet count 360,000/mm3
Hemoglobin A1c 6.3%
Serum
Ferritin 194 ng/mL
Total bilirubin 0.7 mg/dL
Alkaline phosphatase 52 U/L
Aspartate aminotransferase 92 U/L
Alanine aminotransferase 144 U/L
Hepatitis B surface antigen Negative
Hepatitis B core IgM antibody Negative
Hepatitis B surface antibody Positive
Hepatitis C antibody Negative
Antinuclear antibody titers 1:20 (N = < 1:60)
Smooth muscle antibody titers Negative
Anti-LKM1 antibody titers Negative
Transabdominal ultrasonography shows a mildly enlarged, diffusely hyperechoic liver. Which of the following is the most likely underlying cause of these liver abnormalities?

> **Answer Choices:**
>
> (A) Autoimmune liver damage
> (B) Congestive hepatopathy

(C) Insulin resistance
(D) Acetaminophen use

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/9633993a-4c6b-48fc-96e5-a8fdb2f2dc2e

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OpenEvidence Explanation

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The correct answer is **C. Insulin resistance**.

This patient's presentation is classic for **metabolic dysfunction-associated steatotic liver disease (MASLD, formerly NAFLD)**, which is driven by underlying insulin resistance. The key findings supporting this diagnosis include:

- **BMI of 36.3 kg/m²** (class II obesity) with a long history of unsuccessful weight loss attempts
- **Elevated transaminases with ALT > AST** (ALT 144, AST 92; AST:ALT ratio ~0.64, which is typical of MASLD where the ratio is characteristically <0.8) [1]
- **Diffusely hyperechoic liver on ultrasound**, consistent with hepatic steatosis (fatty infiltration)[2]
- **Hepatomegaly** (liver palpated 2–3 cm below the costal margin), present in 50–60% of MASLD patients[3]

- **HbA1c of 6.3%**, in the prediabetes range, reflecting insulin resistance

The workup effectively rules out the other answer choices:

- **Autoimmune liver damage (A):** ANA titers are 1:20 (normal <1:60), smooth muscle antibodies and anti-LKM1 antibodies are negative — all inconsistent with autoimmune hepatitis.[1]
- **Congestive hepatopathy (B):** Vital signs are normal, and there is no mention of heart failure symptoms, jugular venous distension, or peripheral edema. Congestive hepatopathy would not produce a hyperechoic liver on ultrasound.
- **Acetaminophen use (D):** The patient takes only 650 mg every other day, well below the hepatotoxic threshold (maximum recommended dose is 4 g/day for short-term use). This dose would not cause chronic liver injury.

MASLD is the most common cause of mildly elevated transaminases, strongly associated with obesity, metabolic syndrome, and type 2 diabetes.[1][4] Insulin resistance drives hepatic steatosis through increased adipose tissue lipolysis, increased hepatic de novo lipogenesis, and decreased fatty acid oxidation.[3] The alcohol intake described (1–2 glasses of wine 2–3 times per week) falls well below the threshold for alcoholic liver disease (>21 standard drinks/week for men).[5]

Would you like to explore the recommended approach to fibrosis risk stratification in this patient, including the FIB-4 index and indications for further evaluation?

Relevant images

(CONTENT OMITTED)

References

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Question 632

A 41-year-old woman presents with shortness of breath that is worse when she lies on her left side. About 10 days ago, she had an episode of unexplained loss of consciousness. Past medical history is negative and family history is irrelevant. Clinical examination shows a diastolic murmur, which is prominent when she lies on her left side. Jugular venous distention is present, and chest examination reveals fine crackles that do not clear with coughing. Chest X-ray shows pulmonary congestion, and 2-dimensional echocardiogram shows a mass in the left atrium attached to the atrial septum. Which of the following is the most likely diagnosis?

Answer Choices:

(A) Rheumatic fever
(B) Innocent murmur
(C) Non-bacterial thrombotic endocarditis
(D) Atrial myxoma

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/b86221ca-13cd-41d8-9712-c50762663fe0

OpenEvidence Explanation

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The most likely diagnosis is **D. Atrial myxoma**.

This presentation is classic for a **left atrial myxoma**, with every feature pointing to this diagnosis:

- **Left atrial mass attached to the atrial septum on echocardiography** — Cardiac myxomas are found in the left atrium in >75% of cases and are predominantly attached with a stalk to the fossa ovalis (>90% of cases).[1][2]
- **Positional dyspnea (trepopnea)** — The extent of valvular obstruction by a myxoma varies with body position, as the pedunculated mass shifts with gravity. Symptoms worsening when lying on the left side are characteristic, as the tumor prolapses into the mitral valve orifice.[3]
- **Diastolic murmur** — Large myxomas obstruct the mitral valve orifice during diastole, mimicking mitral stenosis. Approximately two-thirds of patients present with obstructive symptoms, and 15% demonstrate a low-frequency diastolic murmur ("tumor plop").[2]
- **Syncope** — If the tumor is large enough and has a long stalk, temporary complete obstruction of the mitral valve orifice may occur, resulting in syncope or even sudden death.[3]
- **Pulmonary congestion and JVD** — These reflect the hemodynamic consequences of left atrial outflow obstruction, with elevated left atrial pressures transmitted to the pulmonary vasculature.[3]

The following figure demonstrates the echocardiographic and pathologic features of cardiac myxoma, including prolapse through the mitral valve during diastole.

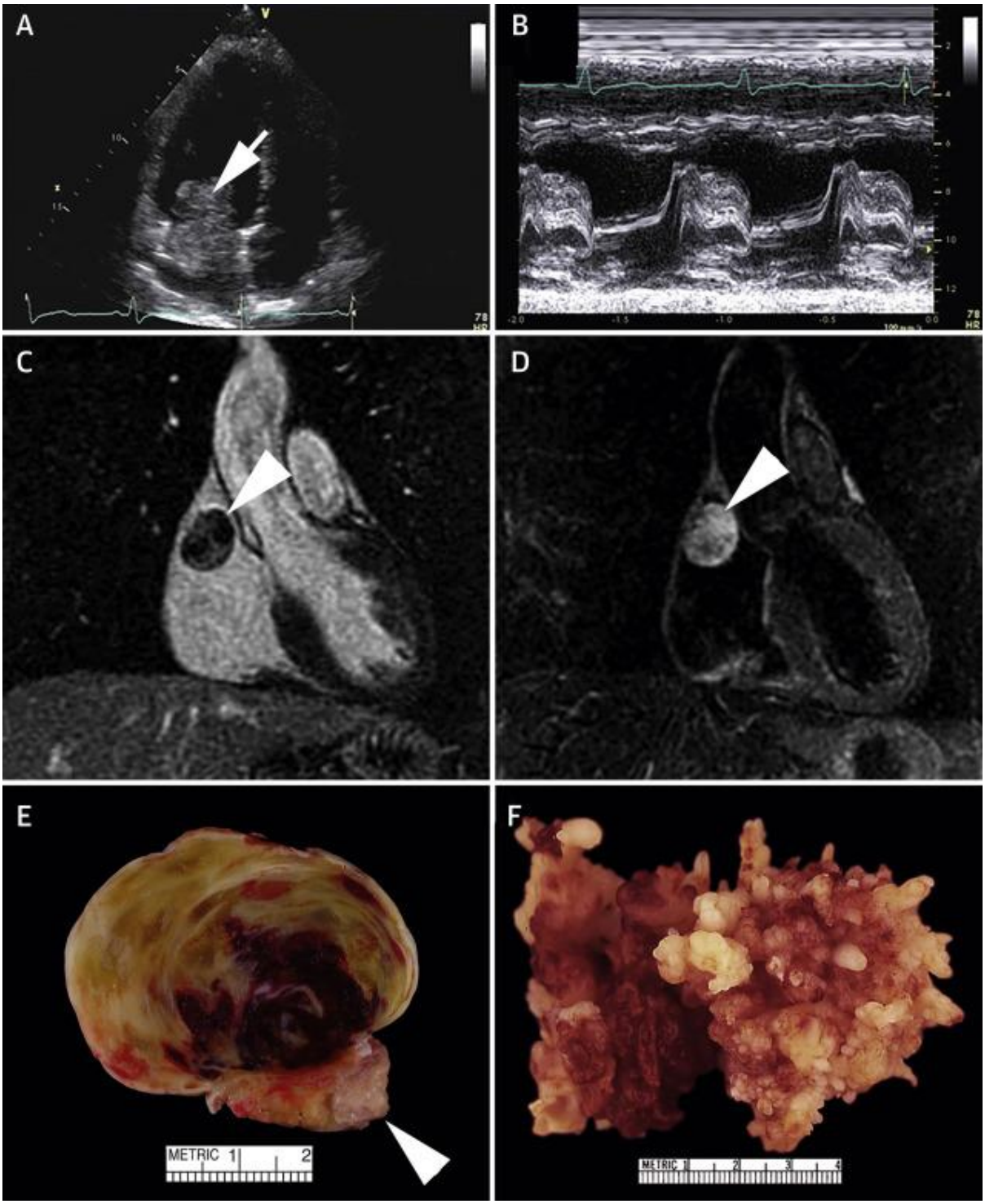


Figure 3. Cardiac Myxoma

Why not the other options?

- **Rheumatic fever (A):** While it can cause a diastolic murmur (mitral stenosis), it would not produce a left atrial mass on echocardiography.
- **Innocent murmur (B):** These are typically systolic, not diastolic, and would not be associated with syncope, pulmonary congestion, or an intracardiac mass.

- **Non-bacterial thrombotic endocarditis (C):** This produces small, sterile vegetations on valve leaflets (not a mass on the atrial septum) and is typically associated with malignancy or hypercoagulable states.

Would you like to explore the surgical management and recurrence rates of cardiac myxomas, including the role of the Carney complex in familial cases?

References

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Question 638

Four days after admission to the hospital for pneumonia, a 68-year-old woman develops abdominal pain and watery, foul-smelling diarrhea. Current medications include intravenous ceftriaxone and oral azithromycin. Stool cultures grow gram-positive, anaerobic rods. She is moved to an isolated hospital room. Sterilization with which of the following agents is most likely to prevent transmission of this pathogen to the next patient who will occupy her room?

Answer Choices:

(A) Chlorine-based solution
(B) Iodine-based solution
(C) Isopropanol-based solution
(D) Quaternary amine-based solution

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/956368b8-0f6e-4805-83a5-2d04ce6c5690

OpenEvidence Explanation

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The answer is **A. Chlorine-based solution**.

This clinical scenario describes **Clostridioides difficile infection (CDI)** — a hospitalized elderly patient on broad-spectrum antibiotics (ceftriaxone and azithromycin) who develops nosocomial diarrhea with stool cultures growing gram-positive, anaerobic rods. *C. difficile* is the most common infectious cause of antibiotic-associated diarrhea in hospitalized patients.[1][2]

The key to this question is that *C. difficile* forms **spores**, which are highly resistant to most common disinfectants. Critically:

- *Alcohol-based (isopropanol) solutions do not inactivate C. difficile spores*. This is why alcohol-based hand sanitizers are insufficient, and soap-and-water handwashing is recommended instead.[3]
- **Quaternary ammonium compounds** are also ineffective against *C. difficile* spores.[4]
- **Iodine-based solutions** have limited sporicidal activity and are not recommended for environmental decontamination of *C. difficile*.
- **Chlorine-based solutions (sodium hypochlorite/bleach)** are the standard recommended sporicidal disinfectant. The SHEA/IDSA 2022 guidelines recommend using an **EPA-approved sporicidal disinfectant, such as diluted (1:10) sodium hypochlorite**, for environmental cleaning and disinfection of rooms occupied by patients with CDI. Laboratory studies confirm that household bleach is the only commonly tested chemical that consistently reduces both vegetative cells and spores across multiple *C. difficile* strains.[5][6]

Would you like to explore the current evidence on fidaxomicin versus vancomycin for treatment of *C. difficile* infection?

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Question 640

A 4-year-old boy presents for a routine checkup. The patient's parents say he was doing well until a few weeks ago at which time he started to complain of daily abdominal cramps and occasional muscle pains. His mother also noticed that he has been less active than usual. The parents deny any complaints of headaches or convulsions. The family lives together in a house built in 1950. The patient's temperature is 36.8°C (98.2°F), blood pressure is 100/70 mm Hg, pulse is 100/min and respirations are 20/min. Abdominal exam shows mild diffuse tenderness to palpation and normal bowel sounds. The patient's height, weight, and head circumference are normal. Laboratory results are as follows:
Hemoglobin 7 g/dL
Mean corpuscular volume (MCV) 72
Lead level (capillary blood) 15 mcg/dL
Lead level (venous blood) 60 mcg/dL
Findings on a peripheral blood smear are shown in the image. Which of the following is the best treatment option for this patient?

Answer Choices:

(A) Trientine
(B) Calcium disodium edetate (EDTA)
(C) Penicillamine
(D) Dimercaptosuccinic acid (DMSA), also known as succimer

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/66551305-5252-40d7-a4a7-8ab782bfb3dd

OpenEvidence Explanation

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The best treatment option for this patient is **D. Dimercaptosuccinic acid (DMSA), also known as succimer**.

This child presents with classic features of **lead poisoning**: abdominal cramps, muscle pains, decreased activity, microcytic anemia (Hb 7 g/dL, MCV 72), and a venous blood lead level of **60 mcg/dL**, living in a pre-1960s home (likely containing lead-based paint). The peripheral blood smear would characteristically show **basophilic stippling** of red blood cells, a hallmark finding of lead poisoning.

Why DMSA (succimer) is the correct answer:

- The CDC and USPSTF recommend chelation therapy for children with blood lead levels **≥45 mcg/dL**. This child's venous level of 60 mcg/dL clearly meets this threshold.[1][2]
- **Succimer (DMSA)** is FDA-approved for treatment of lead poisoning in pediatric patients ≥1 year old with blood lead levels above 45 mcg/dL. It is administered orally (10 mg/kg every 8 hours for 5 days, then every 12 hours for 14 additional days), making it practical for outpatient use in children without encephalopathy.[3]
- In clinical studies, DMSA at 350 mg/m² every 8 hours reduced blood lead levels by **78%**, outperforming $CaNa_2EDTA$ (48% reduction).[3]
- DMSA is described as the "less toxic analog" of dimercaprol and is the most commonly used chelating agent for childhood lead poisoning.[1]

Why the other options are incorrect:

- **A. Trientine** – Used for Wilson disease (copper chelation), not lead poisoning.
- **B. Calcium disodium EDTA** – A valid chelating agent for lead but requires parenteral (IV or IM) administration and is typically reserved for blood lead levels **>70 mcg/dL** or when used in combination with dimercaprol (BAL) for

lead encephalopathy. For a level of 60 mcg/dL without encephalopathy, oral DMSA is preferred.[4]

- **C. Penicillamine** – Has been used for lead chelation but is "less commonly used" due to greater toxicity and is not first-line.[1]

Would you like to explore the specific monitoring parameters and follow-up protocol after initiating succimer therapy in pediatric lead poisoning?

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Question 641

A 39-year-old woman with poorly controlled systemic lupus erythematosus (SLE) presents to her rheumatologist for a follow-up visit. She has had intermittent myalgias, arthralgias, fatigue, and skin rashes over the past 10 years that have acutely worsened over the past year. She works as a school teacher but reports that she has had to miss several days of work due to her symptoms. She has been on hydroxychloroquine for several years but does not feel that it is adequately controlling her symptoms. She does not smoke or drink alcohol. Her temperature is 99.2°F (37.3°C), blood pressure is 130/75 mmHg, pulse is 80/min, and respirations are 18/min. On exam, she is well-appearing and in no acute distress. She has erythematous, raised plaques with keratotic scaling and follicular plugging on her hands. The physician decides to trial the patient on low-dose prednisone to better control her symptoms. At 2 months of follow-up, she reports that her flares have subsided and she has been able to return to work full-time. If this patient continues this medication regimen, she will be at an elevated risk for developing which of the following?

Answer Choices:

(A) Femoral neck fracture
(B) Femoral shaft fracture
(C) Osgood-Schlatter disease
(D) Proximal phalanx fracture

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/0bdf0ba4-ee29-4684-8e19-4cade1feaba3

OpenEvidence Explanation

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The answer is **A. Femoral neck fracture**. Long-term glucocorticoid use causes **glucocorticoid-induced osteoporosis**, which predominantly affects skeletal regions rich in cancellous (trabecular) bone, such as the lumbar spine and **proximal femur** (including the femoral neck).[1][2] This places the patient at elevated risk for osteoporotic fractures at these sites.

Why femoral neck fracture (A) is correct:

Chronic prednisone use increases the risk of hip fracture (which includes femoral neck fractures) by approximately 50% even at low doses (2.5–7.5 mg/day), and by a factor of 7 with continuous use of 10 mg/day for more than 90 days.[1][2] The femoral neck is a classic site for osteoporotic fragility fractures because it is composed largely of trabecular bone, which is preferentially affected by glucocorticoid-mediated bone resorption and impaired bone formation.[1]

Why the other options are incorrect:

- **B. Femoral shaft fracture** — The femoral shaft is composed predominantly of cortical bone and is not a typical site for osteoporotic fragility fractures. Femoral shaft fractures are more commonly associated with high-energy trauma or, rarely, atypical femoral fractures from prolonged bisphosphonate use.
- **C. Osgood-Schlatter disease** — This is an apophysitis of the tibial tubercle seen in adolescents during growth spurts, not a complication of glucocorticoid therapy in adults.
- **D. Proximal phalanx fracture** — Not a recognized site for glucocorticoid-induced osteoporotic fractures.

The ACR 2022 guideline recommends fracture risk assessment soon after initiation of long-term glucocorticoid therapy (≥3 months at doses ≥2.5 mg/day), with consideration of bone-protective therapy including bisphosphonates as first-line treatment.[2][3]

Would you like to explore the specific screening and prevention strategies for glucocorticoid-induced osteoporosis in premenopausal women with SLE?

Relevant images

(CONTENT OMITTED)

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Question 647

A 2-month-old girl is brought to the pediatrician by her concerned father. He states that ever since her uncomplicated delivery she has failed to gain weight, has had chronic diarrhea, and has had multiple bacterial and viral infections. During the course of the workup, an absent thymic shadow is noted and a lymph node biopsy demonstrates the absence of germinal centers. Which of the following is the most likely cause of this patient's symptoms?

> **Answer Choices:**
>
> (A) Defect in ATM gene
> (B) Adenosine deaminase deficiency
> (C) NADPH oxidase deficiency
> (D) Defect in BTK gene

> **Correct Answer:**
>
> **(B)**
>
> **OpenEvidence Response:**
>
> **(B)** ✓

OpenEvidence Link: https://openevidence.com/ask/f6052c1d-2c9d-4880-ab08-b5f8fc4a4b81

OpenEvidence Explanation

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The answer is **B. Adenosine deaminase (ADA) deficiency**. This presentation — a 2-month-old with failure to thrive, chronic diarrhea, recurrent bacterial and viral infections, absent thymic shadow, and absent germinal centers on lymph node

biopsy — is classic for **severe combined immunodeficiency (SCID)**. Among the answer choices, ADA deficiency is the most common autosomal recessive cause of SCID and the only option that produces this phenotype.[1][2][3]

Why ADA deficiency fits:

ADA deficiency causes accumulation of toxic purine metabolites (deoxyadenosine and deoxyATP) that are lymphotoxic to both T and B cells (and NK cells), resulting in a **T^- B^- NK^- SCID** phenotype. This explains the absent thymic shadow (no T-cell development) and absent germinal centers (no functional B cells). Infants present early in life with failure to thrive, chronic diarrhea, and susceptibility to both bacterial and viral infections — precisely as described.[2][4] The 2025 AAAAI/ACAAI/CIS Inborn Errors of Immunity Practice Parameter specifically recommends that ADA enzyme activity be included in the diagnostic evaluation for SCID.[4]

Why the other options are incorrect:

- **A. Defect in ATM gene** — Causes ataxia-telangiectasia, which presents later in childhood with cerebellar ataxia, oculocutaneous telangiectasias, and immunodeficiency. It does not present at 2 months with absent thymic shadow and absent germinal centers.[4]
- **C. NADPH oxidase deficiency** — Causes chronic granulomatous disease (CGD), a phagocyte defect characterized by recurrent catalase-positive bacterial and fungal infections. T- and B-cell function is intact; the thymus and germinal centers are normal.
- **D. Defect in BTK gene** — Causes X-linked agammaglobulinemia (XLA), which affects only B-cell development. XLA presents with absent germinal centers and very low immunoglobulins but has a **normal thymus** and intact T-cell immunity. Additionally, XLA is X-linked and affects males; while this patient is female, the key distinguishing feature is the absent thymic shadow, which is not seen in XLA.[5][6]

Would you like to explore the different genetic subtypes of SCID and how they influence the choice of definitive treatment (e.g., conditioning regimen for hematopoietic stem cell transplant vs. gene therapy)?

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Question 648

A 1-year-old boy is brought to the clinic by his parents for a regular check-up. His weight, height, and head size were found to be in the lower percentile ranges on standard growth curves. His hair is tangled and has a dry, brittle texture. Genetic testing reveals that the patient has a connective tissue disorder caused by impaired copper absorption and transport. The patient's disorder is caused by a mutation in which of the following genes?

> **Answer Choices:**
>
> (A) ATP7A
> (B) COL5A1
> (C) FBN1
> (D) ATP7B

> **Correct Answer:**
>
> **(A)**
>
> **OpenEvidence Response:**
>
> **(A)** ✓

OpenEvidence Link: https://openevidence.com/ask/b218117a-079c-4865-a71e-8521cdfde4e3

OpenEvidence Explanation

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The correct answer is **A. ATP7A**.

The clinical presentation — a 1-year-old boy with failure to thrive (low weight, height, and head circumference), **tangled, dry, brittle hair**, and a connective tissue disorder caused by **impaired copper absorption and transport** — is classic for **Menkes disease** (also known as "kinky hair syndrome"). This X-linked recessive disorder is caused by mutations in the **ATP7A** gene, which encodes a copper-transporting P-type ATPase responsible for intestinal copper absorption and intracellular copper distribution.[1][2][3]

Why the other options are incorrect:

- **B. COL5A1** — Mutations in this gene cause classic Ehlers-Danlos syndrome, a connective tissue disorder characterized by skin hyperextensibility and joint hypermobility, but it is not related to copper metabolism.[4]
- **C. FBN1** — Mutations in fibrillin-1 cause Marfan syndrome, featuring tall stature, arachnodactyly, lens subluxation, and aortic root dilation — again unrelated to copper transport.[4]
- **D. ATP7B** — This gene encodes a different copper-transporting ATPase expressed primarily in the liver. Mutations in ATP7B cause **Wilson disease**, which involves copper accumulation (not deficiency) and typically presents later in life with hepatic and neuropsychiatric symptoms.[2]

In Menkes disease, defective ATP7A protein prevents copper from being absorbed in the intestine and delivered to copper-dependent enzymes such as lysyl oxidase (connective tissue cross-linking), tyrosinase (pigmentation), and cytochrome c oxidase (energy metabolism), explaining the connective tissue abnormalities, characteristic hair changes, neurodegeneration, and failure to thrive.[1][5]

Would you like to explore the current evidence on early copper-histidine replacement therapy and its impact on neurodevelopmental outcomes in Menkes disease?

Relevant images

(CONTENT OMITTED)

References

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Question 649

A 15-year-old girl is brought to the physician because she has not had a menstrual period. There is no personal or family history of serious illness. She is 165 cm (5 ft 5 in) tall and weighs 57 kg (125 lb); BMI is 21 kg/m2. Vital signs are within normal limits. Examination of the breasts shows a secondary mound formed by the nipple and areola. Pubic hair is sparse and lightly pigmented. Abdominal examination shows bilateral firm, nontender inguinal masses. Pelvic examination shows a blind-ended vaginal pouch. Ultrasonography does not show a uterus or ovaries. Which of the following is the most appropriate treatment for this patient's condition?

Answer Choices:

(A) Gonadectomy
(B) Testosterone therapy
(C) Vaginal dilatory therapy
(D) Prednisolone therapy

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/ba71ae6a-4ec1-4bde-b1f5-d1702521c518

OpenEvidence Explanation

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The correct answer is **A. Gonadectomy**.

This clinical presentation — primary amenorrhea, breast development (Tanner stage IV), sparse pubic hair, bilateral inguinal masses, a blind-ended vaginal pouch, and absent uterus/ovaries on ultrasonography — is classic for **complete androgen insensitivity syndrome (CAIS)**. These patients have a 46,XY karyotype with functioning testes (the inguinal masses) that produce testosterone, which is aromatized to estrogen (driving breast development), but the androgen receptor is nonfunctional, resulting in a female phenotype with absent Müllerian structures (due to anti-Müllerian hormone from Sertoli cells).[1]

Gonadectomy is the most appropriate treatment because the retained testes carry a **14–22% lifetime risk of gonadal malignancy** (gonadoblastoma, seminoma), though this risk is very low before age 20.[2][3] Standard management recommends gonadectomy after completion of puberty — this patient has already undergone spontaneous pubertal breast development — followed by lifelong estrogen replacement therapy.[1][4][5]

Why the other options are incorrect:

- **Testosterone therapy (B):** These patients have androgen receptor insensitivity; exogenous testosterone would be ineffective. While some post-gonadectomy patients may use testosterone for libido, it is not the primary treatment.[6]
- **Vaginal dilator therapy (C):** While vaginal dilation may eventually be offered to achieve functional vaginal length for sexual intercourse, it is not the most appropriate initial treatment — gonadectomy to prevent malignancy takes priority.[1][7]
- **Prednisolone therapy (D):** There is no role for glucocorticoid therapy in CAIS (unlike congenital adrenal hyperplasia).

Would you like to explore the evolving debate around timing of gonadectomy versus gonadal surveillance in CAIS, given recent trends toward gonadal retention?

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Question 650

A 51-year-old man presents the emergency room with chest pain. He mentions that the pain started several hours ago and radiates to his left neck and shoulder. He also mentions that he has some difficulty in breathing. He says that he has had similar chest pains before, but nothing seemed to be wrong at that time. He was diagnosed with high cholesterol during that episode and was prescribed medication. He also has a 3-year history of gastritis. The blood pressure is 130/80 mm Hg, respirations are 18/min, and the pulse is 110/min. He seems a little anxious. The physical examination reveals no significant abnormalities. An ECG shows slight changes in the leads. His physician talks to him about the benefits of taking low-dose aspirin daily. Which of the following would be a contraindication to the use of aspirin in this patient?

Answer Choices:

(A) ECG changes
(B) Hypercholesterolemia
(C) Gastritis
(D) Increased pulse rate

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/3921b047-68cb-471c-b7ce-aca02b2ab68f

OpenEvidence Explanation

(CONTENT OMITTED)

The correct answer is **C. Gastritis**.

Gastritis is a contraindication to aspirin use because aspirin irreversibly inhibits cyclooxygenase (COX), reducing prostaglandin synthesis that normally protects the gastric mucosa. In a patient with a 3-year history of gastritis, aspirin would exacerbate mucosal injury and significantly increase the risk of gastrointestinal bleeding.

The 2019 ACC/AHA Guidelines on Primary Prevention of Cardiovascular Disease explicitly recommend against low-dose aspirin in adults at increased risk of bleeding, listing conditions such as **previous gastrointestinal bleeding, peptic ulcer disease, or gastritis** as factors that increase bleeding risk.[1][2] The USPSTF similarly specifies that aspirin for primary prevention should be considered only in patients "not at increased risk for bleeding (e.g., no history of gastrointestinal ulcers)".[3] The ACCP guidelines also reference gastritis as a major GI contraindication to aspirin.[4]

The other answer choices are not contraindications:

- **A. ECG changes** — ECG changes suggesting ischemia would actually support the use of aspirin, not contraindicate it.
- **B. Hypercholesterolemia** — Elevated cholesterol is a cardiovascular risk factor that may favor aspirin use for prevention; it is not a contraindication.
- **D. Increased pulse rate** — Tachycardia in this context likely reflects anxiety or a cardiovascular event and is not a contraindication to aspirin.

Would you like to explore the recommended gastroprotective strategies (e.g., PPI co-therapy) for patients who require aspirin but have GI risk factors?

Relevant images

(CONTENT OMITTED)

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Question 652

An 89-year-old woman is brought to the emergency department by her husband because of diarrhea and weakness for 4 days. She has 2–3 loose stools every day. She has also had 3 episodes of vomiting. She complains of a headache and blurry vision. Three weeks ago, she returned from a cruise trip to the Bahamas. She has congestive heart failure, atrial fibrillation, age-related macular degeneration, type 2 diabetes mellitus, and chronic renal failure. Current medications include warfarin, metoprolol, insulin, digoxin, ramipril, and spironolactone. Her temperature is 36.7°C (98°F), pulse is 61/min, and blood pressure is 108/74 mm Hg. The abdomen is soft, and there is diffuse, mild tenderness to palpation. Laboratory studies show:
Hemoglobin 12.9 g/dL
Leukocyte count 7200/mm3
Platelet count 230,000/mm3
Serum
Na+ 137 mEq/L
K+ 5.2 mEq/L
Glucose 141 mg/dL
Creatinine 1.3 mg/dL
Which of the following is the most appropriate next step in management?

Answer Choices:

(A) Perform hemodialysis
(B) Perform C. difficile toxin assay
(C) Measure serum drug concentration
(D) Administer oral activated charcoal

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/97f9166f-261c-4e00-ac56-82b3d7b284a6

OpenEvidence Explanation

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The correct answer is **C. Measure serum drug concentration**.

This clinical presentation is highly consistent with **digoxin toxicity**. The key features pointing to this diagnosis include:

- **Gastrointestinal symptoms**: Nausea, vomiting, and diarrhea are among the most common manifestations of digoxin toxicity, occurring in 30–70% of overdosed patients.[1][2]
- **Neurological symptoms**: Headache and blurry vision are classic neurological complaints of digoxin toxicity.[3]
- **Bradycardia**: A pulse of 61/min in a patient on digoxin (and metoprolol) raises concern for toxicity-related conduction effects.
- **Hyperkalemia**: Potassium of 5.2 mEq/L is elevated, and hyperkalemia is a recognized feature of digoxin toxicity, especially in patients with impaired renal function.[1][4]
- **Risk factors for toxicity**: This patient has multiple predisposing factors — advanced age, chronic renal failure (creatinine 1.3 mg/dL), low lean body mass (elderly woman), and concurrent use of spironolactone (a potassium-sparing diuretic that can worsen hyperkalemia).[3]

The most appropriate next step is to **measure the serum digoxin concentration** to confirm the clinical suspicion. Toxicity becomes more frequent with levels above 2 ng/mL, though it can occur at lower levels when predisposing factors such as renal impairment and electrolyte abnormalities are present.[2][5]

Why not the other options?

- **A. Hemodialysis** — Digoxin is only slightly dialyzable due to its large volume of distribution, and dialysis is not recommended for digoxin removal.[6][7]
- **B. C. difficile toxin assay** — While diarrhea could suggest C. difficile, the constellation of GI symptoms, visual changes, bradycardia, and hyperkalemia in a patient on digoxin with renal impairment makes digoxin toxicity far more likely.
- **D. Activated charcoal** — This is used for acute ingestions, typically within 1–2 hours. This patient has chronic toxicity from drug accumulation, not an acute overdose, making charcoal inappropriate.

Would you like to explore the management algorithm for confirmed digoxin toxicity, including indications for digoxin-specific Fab antibody fragments?

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Question 653

A 45-year-old woman is brought to the emergency department by her husband due to upper abdominal pain, nausea, and vomiting for the past couple of hours. She had similar episodes in the past, which were often precipitated by food but resolved spontaneously. Her temperature is 38.3°C (101.0°F), heart rate is 96/min, blood pressure is 118/76 mm Hg, and respiratory rate is 16/min. Physical examination reveals tenderness over the right upper quadrant that is severe enough to make her stop breathing when deeply palpated in the area. Lab results show:
Leukocyte count 18,000/mm3 with 79% neutrophils
Aspartate aminotransferase 67 IU/L
Alanine aminotransferase 71 IU/L
Serum amylase 46 U/L
Serum Lipase 55 U/L
Serum calcium 8.9 mg/dL
Ultrasonography of the abdomen is shown below. During the ultrasound exam, the patient complains of tenderness when the probe presses down on her right upper quadrant. Which of the following is the most likely cause of her pain?

Answer Choices:

(A) Acute calculous cholecystitis
(B) Acute acalculous cholecystitis
(C) Acute pancreatitis
(D) Ascending cholangitis

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/950253b2-6727-4c96-acca-bb39c721e1d3

OpenEvidence Explanation

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The most likely cause of this patient's pain is **A. Acute calculous cholecystitis**.

This presentation is classic for acute calculous cholecystitis, supported by several key findings:

- **Murphy's sign**: The patient arrests breathing during deep palpation of the right upper quadrant — this is the clinical Murphy's sign, which is highly specific for acute cholecystitis (LR+ = 11.5–21.3). The tenderness elicited by the ultrasound probe pressing on the RUQ represents the **sonographic Murphy's sign**, further strengthening the diagnosis.[1][2][3]
- **Recurrent postprandial episodes**: Prior similar episodes precipitated by food that resolved spontaneously are consistent with a history of biliary colic from gallstones, which is the typical precursor to acute cholecystitis.[4]
- **Systemic inflammation**: Fever (38.3°C), tachycardia, and leukocytosis (18,000/mm^3 with neutrophilic predominance) indicate an acute inflammatory/infectious process consistent with cholecystitis.[5][6]
- **Mildly elevated transaminases** (AST 67, ALT 71) can occur in acute cholecystitis and do not point toward an alternative diagnosis.[4]
- **Normal amylase and lipase** effectively rule out **acute pancreatitis (C)**, which requires lipase or amylase ≥3 times the upper limit of normal for diagnosis per the Revised Atlanta Classification.[7]

Why not the other options?

- **B. Acute acalculous cholecystitis** — This accounts for only 5–10% of cholecystitis cases and typically occurs in critically ill, hospitalized patients (ICU, post-surgical, septic), not in an otherwise healthy outpatient with recurrent food-triggered episodes.[5]

- **D. Ascending cholangitis** — Charcot's triad (fever, jaundice, RUQ pain) is the hallmark. This patient lacks jaundice, and there is no mention of biliary ductal dilation or elevated bilirubin/alkaline phosphatase, which would be expected.[8]

The following diagnostic algorithm illustrates the clinical approach to differentiating biliary colic from acute cholecystitis based on symptom duration, Murphy's sign, leukocytosis, and ultrasound findings.

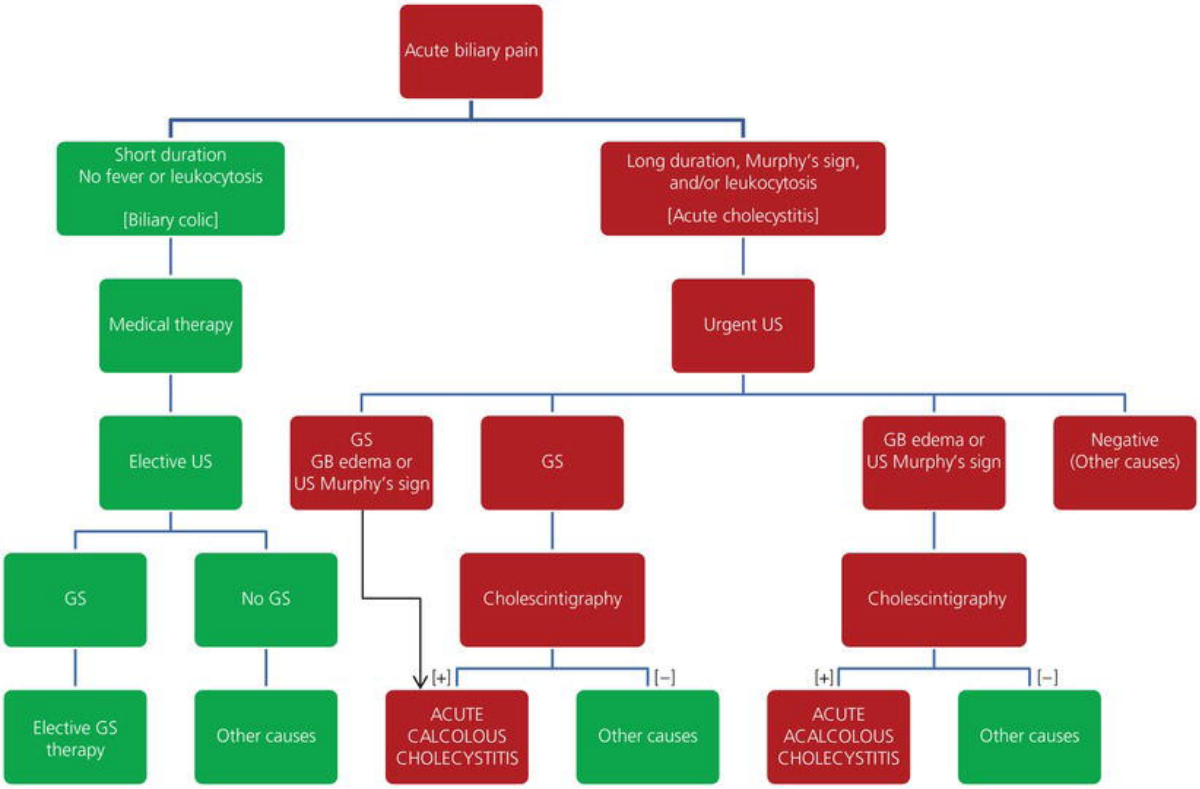


Figure 22. Diagnostic flowchart of patients with acute biliary pain and cholecystitis. After onset of acute biliary pain (biliary colic), a careful evaluation with clinical, laboratory, and imaging tests is necessary for differential diagnosis between simple biliary colic (left part of the algorithm) and acute cholecystitis (right part of the algorithm). In the latter, the presence of leukocytosis and longer pain duration are justified by the ongoing gallbladder inflammation. In addition, associated symptoms, e.g., fever, nausea, and vomiting, are present. Acute cholecystitis, a condition at high risk of complications, requires urgent treatment. GB, gallbladder; GS, gallstones; US, abdominal ultrasound; [–], absent; [+], present. Source: Zakko S, Afdhal N. Pathogenesis, clinical features, and diagnosis of acute cholecystitis. In: Basow DS (ed.). UpToDate. Waltham, MA: UpToDate; 2013. Reproduced with

permission of Wolters Kluwer Health. Copyright © 2013 UpToDate, Inc. For more information, visit www.uptodate.com .

Would you like to explore the current evidence on timing of laparoscopic cholecystectomy (early vs. delayed) and its impact on outcomes in acute calculous cholecystitis?

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Question 655

A 62-year-old woman with a pancreatic insulinoma is being prepared for a laparoscopic enucleation of the tumor. After induction of general anesthesia, preparation of a sterile surgical field, and port placement, the surgeon needs to enter the space posterior to the stomach to access the pancreatic tumor. Which of the following ligaments must be cut in order to access this space?

> **Answer Choices:**
>
> (A) Phrenoesophageal ligament
> (B) Gastrohepatic ligament
> (C) Phrenicocolic ligament
> (D) Ligamentum venosum

> **Correct Answer:**
>
> **(B)**
>
> **OpenEvidence Response:**
>
> **(B)** ✓

OpenEvidence Link: https://openevidence.com/ask/ca483496-a79a-4a8e-9d46-a6331b52f39f

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OpenEvidence Explanation

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The correct answer is **B. Gastrohepatic ligament**.

To access the space posterior to the stomach — the **lesser sac (omental bursa)** — where the pancreas lies, the surgeon must divide a ligament that forms part of its

boundary. The **gastrohepatic ligament** (part of the lesser omentum) connects the liver to the lesser curvature of the stomach and forms the anterior wall of the entrance to the lesser sac. Dividing it provides direct access to the pancreas without needing to retract or mobilize the stomach extensively.

This approach is well-described in the surgical literature. Multiple studies on minimally invasive pancreatic surgery describe the "gastrohepatic ligament approach," in which the gastrohepatic ligament is divided extensively as the first step, and all subsequent dissection around the pancreas is performed through this route — without dividing the gastrocolic ligament or retracting the stomach.[1][2][3] As noted in pancreas allograft retrieval literature, transecting the gastrohepatic ligament provides access to the lesser sac, allowing inspection of the superior border of the pancreas and visualization of the splenic artery and vein.[4]

The omental bursa can be entered through several routes — the hepatogastric (gastrohepatic) ligament, the gastrocolic ligament, the gastrosplenic ligament, or the transverse mesocolon.[5] However, among the answer choices provided, only the gastrohepatic ligament is a valid route to the lesser sac.

The other options are incorrect:

- **A. Phrenoesophageal ligament** — attaches the esophagus to the diaphragm at the hiatus; not relevant to lesser sac access.
- **C. Phrenicocolic ligament** — connects the splenic flexure of the colon to the diaphragm; does not provide access to the space posterior to the stomach.
- **D. Ligamentum venosum** — a remnant of the ductus venosus on the posterior surface of the liver; it is not a surgically divided structure for pancreatic access.

Would you like to explore the specific techniques for intraoperative localization of insulinomas, including the role of intraoperative ultrasound and ICG fluorescence imaging?

Relevant images

(CONTENT OMITTED)

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Question 656

A 55-year-old man is brought to the emergency room by his wife for severe abdominal pain for the past 1 hour. He is unable to give more information about the nature of his pain. His wife says that he has peptic ulcer disease and is being treated with antacids without a good response. She adds that he vomited repeatedly in the last couple of hours, his vomitus being brown/red in color. His temperature is 98.6°F (37°C), respiratory rate is 16/min, pulse is 97/min, and blood pressure is 100/68 mm Hg. A physical exam reveals a tense abdomen with a board like rigidity and positive rebound tenderness. An erect abdominal x-ray is ordered. Which of the following is the most likely diagnosis?

Answer Choices:

(A) Duodenal peptic ulcer
(B) Gastric peptic ulcer
(C) Pancreatitis
(D) Perforated gastric peptic ulcer

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/a5dcd265-0b2c-4503-9bf9-cc39a3cd81ad

OpenEvidence Explanation

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The answer is **D. Perforated gastric peptic ulcer**.

This patient's presentation is classic for a **perforated peptic ulcer**: known peptic ulcer disease inadequately treated with antacids, sudden severe abdominal pain, hematemesis (brown/red vomitus), tachycardia (97/min), relative hypotension (100/68 mmHg), and critically — **board-like rigidity with rebound tenderness**, which are hallmark signs of peritonitis from perforation.[1][2]

Why perforation, not just an uncomplicated ulcer or pancreatitis?

- **Uncomplicated gastric or duodenal ulcer** (options A and B) can cause epigastric pain, nausea, and even upper GI bleeding, but would not produce board-like rigidity and diffuse rebound tenderness — these are signs of peritoneal irritation from leakage of gastric contents into the peritoneal cavity.[1][3]

- **Pancreatitis** (option C) can cause severe abdominal pain and tenderness, but typically presents with epigastric pain radiating to the back, and the degree of rigidity described here ("board-like") is more characteristic of perforation with chemical peritonitis from acidic gastric contents.[1]

- The erect abdominal X-ray is being ordered to look for **free air under the diaphragm (pneumoperitoneum)**, which is the radiographic hallmark of hollow viscus perforation and is found in 30–85% of perforated peptic ulcers on plain films. CT scan has 98% diagnostic accuracy and is the gold standard.[4][5]

The following figure demonstrates the classic radiographic finding of pneumoperitoneum (free air under both hemidiaphragms, indicated by arrows) in a perforated peptic ulcer, along with intraoperative findings.

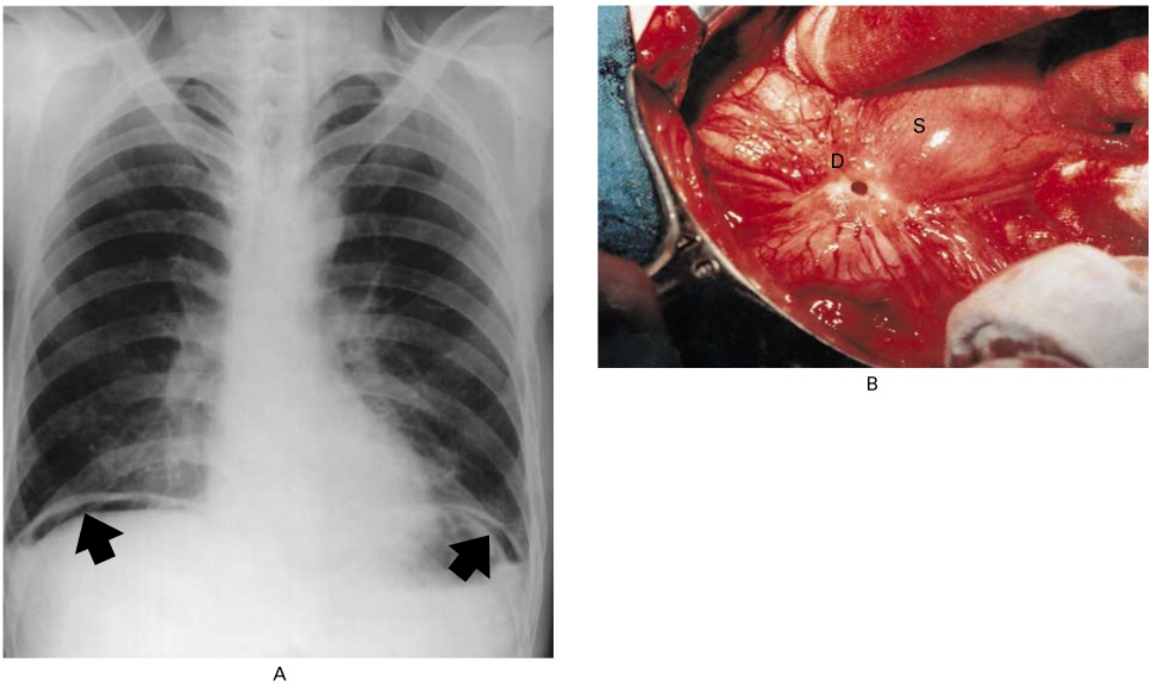


Figure 1.

Used under license from The New England Journal of Medicine.

Notably, every hour of delay in surgical intervention for perforated PUD has been associated with a **2.4% decreased probability of survival**.[5]

Would you like to explore the current surgical management options for perforated peptic ulcer, including laparoscopic versus open repair?

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Question 658

In 2005, a group of researchers believed that prophylactically removing the ovaries and fallopian tubes (bilateral salpingo-oophorectomy) in BRCA-mutation positive women would reduce the chance that they developed breast cancer. To test this hypothesis, they reviewed a database of women who were known to be BRCA-mutation positive and divided the group into those with breast cancer and those without breast cancer. They used data in the registry and surveys about peoples' surgical history to compare the proportion of each population that had undergone a bilateral salpingo-oophorectomy. Based on this data, they reported that women undergoing the procedure had a lower chance of developing breast cancer later in life with an odds ratio of 0.46. This is an example of what type of study design?

Answer Choices:

(A) Meta-analysis
(B) Cross-sectional
(C) Case-control
(D) Genome-wide association study

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/f41b4d6c-edc9-4c99-b8da-1cb48d79642b

OpenEvidence Explanation

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The answer is **C. Case-control**.

This study design is a classic **case-control study** based on several defining features described in the vignette:

- **Starting point is the outcome (disease status):** The researchers began by identifying women who had breast cancer (**cases**) and women who did not (**controls**), both drawn from a registry of BRCA-mutation positive women.
- **Looking backward at exposure:** They then looked retrospectively at each group's history of bilateral salpingo-oophorectomy (the **exposure**) to compare the proportion exposed in cases versus controls.
- **Measure of association is the odds ratio:** Case-control studies yield an **odds ratio** (here, OR = 0.46), not a relative risk, because the study starts with disease status rather than following an exposed cohort forward in time.

Why not the other options?

- **A. Meta-analysis** — A meta-analysis pools data from multiple independent studies using statistical methods; this describes a single study using one registry.
- **B. Cross-sectional** — A cross-sectional study measures exposure and outcome simultaneously at a single point in time (prevalence). Here, the researchers specifically compared a historical exposure (prior surgery) between groups defined by a subsequent outcome, which is the hallmark retrospective design of a case-control study.
- **D. Genome-wide association study (GWAS)** — A GWAS scans the genome for genetic variants associated with a trait; this study examined a surgical intervention, not genetic polymorphisms.

Would you like to explore how the results of case-control studies like this one compare with prospective cohort data on risk-reducing salpingo-oophorectomy in BRCA carriers?

Question 661

A 3-year-old girl is brought to the cardiologist because of sweating and respiratory distress while eating. She is at the 30th percentile for height and 15th percentile for weight. Echocardiography shows a defect in the membranous portion of the interventricular septum and a moderately decreased left ventricular ejection fraction. Physical examination is most likely to show which of the following findings?

> **Answer Choices:**
>
> (A) Systolic murmur that increases with hand clenching
> (B) Systolic murmur that increases with forced exhalation against a closed glottis
> (C) Diastolic murmur preceded by opening snap
> (D) Continuous murmur that is loudest at the second heart sound

> **Correct Answer:**
>
> **(A)**
>
> **OpenEvidence Response:**
>
> **(A)** ✓

OpenEvidence Link: https://openevidence.com/ask/28837755-07bf-4461-a1d2-eb6bcb690228

OpenEvidence Explanation

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The answer is **A. Systolic murmur that increases with hand clenching**.

This child has a **membranous (perimembranous) ventricular septal defect (VSD)** with symptoms of heart failure (sweating and respiratory distress during feeding, failure to thrive, decreased LVEF). A VSD produces a **pansystolic murmur** best heard at the left lower sternal border.[1]

Why hand clenching (isometric handgrip) increases the VSD murmur: Hand clenching increases systemic vascular resistance (afterload), which augments the left-to-right pressure gradient across the VSD, thereby increasing flow through the defect and making the murmur louder. The ACC/AHA valvular heart disease guidelines specifically note that murmurs of MR, VSD, and AR increase with handgrip exercise.[2][3] A landmark NEJM study by Lembo et al. confirmed that the murmurs of mitral regurgitation and VSD are augmented by handgrip (68% sensitivity, 92% specificity) and transient arterial occlusion (78% sensitivity, 100% specificity).[4]

Why the other options are incorrect:

- **B (Valsalva maneuver):** Forced exhalation against a closed glottis (Valsalva) decreases preload, which reduces flow across the VSD and makes most murmurs softer. The notable exceptions where Valsalva increases murmur intensity are hypertrophic obstructive cardiomyopathy and mitral valve prolapse.[2]
- **C (Diastolic murmur with opening snap):** An opening snap followed by a diastolic murmur is characteristic of mitral stenosis, not VSD.
- **D (Continuous murmur loudest at S2):** A continuous "machinery" murmur loudest around the second heart sound describes a patent ductus arteriosus, not a VSD.

Would you like to explore the indications and timing for surgical versus transcatheter closure of perimembranous VSDs in symptomatic children?

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Question 667

A 40-year-old patient is brought into the emergency department after suffering a motor vehicle crash where he was pinned underneath his motorcycle for about 30 minutes before a passerby called 911. While evaluating him per your institution's trauma guidelines, you discover pain upon palpation of his right lower extremity which is much larger than his left counterpart. The patient admits to decreased sensation over his right lower extremity and cannot move his leg. There are no palpable dorsalis pedis or posterior tibial pulses on this extremity, and it is colder and paler in comparison to his left side. Measured compartment pressure of his distal right leg is 35 mm Hg. What is the next best step in this patient's care?

Answer Choices:

(A) Emergent fasciotomy
(B) Venous doppler
(C) Arteriogram
(D) External fixation

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/7eb6463c-aa79-40d1-9dcb-5a3f9ab0d02f

OpenEvidence Explanation

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The answer is **A. Emergent fasciotomy**.

This patient presents with a classic case of **acute compartment syndrome (ACS)** of the right lower extremity following a crush mechanism (pinned under a motorcycle for 30 minutes). The clinical picture is unequivocal: a tense, swollen extremity with the "5 Ps" — **pain, paresthesias, paralysis, pulselessness, and pallor** — along with a measured compartment pressure of **35 mmHg**, which exceeds the widely cited absolute threshold of 30 mmHg for fasciotomy.[1][2]

Why emergent fasciotomy is the correct next step:

- ACS is a surgical emergency. An absolute compartment pressure >30 mmHg is considered an indication for emergency fasciotomy, particularly when supported by unequivocal clinical findings as in this case. Even when using the more specific delta pressure (ΔP = diastolic BP − compartment pressure), a patient with absent distal pulses and neurovascular compromise clearly has critically impaired perfusion.[1][3][4]
- Irreversible nerve and muscle damage can occur within **6 hours** of impaired perfusion, and prompt fasciotomy within 12 hours is critical — over 70% of patients recover normal limb function with timely decompression, compared to only ~10% when fasciotomy is delayed beyond 12 hours.[1][3][5]
- The definitive treatment for ACS of the lower leg is **four-compartment fasciotomy**, typically performed through two incisions.[1]

Why the other options are incorrect:

- **B. Venous Doppler** — This would evaluate for deep vein thrombosis, which does not explain the constellation of elevated compartment pressure, motor/sensory deficits, and absent arterial pulses. It would delay definitive treatment.
- **C. Arteriogram** — While absent pulses raise concern for vascular injury, the elevated compartment pressure and clinical syndrome point to ACS as the primary pathology. Fasciotomy takes priority; vascular assessment can follow decompression. Delaying surgery for an arteriogram risks irreversible tissue necrosis.

- **D. External fixation** — This would be appropriate for fracture stabilization but does not address the compartment syndrome, which is the immediate life- and limb-threatening emergency.

Would you like to explore the specific surgical technique for four-compartment fasciotomy of the lower leg, including incision placement and postoperative wound management?

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Question 669

A 43-year-old male is brought to the emergency department after his son found him vomiting bright red blood. He is visibly intoxicated, and hospital records indicate a long history of alcohol substance abuse treated with antabuse (disulfiram). Vital signs include T 98.4, HR 89, BP 154/92, and RR 20. EGD is notable for mild esophagitis, and a longitudinal esophageal tear at the gastroesophageal junction, with no active bleeding. What is the next best course of action?

Answer Choices:

(A) Cyanoacrylate injection and ligation with banding, IV fluid hydration, and NPO
(B) Conservative management with IV fluid hydration and observation
(C) Esophageal manometry and impedance studies
(D) Calcium channel blockage and Botox injection of the lower esophageal sphincter

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/c850dcb3-2440-4275-9af8-0b81491526b9

OpenEvidence Explanation

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The correct answer is **B. Conservative management with IV fluid hydration and observation**.

This clinical scenario describes a classic **Mallory-Weiss tear** — a longitudinal mucosal laceration at the gastroesophageal junction caused by forceful vomiting (here, in the setting of alcohol intoxication). The critical detail is that the EGD shows **no active bleeding**, which determines the management approach.

Why conservative management is correct:

Guidelines recommend that only Mallory-Weiss tears with **active ongoing bleeding** require endoscopic therapy.[1] A study of 66 patients with non-bleeding Mallory-Weiss tears managed without endoscopic hemostatic therapy found that only 1 patient experienced rebleeding, and that episode did not require intervention.[1] The majority of Mallory-Weiss tears are self-limiting, and most cases do not require urgent endoscopic intervention.[2] Conservative management consists of IV fluid hydration, observation, and supportive care.[3]

Why the other options are incorrect:

- **A (Cyanoacrylate injection and ligation with banding):** Cyanoacrylate is used for **gastric variceal bleeding**, not Mallory-Weiss tears. Endoscopic intervention is unnecessary here given the absence of active bleeding.[1]
- **C (Esophageal manometry and impedance studies):** These are diagnostic tools for esophageal motility disorders (e.g., achalasia) and have no role in the acute management of a Mallory-Weiss tear.
- **D (Calcium channel blockers and Botox injection of the LES):** These are treatments for **achalasia**, not Mallory-Weiss syndrome.

The following figure illustrates the management algorithm for Mallory-Weiss tears, showing that non-bleeding tears require no endoscopic therapy.

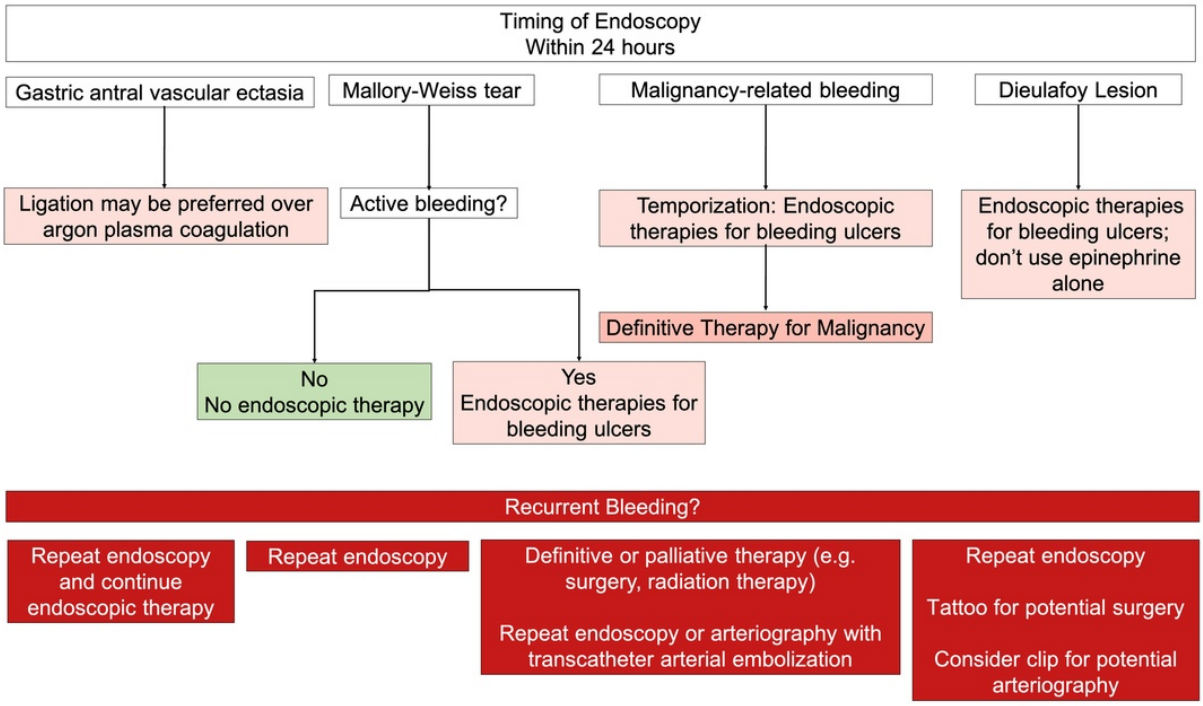


Figure 4. Endoscopic management and post-endoscopic management for patients with acute upper gastrointestinal bleeding from other aetiologies.

Would you like to explore the risk factors that predict rebleeding in Mallory-Weiss syndrome and when to escalate beyond conservative management?

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Question 671

A 19-year-old man with a past medical history significant only for facial acne presents with increased inguinal pruritis. Relevant social history includes participation in school wrestling. He has no significant family history. Other than the pruritic rash, a review of systems is negative. On physical examination, there is an erythematous, well-demarcated patch on his left thigh, over his pubic region, and throughout the perineum. The scrotum is spared. Which of the following is the most likely diagnosis?

Answer Choices:

(A) Tinea corporis
(B) Tinea cruris
(C) Candidal balanitis
(D) Tinea unguium

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/d69e2f1c-81b5-4ea6-baf4-ab8d915732a7

OpenEvidence Explanation

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The correct answer is **B. Tinea cruris**.

This presentation is classic for **tinea cruris** ("jock itch"), a dermatophyte infection of the groin, perineal, and perianal area. Several features in this vignette point directly to this diagnosis:

- **Location**: The erythematous, well-demarcated patch involves the left thigh, pubic region, and perineum — the characteristic distribution of tinea cruris, which affects the inguinal folds and medial thighs.[1][2]
- **Scrotal sparing**: This is a hallmark distinguishing feature of tinea cruris. Dermatophytes typically spare the penis and scrotum, which helps differentiate it from candidal infections (which tend to involve the scrotum with satellite lesions).[1][3]
- **Demographics and risk factors**: A young male wrestler is at high risk for dermatophyte infections due to direct skin-to-skin contact and occlusive, moist environments.[1]
- **Pruritis**: Itch is the predominant complaint in tinea cruris.[1]

The following figure demonstrates the typical appearance of tinea cruris with scrotal sparing:



Figure 2. Tinea cruris. Reprinted with permission from Ely JW, Rosenfeld S, Seabury Stone M. Diagnosis and management of tinea infections. Am Fam Physician. 2014;90(10):705.

Why not the other options?

- **A. Tinea corporis** — refers to dermatophyte infection of the body excluding the groin, scalp, beard, feet, and hands. Since the rash is localized to the groin/perineal area, tinea cruris is the correct classification.[1][4]
- **C. Candidal balanitis** — involves the glans penis and typically does not spare the scrotum; this patient has scrotal sparing and no penile involvement.[1]
- **D. Tinea unguium** — refers to dermatophyte infection of the nails (onychomycosis), which is not described here.[4]

Would you like to explore the recommended topical and systemic treatment options for tinea cruris, particularly in the context of a competitive wrestler who may need clearance to return to sport?

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Question 672

A 6-week-old girl is brought to the pediatrician for a post-natal visit. She was born at 38 weeks gestation to a 25-year-old woman via an uncomplicated spontaneous vaginal delivery. The mother reports that prenatal screening revealed no developmental abnormalities and that the baby has been gaining weight, feeding, stooling, and urinating appropriately. Physical exam of the infant is unremarkable. The mother has a history of polycystic ovarian syndrome and is curious about the development of her daughter's ovaries. Which of the following is true regarding the baby's reproductive system at this time?

Answer Choices:

(A) The baby has not yet developed oocytes
(B) The baby's oocytes are arrested in prophase
(C) The baby's oocytes are arrested in interphase
(D) The baby's oocytes are fully matured

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/5a3b8cd2-4f93-4775-810b-5ae327c256ef

OpenEvidence Explanation

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The correct answer is **B. The baby's oocytes are arrested in prophase**.

During fetal development, oogonia enter meiosis I and progress through the substages of prophase I (leptotene, zygotene, pachytene), ultimately arresting at the **diplotene substage of prophase I** — also called the **dictyate stage**.[1][2][3] By the end of the fetal period, all primary oocytes have formed and are arrested at this stage. At birth, a female newborn has approximately **1–2 million primary oocytes**, all arrested in prophase I of meiosis.[3][4]

These oocytes remain in prophase I arrest for years — from birth until puberty — when a preovulatory luteinizing hormone (LH) surge triggers meiotic resumption in select oocytes during each menstrual cycle.[5][6] At that point, the oocyte completes meiosis I and proceeds to arrest again at **metaphase II** of meiosis II, where it remains until fertilization.[1]

Why the other options are incorrect:

- **A (Not yet developed oocytes):** Oocytes begin developing during fetal life; by 20 weeks gestation, there are 6–7 million oogonia, and by birth all primary oocytes have formed.[3][7]
- **C (Arrested in interphase):** Interphase is the period between cell divisions and is not the stage of oocyte arrest. The arrest occurs specifically in prophase I of meiosis.[2][6]
- **D (Fully matured):** Oocyte maturation does not occur until after puberty, when hormonal signaling triggers meiotic resumption.[4][5]

Would you like to explore how polycystic ovarian syndrome affects folliculogenesis and oocyte quality, given the mother's history of PCOS?

Relevant images

(CONTENT OMITTED)

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Question 673

A 7-year-old boy is brought to the physician because of a 3-week history of burning sensation in his mouth. One year ago, a peripheral blood smear performed during workup of fatigue revealed erythrocytes without central pallor. His father had gallstones, for which he underwent a cholecystectomy at the age of 26 years. Examination shows pallor of the mucosal membranes, mild scleral icterus, a swollen, red tongue, and several mouth ulcers. There is darkening of the skin over the dorsal surfaces of the fingers, toes, and creases of the palms and soles. His spleen is enlarged and palpable 3 cm below the left costal margin. Laboratory studies show a hemoglobin concentration of 9.1 gm/dL, mean corpuscular volume of 104 µm3, and a reticulocyte count of 9%. Which of the following would most likely have prevented this patient's oropharyngeal symptoms?

Answer Choices:

(A) Red blood cell transfusions
(B) Gluten-free diet
(C) Vitamin B12 injections
(D) Folic acid supplementation

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/38e3905a-ef34-4abe-9ea1-3c1ed48c356b

OpenEvidence Explanation

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The answer is **D. Folic acid supplementation**.

This child has **hereditary spherocytosis** (HS) — evidenced by erythrocytes without central pallor (spherocytes), a family history of early-onset gallstones (father's cholecystectomy at age 26), and splenomegaly — who has developed a superimposed **megaloblastic crisis due to folate deficiency**. The oropharyngeal symptoms (glossitis with a swollen red tongue, mouth ulcers, and burning sensation) along with skin hyperpigmentation and macrocytosis (MCV 104) are classic manifestations of folate or B12 deficiency.[1][2][3]

Why folic acid, not B12? In hereditary spherocytosis, chronic hemolysis causes increased red cell turnover, which dramatically increases folate demand. Megaloblastic crises from folate depletion are a well-recognized complication of HS, particularly in growing children.[4] Guidelines recommend that unsplenectomized HS patients take **folic acid 2–3 mg/day until age 5 and 5 mg/day thereafter** to prevent this complication.[4] Prophylactic folic acid supplementation would have prevented the folate deficiency and its associated oropharyngeal manifestations.

The elevated reticulocyte count (9%) confirms ongoing hemolysis, and the macrocytosis in the setting of a known hemolytic anemia points to a superimposed megaloblastic process — most likely folate deficiency given the clinical context of HS. While B12 deficiency can produce identical oral findings, it is not the expected nutritional deficiency in chronic hemolytic anemias; folate depletion is the classic association.[3][4]

Would you like to explore the recommended monitoring and supplementation protocols for children with hereditary spherocytosis?

Relevant images

(CONTENT OMITTED)

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Question 674

An experimental new drug in the treatment of diabetes mellitus type 2 was found to increase the levels of incretins by preventing their degradation at the endothelium. This further increased glucose-dependent insulin production. Which of the following drugs has a mechanism of action most similar to this new experimental drug?

Answer Choices:

(A) Sitagliptin
(B) Glimepiride
(C) Canagliflozin
(D) Pioglitazone

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/0ef2c6fa-4249-4bb2-a4eb-087ff4b80e7d

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OpenEvidence Explanation

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The answer is **A. Sitagliptin**.

The experimental drug described increases incretin levels by **preventing their degradation**, which is the defining mechanism of **DPP-4 (dipeptidyl peptidase-4) inhibitors**. Sitagliptin is a DPP-4 inhibitor that works by blocking the enzyme

DPP-4, which normally degrades incretins (GLP-1 and GIP) at the vascular endothelium. By inhibiting this enzyme, sitagliptin prolongs incretin activity, leading to **glucose-dependent insulin secretion** and suppression of glucagon — exactly matching the described experimental drug.

The other options differ in mechanism:

- **B. Glimepiride** — a sulfonylurea that stimulates insulin release from pancreatic beta cells by closing ATP-sensitive K^+ channels, independent of glucose levels.
- **C. Canagliflozin** — an SGLT2 inhibitor that reduces glucose reabsorption in the proximal renal tubule, promoting glucosuria.
- **D. Pioglitazone** — a thiazolidinedione that activates PPARγ receptors, improving insulin sensitivity in peripheral tissues.

Would you like to explore how DPP-4 inhibitors compare to GLP-1 receptor agonists in terms of efficacy and cardiovascular outcomes in type 2 diabetes?

Question 675

A 60-year-old man with severe persistent asthma since the age of 14 presents with an acute exacerbation of shortness of breath, wheezing, and coughing over the last several days. His asthmatic symptoms are usually well controlled with regular high-dose inhaled triamcinolone, but over the last week or so he has developed a nocturnal cough and mild wheezing despite good compliance with controller medications. A review of several spirometry reports suggest of bronchial asthma with a partial irreversible airway obstruction. Which of the following is most likely to be associated with the recent loss of asthma control in this patient?

Answer Choices:

(A) Airway epithelial shedding
(B) Airway smooth muscle atrophy
(C) Airway remodeling
(D) Airway hyperresponsiveness

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/8b9106fa-fbd9-46f4-96b5-25a68f8b512f

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OpenEvidence Explanation

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The answer is **C. Airway remodeling**.

In a patient with **long-standing severe persistent asthma** (46 years of disease) who develops loss of control despite good compliance with high-dose inhaled corticosteroids, and whose spirometry shows **partial irreversible airway obstruction**, the most likely explanation is **airway remodeling** — the progressive structural changes that occur in chronically inflamed airways and lead to fixed airflow limitation that is poorly responsive to standard anti-inflammatory therapy.

Why airway remodeling is correct:

Airway remodeling refers to the architectural changes of the airway that result in fixed airflow limitation and reduced treatment reversibility.[1] These structural changes include subepithelial fibrosis, extracellular matrix deposition, airway smooth muscle **hypertrophy and hyperplasia** (not atrophy), goblet cell hyperplasia, and increased vascularity.[2][3] Remodeling is proportionally related to the duration and severity of disease, making this patient — with nearly five decades of severe asthma — a classic example.[3] Importantly, airway remodeling contributes to airway narrowing and diminished bronchodilator responsiveness, explaining why his symptoms are breaking through despite adequate controller therapy.[4][5]

Why the other options are less appropriate:

- **A. Airway epithelial shedding** — While epithelial disruption is a component of asthma pathology, it is part of the broader remodeling process rather than an independent cause of progressive, irreversible obstruction.[6][7]
- **B. Airway smooth muscle atrophy** — This is incorrect; asthma causes smooth muscle **hypertrophy and hyperplasia**, not atrophy. Increased smooth muscle mass is a hallmark of remodeling.[2][5]
- **D. Airway hyperresponsiveness (AHR)** — AHR is a functional hallmark of asthma but does not explain the **irreversible** component of obstruction seen on spirometry. AHR is typically responsive to corticosteroids, whereas this patient's symptoms are breaking through despite treatment. AHR itself is partly a downstream consequence of structural remodeling.[3][7]

The key clinical clue is the **partial irreversible obstruction** on spirometry in a patient with decades of severe disease — this directly points to structural airway remodeling as the underlying mechanism for loss of control.

Would you like to explore the evidence on whether biologic therapies can modify or reverse airway remodeling in long-standing severe asthma?

Relevant images

(CONTENT OMITTED)

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Question 680

A 25-year-old man presents to the office because of extreme fatigue for the past 2 days. He is also worried about his skin looking yellow. He does not have any other complaints and denies fever and headache. He admits to using illicit intravenous drugs in the past. He does not have any immunization records because he moved from Africa to the US at the age of 18. His vital signs are as follows: heart rate 72/min, respiratory rate 14/min, temperature 37.9°C (100.2°F), and blood pressure 100/74 mm Hg. Physical examination is not significant except for mild diffuse abdominal tenderness. His blood is drawn for routine tests and shows an alanine aminotransferase level (ALT) of 2,000 IU/L. A hepatitis viral panel is ordered which shows:
Anti-HAV IgM negative
HBsAg positive
Anti-HBs negative
IgM anti-HBc positive
Anti-HCV negative
Anti-HDV negative
What is the most likely diagnosis?

Answer Choices:

(A) Past hepatitis B infection
(B) Acute hepatitis A
(C) Acute hepatitis D superinfection
(D) Acute hepatitis B

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/1ada9b8c-a811-4960-b554-ef97c0d0a952

OpenEvidence Explanation

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The correct answer is **D. Acute hepatitis B**.

The serologic pattern in this case — **HBsAg positive, anti-HBs negative, and IgM anti-HBc positive** — is the classic profile of **acute hepatitis B infection**.[1][2] The presence of **IgM anti-HBc** is the key marker that distinguishes acute from chronic HBV infection, as it indicates recent infection and remains detectable for approximately 6 months.[3][4] The clinical presentation (fatigue, jaundice, low-grade fever, diffuse abdominal tenderness, and markedly elevated ALT of 2,000 IU/L) is consistent with symptomatic acute hepatitis B, which occurs in approximately 30% of immunocompetent adults.[1]

The following figure illustrates the diagnostic algorithm for interpreting HBV serologic markers:

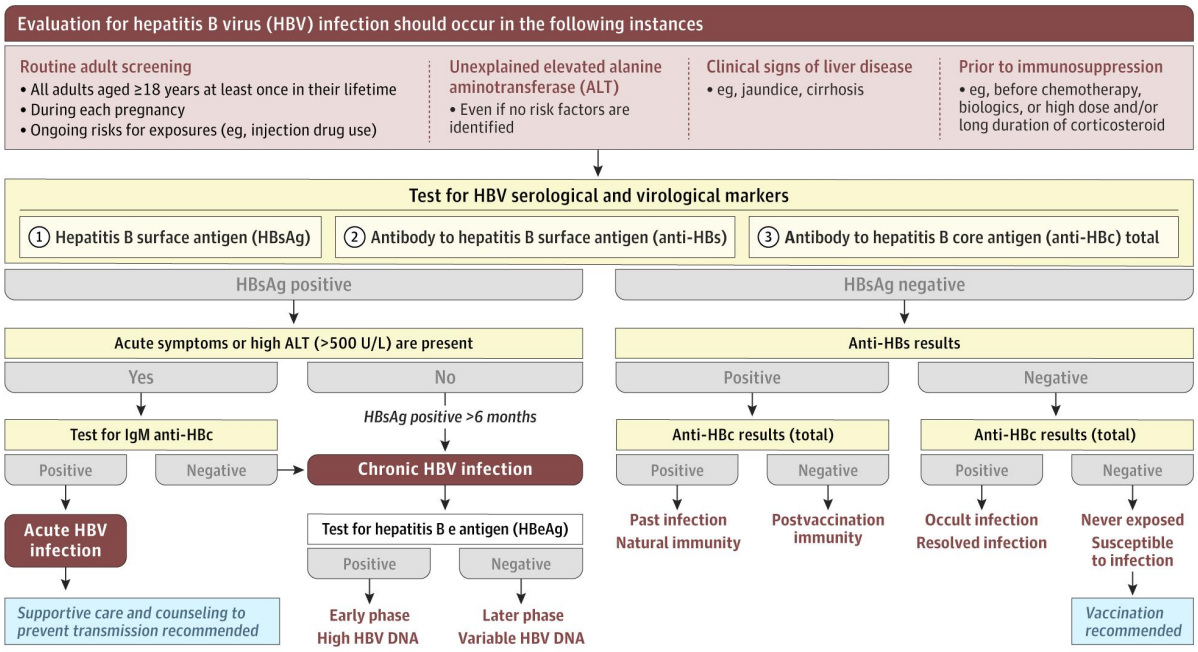


Figure 3. Chronic Hepatitis B Management

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Why the other options are incorrect:

- **A. Past hepatitis B infection** — A resolved infection would show **anti-HBs positive** and **anti-HBc (IgG) positive**, with **HBsAg negative**. This patient has the opposite pattern.[6]
- **B. Acute hepatitis A** — Anti-HAV IgM is **negative**, ruling out acute HAV infection.
- **C. Acute hepatitis D superinfection** — HDV requires HBV coinfection to replicate. Anti-HDV is **negative** in this case, excluding HDV. Additionally, a superinfection implies pre-existing chronic HBV, which would show IgG (not IgM) anti-HBc.[3]

This patient's risk factors — IV drug use and immigration from Africa (an HBV-endemic region) without immunization records — are consistent with acquisition of HBV through parenteral exposure.[7]

Would you like to explore the management approach for acute hepatitis B, including indications for antiviral therapy and monitoring for progression to chronic infection?

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Question 681

A 29-year-old female presents to her primary care provider with an aching pain in her left leg that has progressively gotten worse over several days. She recently had an unfortunate sporting incident resulting in large bruises along both legs and lower thighs. An X-ray after the event was negative for fracture. Past medical history is positive for systemic lupus erythematosus. She also has a history of one spontaneous abortion at 12 weeks gestation. Today, her heart rate is 90/min, respiratory rate is 17/min, blood pressure is 119/80 mm Hg, and temperature is 37.0°C (98.6°F). On physical examination, her left leg appears pink and slightly swollen. Homan's sign is positive. A Doppler ultrasound reveals a thrombus in the left popliteal vein. Her lab results are as follows:
Platelets 250,000/mm3
Prothrombin Time 14 sec
Partial Thromboplastin Time 90 sec
Mixing study (PTT) 89 sec
What is the most likely cause of the patient's condition?

Answer Choices:

(A) Antibodies directed against platelet glycoprotein IIb/IIIa
(B) Antibodies directed against phospholipids
(C) Antibodies directed against endothelial cells
(D) Vitamin K deficiency

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/3f2c679e-0626-4c18-b166-e8a6e4b8d368

OpenEvidence Explanation

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The most likely cause is **B. Antibodies directed against phospholipids**.

This patient presents with a classic picture of **antiphospholipid syndrome (APS)** in the setting of systemic lupus erythematosus (SLE). The key findings that point to this diagnosis include:

- **SLE** with a history of **spontaneous abortion at 12 weeks** (pregnancy loss after 10 weeks is characteristic of APS, as losses before 10 weeks are more commonly attributed to chromosomal defects)[1]
- **Deep vein thrombosis** (popliteal vein thrombus confirmed on Doppler ultrasound)
- **Markedly prolonged PTT (90 sec)** with a **normal PT (14 sec)**
- **Mixing study that does not correct** (PTT remains 89 sec), indicating the presence of an inhibitor rather than a factor deficiency[2][3]

This laboratory pattern is the hallmark of a **lupus anticoagulant**, which is caused by antiphospholipid antibodies. These antibodies bind to phospholipid-binding plasma proteins (primarily β2-glycoprotein I and prothrombin) and paradoxically prolong phospholipid-dependent coagulation assays in vitro while promoting thrombosis in vivo.[4][5] The mixing study is critical here: if the prolonged PTT were due to a factor deficiency (as in vitamin K deficiency, answer D), the addition of normal plasma would correct the clotting time. The failure to correct confirms an inhibitor is present.[2][3]

Why the other answers are incorrect:

- **A. Antibodies against platelet glycoprotein IIb/IIIa** — This is the mechanism of immune thrombocytopenic purpura (ITP), which presents with thrombocytopenia and bleeding, not thrombosis. This patient's platelet count is normal.

- **C. Antibodies against endothelial cells** — While anti-endothelial cell antibodies can occur in vasculitis, they do not produce this characteristic coagulation profile with prolonged PTT and non-correcting mixing study.

- **D. Vitamin K deficiency** — This would prolong both PT and PTT, and the mixing study would correct with the addition of normal plasma (since the deficiency would be corrected by providing the missing factors).

Lupus anticoagulant is the strongest antiphospholipid antibody predictor of venous thrombosis in SLE patients, with an OR of 6.17 (95% CI 2.77–13.76) for venous thrombotic events.[6] Approximately 30–40% of SLE patients have antiphospholipid antibodies, and the combination of thrombosis plus pregnancy morbidity in the presence of these antibodies defines the antiphospholipid syndrome.[7][8]

Would you like to explore the recommended anticoagulation strategies and monitoring for antiphospholipid syndrome, particularly regarding the choice between warfarin and direct oral anticoagulants?

Relevant images

(CONTENT OMITTED)

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Question 683

A 30-year-old man is brought to the emergency department with complaints of fever (41.5°C (106.7°F)) and diarrhea for the past 12 hours. There is no history of headaches, vomiting, or loss of consciousness. The past medical history is unobtainable due to a language barrier (the patient recently immigrated from abroad), but his wife says her husband had a motor vehicle accident when he was a teenager that required surgery. He is transferred to the ICU after a few hours in the ED because of dyspnea, cyanosis, and near-collapse. There are no signs of a meningeal infection. The Blood pressure was 70/30 mm Hg at the time of transfer. A chest X-ray at the time of admission showed interstitial infiltrates without homogeneous opacities. The initial laboratory results reveal metabolic acidosis, leukopenia with a count of 2,000/mm^3, thrombocytopenia (15,000/mm^3), and a coagulation profile suggestive of disseminated coagulation. A peripheral smear was performed and is shown below. Despite ventilatory support, administration of intravenous fluids, antibiotics, and vasopressor agents, the patient died the next day. A gram stain from an autopsy specimen of the lungs revealed gram-positive, lancet-shaped diplococci occurring singly or in chains. Which of the following organisms is most likely?

Answer Choices:

(A) Staphylococcus aureus
(B) Streptococcus pyogene
(C) Streptococcus pneumoniae
(D) Non-typeable H. influenzae

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/ad5b8a21-7e86-4925-a429-35b58761e7cb

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OpenEvidence Explanation

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The answer is **C. Streptococcus pneumoniae**.

The autopsy Gram stain revealing **gram-positive, lancet-shaped diplococci occurring singly or in chains** is the classic morphologic description of *Streptococcus pneumoniae*.[1][2][3] No other answer choice matches this morphology:

- *Staphylococcus aureus* appears as gram-positive cocci in **clusters** (grape-like), not lancet-shaped diplococci.
- *Streptococcus pyogenes* forms gram-positive cocci in **chains**, but they are round, not lancet-shaped.
- *Non-typeable H. influenzae* is a **gram-negative** coccobacillus, not gram-positive.

Clinical reasoning supporting the diagnosis: This case represents a classic presentation of **overwhelming post-splenectomy infection (OPSI)**. The key clue is the history of a motor vehicle accident as a teenager requiring surgery — this strongly suggests a traumatic splenectomy. The fulminant course — fever, diarrhea as a nonspecific prodrome, followed by rapid deterioration with septic shock (BP 70/30), DIC (thrombocytopenia 15,000/mm^3, coagulopathy), leukopenia, metabolic acidosis, and death within 24 hours — is the hallmark of OPSI.[4]

S. pneumoniae is the most common pathogen causing OPSI, identified in **42% of cases** in a prospective multicenter cohort study, with mortality as high as 50%.[4][5] The peripheral smear referenced in the question likely showed organisms visible in the blood — a finding described in high-grade pneumococcal

bacteremia in asplenic patients.[4] The risk of OPSI persists for life after splenectomy, with a median interval of 6 years (range 1 month to 50 years).[5][6]

Would you like to explore the current vaccination and prophylaxis guidelines for asplenic patients to prevent overwhelming post-splenectomy infection?

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Question 684

A 12-year-old girl is brought to the emergency department 3 hours after the sudden onset of colicky abdominal pain and vomiting. The patient also manifests symptoms of redness and swelling of the face and lips without pruritus. Her symptoms began following a tooth extraction earlier in the morning. She had a similar episode of facial swelling after a bicycle accident 1 year ago, which resolved within 48 hours without treatment. Vital signs are within normal limits. Examination shows a nontender facial edema, erythema of the oral mucosa, and an enlarged tongue. The abdomen is soft, and there is tenderness to palpation over the lower quadrants. An abdominal ultrasound shows segmental thickening of the intestinal wall. Which of the following is the most likely cause of this patient's condition?

Answer Choices:

(A) Autoantibody-mediated tissue damage
(B) Complement inhibitor deficiency
(C) Drug-induced bradykinin excess
(D) Mast-cell activation

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/1aa8e454-40cb-43d1-8e5a-c978c1f5f6e1

OpenEvidence Explanation

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The correct answer is **B. Complement inhibitor deficiency**.

This presentation is classic for **hereditary angioedema (HAE)** due to **C1 inhibitor (C1-INH) deficiency**. The key features pointing to this diagnosis include:

- **Nonpruritic** facial and lip swelling (distinguishing it from histamine/mast cell–mediated angioedema, which typically presents with urticaria and pruritus)[1][2]
- **Trauma-triggered episodes** — the current attack followed a tooth extraction, and the prior episode occurred after a bicycle accident. Minor trauma and stress are well-recognized precipitants of HAE attacks[3][4]
- **Abdominal symptoms** — colicky pain, vomiting, and segmental intestinal wall thickening on ultrasound reflect submucosal bowel edema, a hallmark of HAE abdominal attacks[5][6]
- **Self-resolving prior episode** within 48 hours, consistent with the typical HAE attack duration of 48–72 hours[6]
- **Age of onset in childhood** — HAE typically develops between ages 8 and 12 years[2]

Why not the other options?

- **A (Autoantibody-mediated tissue damage):** Acquired C1-INH deficiency involves autoantibodies but is associated with lymphoproliferative or autoimmune disorders, typically in older adults — not a 12-year-old with recurrent trauma-triggered episodes.[1]
- **C (Drug-induced bradykinin excess):** ACE inhibitor–associated angioedema causes bradykinin accumulation by reducing its degradation, but there is no mention of ACE inhibitor use, and the recurrent, trauma-triggered pattern with abdominal involvement points to HAE.[7]
- **D (Mast-cell activation):** Mast cell–mediated angioedema is histaminergic and typically presents with **urticaria and pruritus**, responds to antihistamines and epinephrine, and does not cause the characteristic intestinal wall thickening seen here.[1][2]

The underlying mechanism in HAE types I and II is a deficiency of functional C1-INH, which leads to uncontrolled activation of the plasma contact system and excessive **bradykinin** generation — the direct mediator of the angioedema.[2]

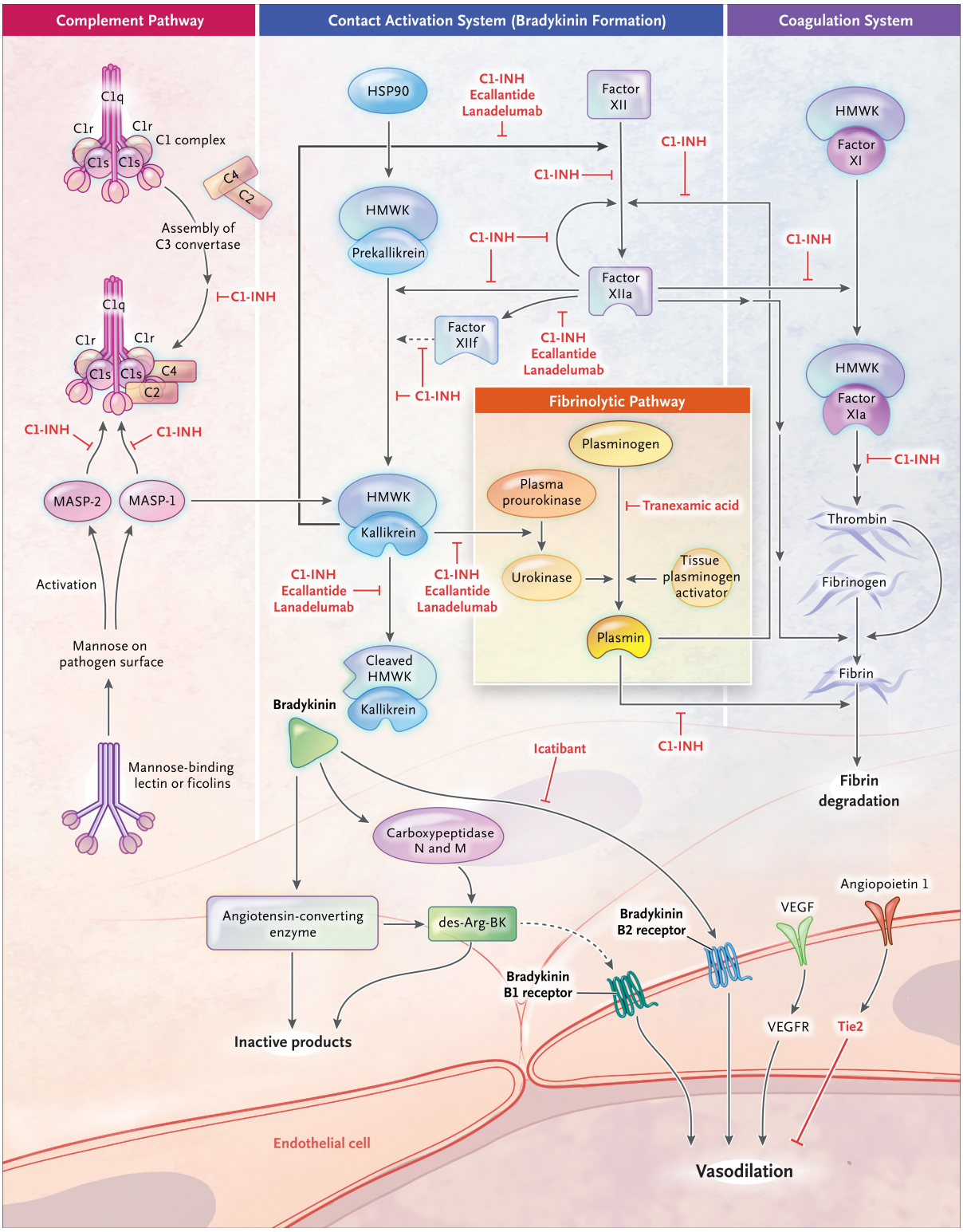


Figure 1. Contact, Complement, and Fibrinolytic Systems in Hereditary Angioedema (HAE) and Targets for Available Therapy.

Used under license from The New England Journal of Medicine.

Would you like to explore the acute and prophylactic treatment options for hereditary angioedema in pediatric patients?

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Question 689

A 33-year-old man presents to the infectious diseases clinic for follow-up. He was recently admitted to the hospital with fever, shortness of breath, and cough, and was found to have Pneumocystic jirovecii pneumonia and a new diagnosis of HIV. His CD4 count is 175, viral load is pending. As part of routine laboratory studies given his new diagnosis, an RPR was found to be positive with a titer of 1:64, and this is confirmed with a positive FTA-ABS. He is unsure when or how he acquired HIV or syphilis. His neurological examination is normal, and he has no symptoms. Which of the following is the most appropriate next step in management:

Answer Choices:

(A) Perform lumbar puncture, treat based on presence or absence of CNS disease
(B) Treat with three weekly injections of penicillin, obtain titers in 3 months
(C) Treat with three weekly injections of penicillin, obtain titers in 6 months
(D) Treat with a single injection of penicillin, obtain titers in 6 months

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/c4e42578-5916-4a50-b89c-8fff37622793

OpenEvidence Explanation

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The correct answer is **C. Treat with three weekly injections of penicillin, obtain titers in 6 months**.

Key reasoning:

This patient has a new diagnosis of syphilis with an unknown duration of infection. Since he is unsure when he acquired syphilis and there is no documentation of prior negative serologies or symptoms consistent with early syphilis, this must be classified as **latent syphilis of unknown duration**. Per CDC STI Treatment Guidelines, the recommended treatment for late latent syphilis or latent syphilis of unknown duration in persons with HIV is **benzathine penicillin G 7.2 million units total, administered as 3 doses of 2.4 million units IM at 1-week intervals**.[1]

Why not the other options?

- **A (Lumbar puncture first):** The CDC does not recommend routine CSF examination in neurologically asymptomatic patients with latent syphilis and HIV, as it has not been associated with improved clinical outcomes. While this patient does have risk factors for CSF abnormalities (RPR ≥1:32 and CD4 ≤350), current guidelines state that in the absence of neurologic signs or symptoms, lumbar puncture is not indicated.[1][2][3]

- **B (Three weekly injections, titers at 3 months):** While the treatment regimen of three weekly injections is correct, the CDC recommends serologic follow-up at **6, 12, 18, and 24 months** after therapy for HIV-positive patients with latent syphilis. The 3-month follow-up interval applies to primary and secondary syphilis in HIV-positive patients, not latent syphilis of unknown duration.[1]

- **D (Single injection, titers at 6 months):** A single injection of benzathine penicillin G is appropriate only for early syphilis (primary, secondary, or early latent within the past 12 months). Since the duration of infection is unknown, this patient requires the extended 3-dose regimen.[1][2]

Would you like to explore the indications and yield of lumbar puncture in HIV-positive patients with syphilis who have high RPR titers and low CD4 counts but no neurologic symptoms?

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Question 693

A 38-year-old woman presents to her physician's clinic for recurrent episodes of chest pain that wakes her from her sleep. While usually occurring late at night, she has also had similar pains during the day at random times, most recently while sitting at her desk in her office and at other times while doing the dishes at home. The pain lasts 10–15 minutes and resolves spontaneously. She is unable to identify any common preceding event to pain onset. The remainder of her history is unremarkable and she takes no regular medications. She works as an accountant. There is no history of smoking or drug use, however, she does consume 5 alcoholic drinks per week. Examination reveals: pulse 70/min, respirations 16/min, and blood pressure 120/70 mm Hg. A physical examination is unremarkable. Which of the following would be effective in reducing her symptoms?

Answer Choices:

(A) Aspirin
(B) Isosorbide dinitrate
(C) Heparin
(D) Propranolol

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/4d484a0c-0856-42f3-aefb-72d8c8fda817

OpenEvidence Explanation

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The answer is **B. Isosorbide dinitrate**.

This clinical presentation — recurrent chest pain occurring at rest (including during sleep), in a young woman without traditional cardiovascular risk factors, with episodes that are transient (10–15 minutes) and resolve spontaneously without an identifiable exertional trigger — is classic for **variant (Prinzmetal's) angina**, which is caused by coronary artery vasospasm.

Why isosorbide dinitrate is correct: Coronary spasm is highly responsive to nitrates and calcium channel blockers, which are considered first-line therapies.[1][2][3] Nitrates such as isosorbide dinitrate act as vasodilators, directly relaxing coronary smooth muscle and relieving vasospasm.[4]

Why the other options are incorrect:

- **A. Aspirin** — Aspirin has not been shown to reduce major adverse cardiovascular events in vasospastic angina without significant coronary artery disease. It may even worsen vasospasm via prostacyclin inhibition.[5]
- **C. Heparin** — Anticoagulation does not address the underlying mechanism of coronary vasospasm and has no role in the management of variant angina.
- **D. Propranolol** — Beta-blockers are **contraindicated** in vasospastic angina. They can precipitate unopposed alpha-adrenergic–mediated vasoconstriction, worsening coronary spasm. A study directly demonstrated that propranolol did not suppress but rather aggravated exercise-induced attacks in patients with variant angina, while nifedipine (a calcium channel blocker) suppressed them.[4][6][7]

Would you like to explore the diagnostic workup for suspected Prinzmetal's angina, including the role of provocative testing with ergonovine or acetylcholine?

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Question 694

A 16-year-old male presents to his pediatrician with complaints of malaise, fatigue, sore throat, and fever over the last several days. His vital signs are as follows: T 39.1 C, HR 82, BP 122/76, RR 14, and SpO2 99%. Physical examination is significant for splenomegaly, tonsillar exudate, and posterior auricular lymphadenopathy. The tonsils are not notably enlarged. Laboratory work-up shows an elevated lymphocyte count, atypical lymphocytes on a peripheral blood smear, and a positive heterophile antibody screen. Which of the following is the best management of this patient's condition?

Answer Choices:

(A) Bed rest and activity limitation
(B) Ganciclovir
(C) Amoxicillin
(D) Prednisone

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/5d58497f-ae6b-4243-a360-465c88b9fd83

OpenEvidence Explanation

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The best answer is **A. Bed rest and activity limitation**. This presentation — a 16-year-old with fever, sore throat, tonsillar exudate, posterior auricular lymphadenopathy, splenomegaly, atypical lymphocytes, and a positive heterophile antibody test — is classic for **infectious mononucleosis (IM)** caused by Epstein-Barr virus (EBV). Management is **supportive care**, with activity restriction to reduce the risk of splenic rupture.

Why the other options are incorrect:

- **B. Ganciclovir** — Antiviral therapy has not been shown to diminish the severity or duration of IM symptoms. A Cochrane review found no benefit of antivirals for uncomplicated IM.[1]
- **C. Amoxicillin** — Amoxicillin (and other aminopenicillins) should be specifically avoided in IM, as they cause a characteristic **pruritic maculopapular rash** in a high proportion of patients with EBV infection. Antibiotics are only indicated if concurrent streptococcal pharyngitis is confirmed, and in that case, a non-penicillin agent should be used.[2]
- **D. Prednisone** — Corticosteroids are **not indicated for uncomplicated IM**. They are reserved for specific complications such as impending airway obstruction from tonsillar hypertrophy, severe thrombocytopenia, hemolytic anemia, or myocarditis. This patient's tonsils are not notably enlarged, so there is no indication for steroids.[3][4][5]

Key management principles for IM:

IM is self-limiting, typically resolving within 2–8 weeks. Treatment centers on acetaminophen or NSAIDs for fever and throat discomfort, adequate hydration and nutrition, and rest — though strict bed rest is not necessary.[5] The most important counseling point is **avoidance of contact/collision sports and heavy exertion for at least 3 weeks** from symptom onset due to the risk of splenic rupture, which occurs in 0.1–0.2% of cases but can be fatal.[3][5][6] Return to activity should be guided by shared decision-making once the patient is afebrile and clinically improved.[4][6]

> "Although getting adequate rest is prudent, bed rest is unnecessary. Patients may excrete high levels of EBV in their saliva in the year after the onset of infectious mononucleosis, but special precautions against

transmission of EBV are not necessary, since most people are EBV-seropositive."

—Katherine Luzuriaga, M.D. et al., University of Massachusetts Medical School. Infectious Mononucleosis. N Engl J Med. May 27, 2010.

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Would you like to explore the evidence on timing and criteria for safe return to contact sports in adolescents with infectious mononucleosis and splenomegaly?

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Question 696

A 38-year-old woman presents to her primary care physician for her yearly exam. Her only complaint is difficulty losing weight. Her BMI is 34 kg/m^2. In addition to a standard physical exam, the physician orders a glucose tolerance test. The woman's fasting blood glucose level is 120 mg/dL and two-hour post 75g glucose load blood glucose level is 190 mg/dL. The physician informs the patient that she is pre-diabetic or at risk of developing diabetes and recommends lifestyle modification with follow-up in 6 months. Which of the following endogenous signaling molecules or receptors will increase insulin sensitivity in this patient?

Answer Choices:

(A) Catecholamines
(B) Glucagon
(C) Glucocorticoids
(D) Peroxisome proliferator-activated receptor gamma

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/c5032794-254c-4a6b-9503-e488e5fc5363

OpenEvidence Explanation

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The answer is **D. Peroxisome proliferator-activated receptor gamma (PPARγ)**.

PPARγ is a nuclear receptor that serves as a key regulator of **insulin sensitivity** in major glucose-utilizing tissues including adipose tissue, liver, and skeletal muscle.[1][2][3] Activation of PPARγ increases insulin sensitivity through several mechanisms:

- **Upregulation of GLUT4 translocation** to the cell surface, increasing glucose uptake in adipocytes and muscle cells[2]
- **Promotion of adipocyte differentiation and lipid storage** in adipose tissue, which protects peripheral tissues (liver, muscle) from lipotoxicity caused by ectopic fat accumulation[3]
- **Regulation of adipokines** such as adiponectin (which enhances insulin sensitivity) and suppression of pro-inflammatory cytokines like TNFα and resistin that promote insulin resistance[2][3]

This is the basis for the thiazolidinedione (TZD) drug class (e.g., pioglitazone, rosiglitazone), which are synthetic PPARγ agonists used clinically to treat type 2 diabetes by improving insulin sensitivity.[1][4]

The other three options all **decrease** insulin sensitivity (i.e., they are counter-regulatory hormones that promote insulin resistance):

- **Catecholamines** (A) antagonize insulin by stimulating gluconeogenesis, glycogenolysis, and lipolysis, and by inhibiting peripheral glucose uptake via β-adrenergic mechanisms.[5][6]
- **Glucagon** (B) opposes insulin action primarily in the liver by promoting hepatic glucose output.[5]
- **Glucocorticoids** (C) induce insulin resistance by reducing glucose transporter number/efficacy and by increasing circulating glucagon and free fatty acids; clinically, Cushing's syndrome (glucocorticoid excess) is associated with glucose intolerance and insulin resistance.[5][7][8]

Would you like to explore the specific mechanisms by which thiazolidinediones improve insulin sensitivity in prediabetic patients and the evidence for their use in diabetes prevention?

Relevant images

(CONTENT OMITTED)

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Question 697

A 35-year-old male presents to the emergency department for evaluation of hemoptysis. A chest X-ray reveals bilateral focal pulmonary consolidation. On further questioning, he admits having hematuria. Urinalysis shows RBC casts and 400 mL of urine is excreted in 24 hours. What is the most likely cause of hemoptysis and hematuria in this patient?

Answer Choices:

(A) Anti-Smith antibodies
(B) Anti-neutrophil antibodies
(C) Anti-mitochondrial antibodies
(D) Anti-glomerular basement membrane antibodies

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/7ac51550-8605-4e63-87f8-ba5f0a3e7977

OpenEvidence Explanation

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The answer is **D. Anti-glomerular basement membrane (anti-GBM) antibodies**.

This presentation — hemoptysis with bilateral pulmonary consolidation, hematuria with **RBC casts**, and oliguria (400 mL/24 hours) in a young male — is the classic **pulmonary-renal syndrome of Goodpasture disease** (anti-GBM

disease). Anti-GBM antibodies target the noncollagenous (NC1) domain of the α3 chain of type IV collagen, which is present in both glomerular and alveolar basement membranes, explaining the simultaneous lung and kidney involvement. [1][2]

Why the other options are incorrect:

- **A. Anti-Smith antibodies** — These are highly specific for systemic lupus erythematosus (SLE). While SLE can cause a pulmonary-renal syndrome, it typically presents with additional systemic features (rash, arthritis, serositis) and is far more common in women.
- **B. Anti-neutrophil antibodies (ANCA)** — ANCA-associated vasculitides (granulomatosis with polyangiitis, microscopic polyangiitis) can also cause a pulmonary-renal syndrome. However, the classic board-style presentation of a young male with hemoptysis, rapidly progressive glomerulonephritis with RBC casts, and oliguria points most directly to Goodpasture disease. Notably, some patients with anti-GBM disease are also ANCA-positive (~10–30%), but anti-GBM antibodies are the primary pathogenic driver in this scenario.[3][4]
- **C. Anti-mitochondrial antibodies** — These are associated with primary biliary cholangitis, a hepatic condition unrelated to pulmonary-renal syndromes.

Key clinical features supporting anti-GBM disease:

- Anti-GBM disease with pulmonary involvement is more frequent in **men (~80%)** and typically occurs in younger patients.[2]
- RBC casts indicate glomerular origin of hematuria, and ~80% of patients have crescents in more than half of their glomeruli.[2]
- Oliguria at presentation reflects the severity and rapidity of glomerular injury.[3]
- Treatment requires urgent plasmapheresis to remove circulating anti-GBM antibodies combined with immunosuppression (corticosteroids and cyclophosphamide).[1][5]

Would you like to explore the prognostic factors and treatment thresholds that determine renal recovery in anti-GBM disease?

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Question 699

A 25-year-old female presents to her primary care physician complaining of double vision. She first started seeing double after a long day at her work as a radiation technologist. Since then, her vision has appeared to worsen in the evenings. She has also felt worsening fatigue despite no change in her work hours or sleep habits. She has a history of type I diabetes mellitus and her most recent hemoglobin A1c was 7.4%. Her family history is notable for Sjogren's syndrome in her mother and hypertension, hyperlipidemia, and carotid dissection in her father. Her temperature is 98.9°F (37.2°C), blood pressure is 105/70 mmHg, pulse is 75/min, and respirations are 16/min. On examination, her pupils are equally round and reactive to light. Extraocular movements are intact. Mild ptosis is noted bilaterally but worse on the left. A visual acuity test reveals no abnormalities. Which of the following medications is most appropriate in the management of this patient?

Answer Choices:

(A) Pyridostigmine
(B) Physostigmine
(C) Hydrocortisone
(D) Azathioprine

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/99b58f53-f9ac-407d-bc8a-b3619229d42f

OpenEvidence Explanation

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The correct answer is **A. Pyridostigmine**.

This clinical vignette describes a young woman with **diplopia that worsens in the evening**, bilateral ptosis, and progressive fatigue — classic features of **myasthenia gravis (MG)**. The hallmark of MG is fatigable weakness that worsens with sustained activity and improves with rest, which explains the pattern of symptoms worsening at the end of the day. The association with type 1 diabetes and a family history of Sjögren's syndrome further supports an autoimmune predisposition.

Pyridostigmine, an acetylcholinesterase inhibitor, is the **first-line pharmacologic agent** in most patients with MG.[1][2][3] It works by inhibiting acetylcholinesterase, thereby prolonging acetylcholine activity at the neuromuscular junction and improving neuromuscular transmission.[1] The International Consensus Guidance for Management of MG states that pyridostigmine should be part of the initial treatment in most patients, and for those with mild disease who achieve near-full remission with symptomatic therapy, no additional drug therapy is recommended.[2][3]

Why not the other options?

- **B. Physostigmine** — This is also a cholinesterase inhibitor but crosses the blood-brain barrier (tertiary amine) and is used primarily for anticholinergic toxicity (e.g., atropine overdose), not MG. Pyridostigmine (a quaternary ammonium compound) acts peripherally and is preferred for MG.

- **C. Hydrocortisone** — While corticosteroids are used in MG, they are reserved for patients who do not meet treatment goals after an adequate trial of pyridostigmine. Corticosteroids are not first-line initial therapy.[2][4]

- **D. Azathioprine** — This is a nonsteroidal immunosuppressive agent used as a steroid-sparing agent in MG, but it is added only when corticosteroids

alone are insufficient, contraindicated, or cause significant side effects. It is not appropriate as initial monotherapy.[2][5]

Would you like to explore the diagnostic workup for suspected myasthenia gravis, including the role of acetylcholine receptor antibody testing and repetitive nerve stimulation?

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Question 700

A 76-year-old woman visits a physician for a general medical examination. She is asymptomatic. Six months prior, she had a cerebral stroke with left hemiparesis, from which she has almost completely recovered with physiotherapy. She has a history of hypertension and atrial fibrillation (AF). She has no significant ischemic, valvular, or structural heart disease. She takes metoprolol, amlodipine, warfarin, and atorvastatin. Blood pressure is 125/70 mm Hg, pulse is 75/min with an irregular rhythm. Respirations are 13/min. She has a minor limp and weakness in her left arm and leg. Heart exam shows no abnormalities other than irregular beats. To assess adherence and therapeutic efficacy in this patient, which of the following studies should be ordered?

Answer Choices:

(A) Echocardiogram
(B) International normalized ratio
(C) Partial thromboplastin time
(D) Serum drug levels

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/9536cbb7-2336-4f5e-bf94-22598a8134b0

OpenEvidence Explanation

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The answer is **B. International normalized ratio (INR)**.

The **INR** is the standard test used to monitor both adherence and therapeutic efficacy in patients taking **warfarin**. This patient has nonvalvular atrial fibrillation with a history of prior stroke and is on warfarin for stroke prevention — making routine INR monitoring essential.

The 2023 ACC/AHA/ACCP/HRS Guideline for the Management of Atrial Fibrillation gives a **Class I recommendation** that patients with AF receiving warfarin should maintain a **target INR of 2.0 to 3.0**, with routine INR monitoring to optimize time in therapeutic range and minimize risks of thromboembolism and major bleeding.[1] The INR should be determined at least weekly during initiation and **at least monthly** once stable.[2] A systematic review of 47 studies demonstrated that time in therapeutic INR range was negatively correlated with both thromboembolism risk ($R = -0.59$, $P = 0.01$) and major bleeding risk ($R = -0.59$, $P = 0.002$).[3]

Why the other options are incorrect:

- **A. Echocardiogram** — The patient has no significant valvular or structural heart disease and is asymptomatic. An echocardiogram would not assess warfarin adherence or efficacy.
- **C. Partial thromboplastin time (PTT)** — PTT monitors **heparin** therapy (unfractionated heparin), not warfarin. Warfarin affects the extrinsic pathway, which is measured by the **prothrombin time (PT)/INR**, not the PTT.
- **D. Serum drug levels** — Warfarin is not monitored by serum drug levels. Its therapeutic effect is assessed functionally via the INR, which reflects the degree of anticoagulation achieved.

Would you like to explore whether this patient's current warfarin therapy should be transitioned to a DOAC given her stroke history and CHA_2DS_2-VASc score?

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Question 702

Accurate and rapid identification of individuals with tuberculosis (TB) is crucial to accomplishing the goal of the World Health Organization (WHO) to eliminate this disease. One of the key strategies for the detection of TB is the use of tuberculin skin testing as a globally pertinent screening method, due to its low cost and technical simplicity. A study from Brazil demonstrated 76.7% accuracy, 67.9% sensitivity, 84.4% specificity, 79.1% positive predictive value, and 75% negative predictive value when using 5-mm skin elevation as a threshold, or cut-off, point for the screening test (following intradermal injection). Lowering the cut-off point to 4 mm would also result in an increase in which test property?

Answer Choices:

(A) Convergent validity
(B) Discriminant validity
(C) Negative predictive value
(D) Test specificity

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/919873f6-6473-4d35-a734-943b7e147fd5

OpenEvidence Explanation

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The answer is **C. Negative predictive value**.

Lowering the cut-off point from 5 mm to 4 mm makes the test criterion less stringent for declaring a result "positive." This fundamental trade-off in diagnostic testing means that **lowering the threshold increases sensitivity** (more true positives are captured) while **decreasing specificity** (more false positives occur).[1][2][3] This inverse relationship between sensitivity and specificity at different cut points is a core principle illustrated by the receiver operating characteristic (ROC) curve.

The following ROC curve figure illustrates how shifting the threshold along the curve changes the trade-off between sensitivity and specificity:

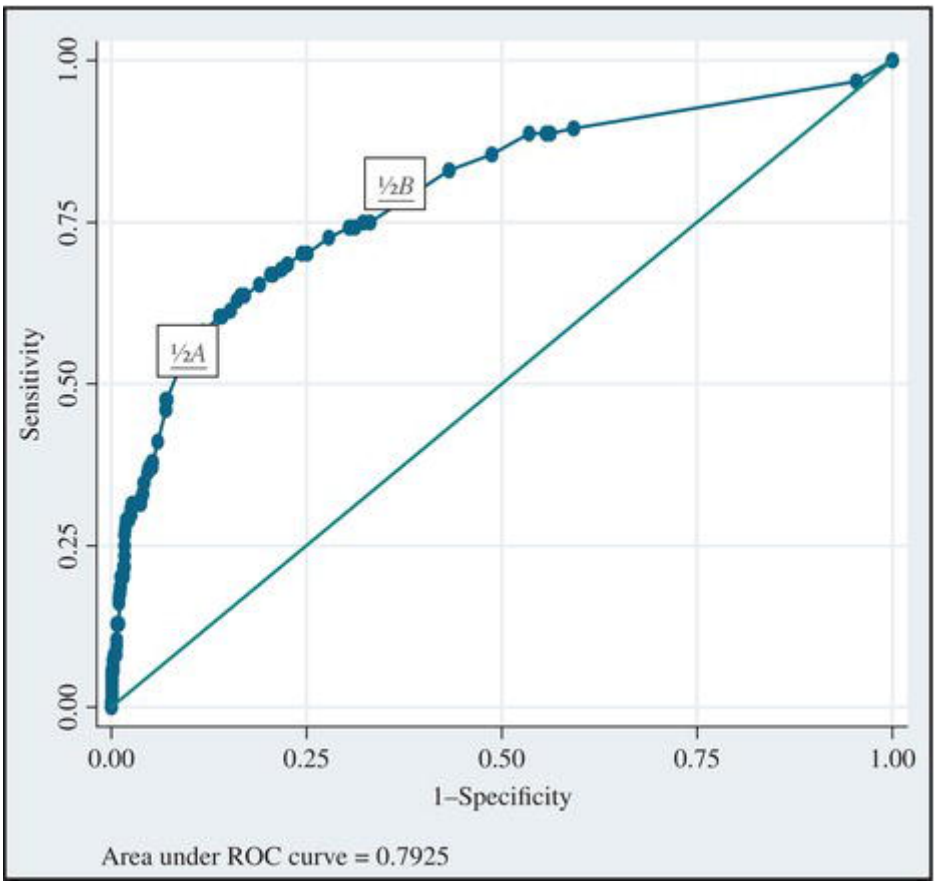


Figure 3. Receiver operator characteristic (ROC) curve. Note: A and B are two specific points on the ROC curve. The slope of the line between the two is the interval likelihood ratio.

With increased sensitivity, the test correctly identifies a greater proportion of truly infected individuals, which means fewer false negatives. Since **negative predictive value (NPV)** is defined as true negatives / (true negatives + false negatives), a reduction in false negatives directly increases the NPV.[1][5] This is consistent with the data from the TST study cited in the question: at a 5-mm

cut-off, the NPV was 75%, and lowering the threshold to 4 mm would capture additional true positives (reducing false negatives), thereby improving the NPV.

The other options are incorrect:

- **A (Convergent validity)** and **B (Discriminant validity)** are psychometric properties related to construct validity, not properties affected by shifting a diagnostic cut-off point.
- **D (Test specificity)** would actually decrease with a lower cut-off, as more non-diseased individuals would be incorrectly classified as positive.[1][2]

Would you like to explore how different TST cut-off thresholds are applied in clinical practice based on patient risk stratification?

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Question 704

A one-week-old, full-term infant born by uncomplicated vaginal delivery is brought to a pediatrician by his mother, who notes that her daughter's skin appears yellow. She reports that the child cries several times per day and sleeps 7-8 hours at night, uninterrupted. She has been breastfeeding exclusively and feels that he has been feeding well. Which of the following is the best treatment for this condition?

> **Answer Choices:**
>
> (A) Phenobarbital administration
> (B) Plasma exchange
> (C) Switch from breast milk to formula
> (D) Continue normal breast feeding

> **Correct Answer:**
>
> **(D)**
>
> **OpenEvidence Response:**
>
> **(D)** ✓

OpenEvidence Link: https://openevidence.com/ask/ba965bae-e11b-4745-be6f-11ad908e652a

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OpenEvidence Explanation

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The correct answer is **D. Continue normal breastfeeding**.

This clinical scenario describes **breast milk jaundice**, a benign condition that presents in the first 1–2 weeks of life in an otherwise healthy, well-feeding

breastfed infant. It is distinct from "breastfeeding jaundice" (suboptimal intake hyperbilirubinemia), which peaks at days 3–5 and is associated with inadequate milk intake and excess weight loss. Breast milk jaundice is characterized by prolonged unconjugated hyperbilirubinemia that can persist up to 3 months and is almost always nonpathologic.[1][2]

Why continue breastfeeding?

The AAP guidelines emphasize that breast milk jaundice occurring in a healthy, thriving infant who is gaining weight appropriately and stooling frequently requires **no treatment**.[2] Breastfed infants who are adequately hydrated should not routinely receive formula supplementation.[1] Mothers of jaundiced newborns are more than twice as likely to stop breastfeeding, and positive encouragement from clinicians is one of the strongest predictors of continued breastfeeding.[3] Switching to formula (option C) is not indicated in this scenario.

Why not the other options?

- **Phenobarbital (A):** Not part of standard management for physiologic or breast milk jaundice.
- **Plasma exchange (B):** Reserved for severe hemolytic disease or exchange transfusion-level hyperbilirubinemia, not applicable here.
- **Switch to formula (C):** Discontinuation of breastfeeding is not necessary for breast milk jaundice. The AAP explicitly states that the need for phototherapy in an otherwise healthy infant is not an indication for formula supplementation unless bilirubin levels are approaching exchange transfusion thresholds.[2]

One important clinical note: the mother reports the infant sleeps 7–8 hours uninterrupted at night, which may suggest suboptimal feeding frequency. The AAP recommends breastfeeding at least 8 times per 24 hours.[1][4] While the best answer among the choices is to continue breastfeeding, in practice, counseling to increase feeding frequency (including waking the infant for nighttime feeds) would be an important component of management.

Would you like to explore the AAP's updated phototherapy thresholds and when escalation of care is indicated in neonatal hyperbilirubinemia?

Relevant images

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Question 705

A 35-year-old woman arrives to the clinic complaining of progressive urinary leakage that has occurred for the past 1 year. At first, she would notice leakage only during athletic exercise, but now the incontinence occurs even when she laughs or coughs. The patient states that she goes to the bathroom more frequently to try to prevent “wetting myself.” She wakes up once a night to urinate. She denies dysuria, hematuria, abdominal pain, and abnormal vaginal discharge. The patient has bipolar syndrome and takes lithium. She had an uncomplicated vaginal delivery 10 years ago and a cesarean section 4 years ago. She has had no other surgeries. She drinks at least 6 glasses of water a day but may drink more on days she goes for a long run. She also has a large coffee in the morning and another coffee mid-day if she “needs to focus.” The patient denies tobacco, alcohol, and other recreational drug use. Pelvic examination and speculum examination are unremarkable. When that patient is asked to Valsalva, leakage of urine is observed. A urinalysis, including specific gravity, is within normal limits. A beta-human chorionic gonadotropin is negative. Which of the following is the most likely cause of the patient’s symptoms?

Answer Choices:

(A) Diabetic polyuria
(B) Primary polydipsia
(C) Urethral hypermobility
(D) Vescicovaginal fistula

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/52afba5a-e785-48eb-92cb-a45031d121cf

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OpenEvidence Explanation

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The correct answer is **C. Urethral hypermobility**.

This patient presents with classic **stress urinary incontinence (SUI)** — progressive leakage initially with exercise, now with coughing and laughing, and a positive Valsalva leak test on examination. The most common mechanism of SUI in premenopausal women is **urethral hypermobility**, which results from loss of support of the pelvic-floor musculature or vaginal connective tissue, such that the urethra and bladder neck do not close sufficiently in response to increases in intraabdominal pressure.[1][2]

Why urethral hypermobility fits best:

- The hallmark of SUI is involuntary urine loss with increased abdominal pressure (coughing, sneezing, exercise), exactly as described.[1][2]
- Vaginal delivery is a major risk factor for SUI, conferring approximately twice the risk compared with cesarean delivery. This patient had a prior vaginal delivery.[1][3]
- The positive Valsalva leak test objectively confirms stress incontinence.[1]
- The pelvic and speculum exams are unremarkable, ruling out significant prolapse or fistula.

Why the other options are incorrect:

- **A. Diabetic polyuria** — The urinalysis (including specific gravity) is normal, with no glycosuria. Polyuria would cause frequency and large volumes but not provocation-specific leakage with Valsalva.

- **B. Primary polydipsia** — While lithium can cause nephrogenic diabetes insipidus (leading to polydipsia/polyuria), the normal urinalysis with normal specific gravity argues against this. Additionally, primary polydipsia would not explain leakage specifically triggered by coughing and exercise.

- **D. Vesicovaginal fistula** — A fistula would cause continuous, unprovoked leakage rather than stress-provoked incontinence, and the speculum exam would typically reveal the fistula or continuous vaginal discharge. The exam here was unremarkable.[1]

Would you like to explore the first-line behavioral and conservative management strategies for stress urinary incontinence?

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Question 707

A 47-year-old woman presents to a physician for evaluation of vomiting and diarrhea for 2 days. Her symptoms began following a company picnic a few days ago. Initially, she was unable to tolerate any solids or liquids by mouth, but now has been able to drink sips of water. She had a mild headache, which was relieved with acetaminophen. The past medical history is unremarkable. She does not take any medications. The blood pressure is 120/60 mm Hg and the heart rate is 60/min. On examination, the mucous membranes are dry and the eyes are slightly sunken. Where is most of the sodium reabsorbed in this patient's kidneys?

> **Answer Choices:**
>
> (A) Distal tubule
> (B) Descending limb of loop of Henle
> (C) Proximal tubule
> (D) Ascending limb of loop of Henle

> **Correct Answer:**
>
> (C)
>
> **OpenEvidence Response:**
>
> (C) ✓

OpenEvidence Link: https://openevidence.com/ask/dd77df15-5e88-4c99-9fce-2d01d0cb5896

OpenEvidence Explanation

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The correct answer is **C. Proximal tubule**.

The **proximal tubule reabsorbs approximately 65–67% of filtered sodium**, making it the site of greatest sodium reabsorption in the nephron.[1][2][3] This is a consistent finding across renal physiology: the proximal tubule handles the bulk of sodium reabsorption via the Na^+/H^+ exchanger (NHE3) on the apical membrane, driven by the basolateral Na^+-K^+-ATPase.[3][4]

In this clinical scenario — a patient with signs of volume depletion (dry mucous membranes, sunken eyes) from vomiting and diarrhea — the kidneys would be maximizing sodium reabsorption to preserve extracellular volume. Notably, in hypovolemic states, circulating angiotensin II and catecholamines can increase proximal tubular sodium reabsorption from the baseline ~66% up to **80%**, further emphasizing the proximal tubule's dominant role.[2]

The following figure illustrates the sites of sodium reabsorption along the nephron and the corresponding diuretic sites of action:

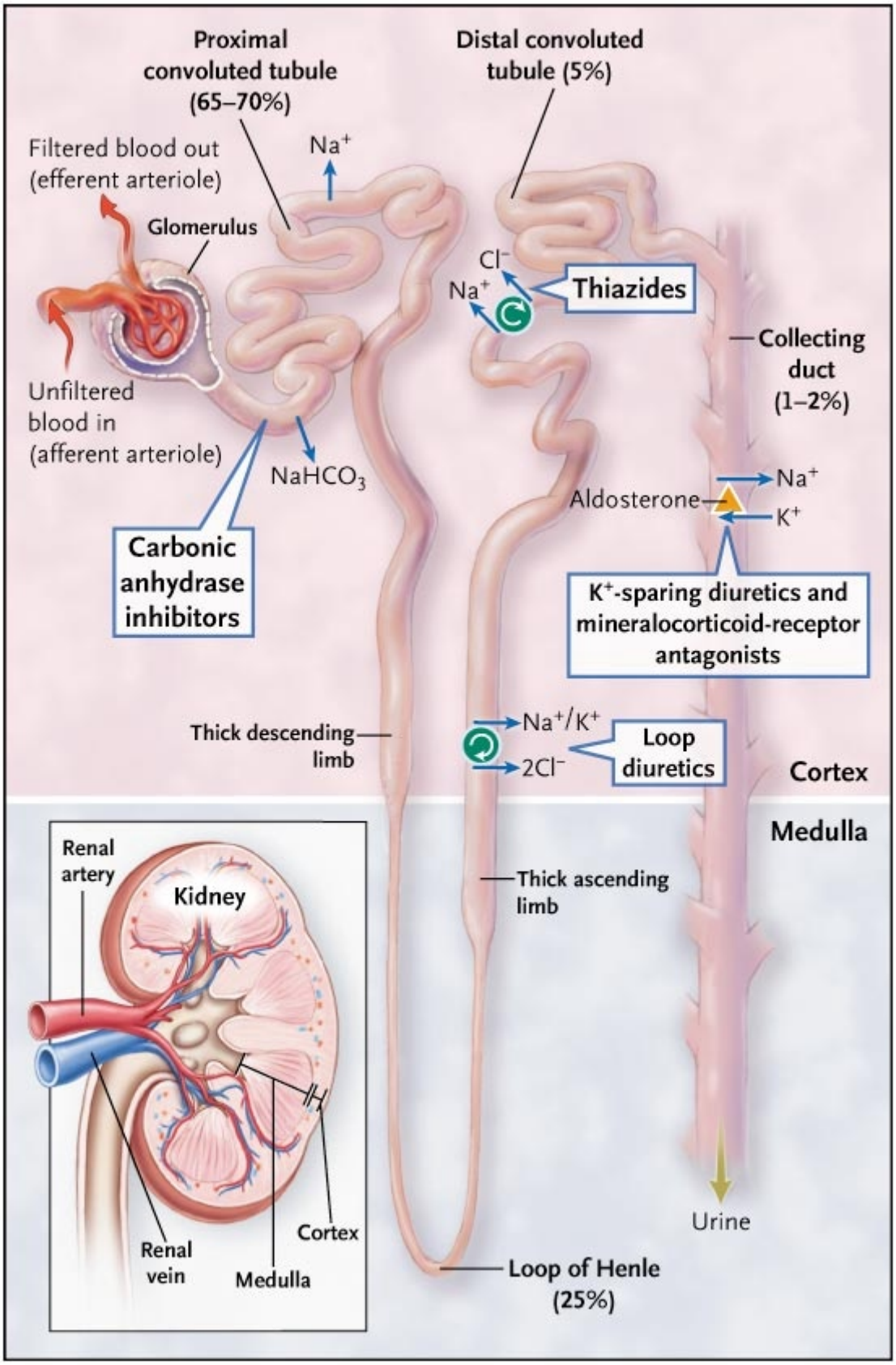


Figure 1. Sites of Diuretic Action in the Nephron.

Used under license from The New England Journal of Medicine.

Why the other options are incorrect:

- **A. Distal tubule** — Reabsorbs only ~5–10% of filtered sodium via the NaCl cotransporter (NCC)[3][6]
- **B. Descending limb of loop of Henle** — Permeable primarily to water, not a significant site of active sodium reabsorption[3]
- **D. Ascending limb of loop of Henle** — Reabsorbs ~20–30% of filtered sodium via NKCC2, making it the second largest site, but still far less than the proximal tubule[3][7][8]

Would you like to explore how angiotensin II and other neurohormonal mechanisms upregulate proximal tubular sodium reabsorption during hypovolemic states?

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Question 708

A one-week-old boy presents with yellow sclerae, severe lethargy, and decreased muscle tone. His mother notes that the symptoms started shortly after birth and have been progressively worsening. The patient is breast fed and takes no medications. His labs are within normal limits with the exception of his liver function tests as follows:

ALT: 8 U/ L
AST: 10 U/L
Alkaline phosphatase: 50 U/L
Albumin: 3.7 g/dL
Total protein: 6.7 g/dL
Bilirubin, total: 29.4 mg/dL
Bilirubin, unconjugated: 29.2 mg/dL
Bilirubin, conjugated: 0.2 mg/dL

The boy is taken immediately for treatment. What is the most likely underlying cause of his condition?

Answer Choices:

(A) Absence of UDP-glucuronosyltransferase-1A1
(B) Alteration in the ankyrin protein
(C) Reduction in UDP-glucuronosyltransferase-1A1 activity
(D) Deficiency in glucocerebrosidase

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/756c773c-64d7-49dc-8489-27c541c3ce58

OpenEvidence Explanation

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The correct answer is **A. Absence of UDP-glucuronosyltransferase-1A1**, consistent with **Crigler-Najjar syndrome type I**.

This neonate presents with dangerously elevated **unconjugated bilirubin (29.2 mg/dL)** with onset shortly after birth, progressive worsening, severe lethargy, decreased muscle tone (signs of early bilirubin encephalopathy/kernicterus), and otherwise normal liver function tests — a classic presentation of Crigler-Najjar syndrome type I (CN-I).

Why answer A is correct:

Crigler-Najjar syndrome type I is caused by **complete absence** of UDP-glucuronosyltransferase-1A1 (UGT1A1) enzyme function due to biallelic loss-of-function mutations in the UGT1A1 gene. This results in the inability to conjugate bilirubin, leading to severe unconjugated hyperbilirubinemia from birth with total bilirubin levels typically ranging from 20–50 mg/dL. Jaundice is apparent from birth and progressively accumulates, posing a high risk of kernicterus.[1][2] The neurological signs in this infant (lethargy, hypotonia) suggest early bilirubin-induced neurologic dysfunction.[3]

Why the other answers are incorrect:

- **C. Reduction in UGT1A1 activity** — This describes either Crigler-Najjar syndrome type II (CN-II, <20% enzyme activity) or Gilbert syndrome (~30% activity). CN-II produces milder hyperbilirubinemia (typically <20 mg/dL), and Gilbert syndrome causes only mild, intermittent jaundice. Neither would produce this degree of hyperbilirubinemia with neurological compromise in the first week of life.[2][4]

- **B. Alteration in the ankyrin protein** — Ankyrin defects cause hereditary spherocytosis, a hemolytic anemia. While this can cause neonatal jaundice, it would be expected to show evidence of hemolysis (anemia, reticulocytosis, elevated LDH) rather than isolated unconjugated hyperbilirubinemia with otherwise normal labs.

- **D. Deficiency in glucocerebrosidase** — This causes Gaucher disease, a lysosomal storage disorder that does not typically present with isolated severe unconjugated hyperbilirubinemia in the first week of life.

The key distinguishing features pointing to CN-I are the **extreme** unconjugated bilirubin level, onset from birth with progressive worsening, normal hepatic transaminases, and early neurological signs — all consistent with complete absence rather than mere reduction of UGT1A1 activity.[1][5]

Would you like to explore the management differences between Crigler-Najjar syndrome types I and II, including the role of phototherapy, plasmapheresis, and liver transplantation?

Relevant images

(CONTENT OMITTED)

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6. Neonatal Jaundice. Rebecca Puddifoot. Chapter 11.1

7. Approach to the patient with abnormal liver chemistries or jaundice. Yumi Ando, Joseph Ahn. Chapter 38

Question 710

A 62-year-old man comes to the emergency department because of right-sided back pain, nausea, and dark urine. He reports alternating episodes of decreased urine output followed by a temporary increase in urine output for the past 2 days. In the past year, he has had two urinary tract infections. He has Crohn disease and underwent a small bowel resection 5 years ago. He currently takes mesalamine and a multivitamin. His father had recurrent kidney stones. His vital signs are within normal limits. Examination shows right costovertebral angle tenderness. Urinalysis shows 70 RBC/hpf and envelope-shaped crystals. A CT scan of the abdomen shows a 6-mm stone in the proximal right ureter and two 4-mm stones in the left kidney. Which of the following factors has most likely contributed most to this patient's current condition?

Answer Choices:

(A) Parathyroid gland adenoma
(B) Excess vitamin D
(C) Malabsorption of fatty acids
(D) High urine pH

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/eb37aaee-5816-46e5-9fd5-d35e32d38d44

OpenEvidence Explanation

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The answer is **C. Malabsorption of fatty acids**.

The envelope-shaped crystals on urinalysis are pathognomonic for **calcium oxalate**, and this patient's history of Crohn disease with prior small bowel resection points directly to **enteric hyperoxaluria** as the mechanism driving stone formation.

Mechanism of enteric hyperoxaluria: Small bowel resection (particularly ileal) causes fat malabsorption, which leads to calcium oxalate nephrolithiasis through two synergistic pathways:[1][2][3]

1. **Calcium saponification** — Unabsorbed free fatty acids bind intraluminal calcium, preventing calcium from complexing with dietary oxalate. This leaves more soluble (free) oxalate available for absorption across the colonic mucosa.

2. **Increased colonic permeability** — Unabsorbed bile salts and fatty acids act as detergents on the colonic epithelium, increasing its permeability to oxalate and further enhancing oxalate absorption.

The net result is markedly elevated urinary oxalate excretion (often >100 mg/day), which drives calcium oxalate supersaturation and stone formation.[1][2] Additional urinary risk factors in these patients include low urine volume, hypocitraturia, and acidic urine pH.[4][5]

Why not the other options?

- **A (Parathyroid adenoma)** — Primary hyperparathyroidism causes calcium phosphate or calcium oxalate stones, but typically presents with hypercalcemia and would not explain envelope-shaped crystals in this clinical context.

- **B (Excess vitamin D)** — Could cause hypercalciuria, but there is no indication of vitamin D excess; multivitamins contain standard doses.

- **D (High urine pH)** — High urine pH favors calcium phosphate stones, not calcium oxalate. In fact, patients with enteric hyperoxaluria tend to have low urine pH.[4]

Would you like to explore the specific dietary and pharmacologic strategies for preventing recurrent calcium oxalate stones in patients with enteric hyperoxaluria?

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Question 712

A 29-year-old woman, gravida 3, para 2, at 24 weeks' gestation comes to the emergency department because of vaginal bleeding and mild pelvic pain for 2 hours. Her current pregnancy was achieved by means of in vitro fertilization due to azoospermia in her partner. Prenatal course has been uncomplicated with regular prenatal visits. After a period of having avoided sexual intercourse during her early pregnancy, she resumed sexual activity with her partner at week 22 of gestation. Her first child was delivered by lower segment transverse cesarean section because of a nonreassuring fetal heart rate; her other child was delivered vaginally. She has had abnormal Pap smears due to HPV in the past. Her pulse is 82/min, respirations are 18/min, and blood pressure is 134/76 mm Hg. The abdomen is nontender, the uterus is consistent with 24 weeks' gestation, and the fetus is in a cephalic presentation. There are traces of blood on the vulva and the introitus. Speculum examination shows a tender, bruised cervix, with a closed cervical os. Fetal heart rate is 166/min and CTG shows a reassuring fetal heart rate tracing. Ultrasound shows a uniformly echogenic placenta located at the fundal end of the posterior uterine wall. What is the most likely cause of this patient's antepartum bleeding?

Answer Choices:

(A) Pedunculated cervical growth
(B) Inflammation of the cervix
(C) Cervical trauma
(D) Premature separation of the placenta

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/33369d73-a384-44de-b4b1-78500adf797a

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OpenEvidence Explanation

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The most likely cause of this patient's antepartum bleeding is **C. Cervical trauma**.

Several key clinical features point to this diagnosis:

1. **Speculum findings**: The cervix is described as **tender and bruised**, which is direct evidence of mechanical trauma to the cervix. This is the most specific finding in the vignette.
2. **Recent resumption of sexual intercourse**: The patient resumed sexual activity at 22 weeks after a period of abstinence. The pregnant cervix is highly vascular and friable, making it susceptible to postcoital trauma and bleeding.[1][2]
3. **Normal placental location**: Ultrasound shows the placenta at the **fundal end of the posterior uterine wall**, effectively ruling out placenta previa.[1]
4. **Against placental abruption (option D)**: The abdomen is nontender, there is no uterine hypertonicity, the CTG is reassuring, and the placenta is normally located without evidence of retroplacental clot. While IVF and multiparity are risk factors for abruption, the clinical presentation does not support this diagnosis.[1]
5. **Against cervical inflammation/cervicitis (option B)**: Although the patient has a history of abnormal Pap smears due to HPV, cervicitis would present with discharge, erythema, and friability rather than a **bruised** cervix. The bruising specifically implies mechanical injury rather than an inflammatory process.[1]
6. **Against pedunculated cervical growth/polyp (option A)**: No cervical mass or polyp was noted on speculum examination, making this unlikely.

The combination of recent coital activity, a bruised and tender cervix on speculum exam, trace bleeding, and an otherwise reassuring clinical picture (stable vitals, nontender abdomen, reassuring fetal heart tracing, normal placental position) is most consistent with **postcoital cervical trauma**.

Would you like to explore the management approach and counseling recommendations for postcoital bleeding during pregnancy?

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Question 713

A 16-year-old boy is rushed to the emergency room with acute vomiting and abdominal pain that began earlier today. His parents say that the boy was doing well until two days ago when he told them that he was feeling unwell. He has diabetes and takes insulin but stopped taking it when he began to feel poorly two days ago. His temperature is 37°C (98.6°F), respirations are shallow and rapid with a rate of 33/min, pulse is 107/min, and blood pressure is 101/68 mm Hg. He appears severely dehydrated, showing signs of fatigue, and poor skin turgor. His breath has a fruity smell to it. His blood glucose level is 691 mg/dL. Blood is drawn for labs and the results are given below:
Serum:
pH: 7.21
pCO2: 32 mm HG
HCO 3-: 15.2 mEq/L
Sodium: 122 mEq/L
Potassium: 5.8 mEq/L
Urinalysis is positive for ketone bodies. What is the most appropriate immediate step in the management of this patient?

Answer Choices:

(A) Administer IV fluids and insulin
(B) Administer IV antibiotics
(C) Administer IV fluids with oral antidiabetic medications
(D) Administer potassium and magnesium

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/810fb116-d5ea-4e2f-97f7-feba15766180

OpenEvidence Explanation

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The correct answer is **A. Administer IV fluids and insulin**.

This patient presents with classic **diabetic ketoacidosis (DKA)**: a known diabetic who stopped insulin, now with hyperglycemia (glucose 691 mg/dL), metabolic acidosis (pH 7.21, HCO_3^- 15.2 mEq/L), ketonuria, Kussmaul respirations, dehydration, and fruity breath. The cornerstone of DKA management is **IV fluid resuscitation followed by IV insulin**, along with electrolyte monitoring and replacement.[1][2]

Why the other options are incorrect:

- **B (IV antibiotics):** There is no evidence of infection in this presentation. The precipitant is clearly insulin omission, not sepsis. Antibiotics are not indicated.
- **C (IV fluids with oral antidiabetic medications):** Oral antidiabetic agents have no role in acute DKA management. Insulin is required to suppress ketogenesis and resolve the acidosis.[1][2]
- **D (Administer potassium and magnesium):** Although patients with DKA have total body potassium depletion, this patient's serum potassium is **5.8 mEq/L** (elevated). The hyperkalemia is a result of insulin deficiency, acidosis, and volume depletion causing transcellular potassium shifts. Potassium supplementation should be withheld when serum K^+ is >5.3 mEq/L and only added to IV fluids once levels fall below the upper limit of normal. Insulin administration will itself help correct the hyperkalemia by driving potassium intracellularly.[2][3]

Key management sequence in DKA:

1. **IV fluid resuscitation** with isotonic saline is initiated first to restore circulatory volume[1][2]
2. **IV insulin** is started 1–2 hours after fluid initiation (0.05–0.1 units/kg/hr in pediatric patients)[2]
3. **Potassium** is added to IV fluids once levels drop below the upper limit of normal and urine output is established[2]
4. **Dextrose** is added to IV fluids when blood glucose reaches 250 mg/dL to prevent hypoglycemia while continuing insulin for acidosis resolution[2]

Would you like to explore the specific monitoring parameters and cerebral edema risk considerations unique to pediatric DKA management?

Relevant images

(CONTENT OMITTED)

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Question 715

A mother brings her 6-year-old daughter to the pediatrician to discuss her child's sleeping troubles. Three times now in the last month the child has begun screaming and crying in the middle of the night. When the parents rush to the child's room, they find her crying inconsolably. They try to ask her what is wrong, but she does not respond and persists crying for approximately 20 minutes, after which she goes back to sleeping comfortably. Upon awaking the following morning, she has no recollection of the night's events. Which of the following is true about these episodes?

Answer Choices:

(A) They will be persistent into adulthood
(B) They occur only during non-REM sleep
(C) They are associated with child abuse
(D) They are associated with later development of a mood disorder

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/70b3a12d-7a3d-43cc-87a1-822e3969e837

OpenEvidence Explanation

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The correct answer is **B. They occur only during non-REM sleep**.

This clinical vignette describes classic **sleep terrors** (pavor nocturnus): sudden onset of screaming and crying in the middle of the night, inconsolability, unresponsiveness to parental attempts at communication, self-limited episodes lasting ~20 minutes, and complete amnesia for the event the following morning.

Why B is correct: Sleep terrors are classified as a **disorder of arousal from NREM sleep**, occurring almost exclusively during slow-wave sleep (NREM stage 3, or N3).[1][2][3] They typically arise during the first third of the night, when slow-wave sleep predominates.[4] This is a key distinguishing feature from nightmares, which occur during REM sleep in the second half of the night and are associated with dream recall upon awakening.[5]

Why the other options are incorrect:

- **A (Persistent into adulthood):** Sleep terrors are characteristically self-limited and typically resolve by adolescence. The DSM-5 notes remission rates between 50% and 65%, with prevalence dropping to only 0.6% in the 10–18 age group. The condition is considered benign and age-related, likely reflecting neurodevelopmental immaturity of cortical inhibitory circuits.[3][4]

- **C (Associated with child abuse):** While childhood maltreatment is associated with nightmares and insomnia symptoms, sleep terrors in the vast majority of cases **do not indicate the presence of a primary underlying psychological problem or trauma**. Although some associations with stress and bullying have been observed, sleep terrors are not specifically associated with child abuse.[1][6][7]

- **D (Associated with later development of a mood disorder):** While some studies have noted associations between sleep terrors and anxiety symptoms in children, a specific causal correlation between sleep terrors and later psychiatric disorders has not been demonstrated. The condition is generally considered benign and self-limiting.[1][3]

Would you like to explore the distinguishing features between sleep terrors and nocturnal seizures, which is an important differential to consider in pediatric parasomnias?

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Question 717

Two hours after admission to the hospital for dialysis, a 63-year-old woman has severe pain in her lower back. The pain is 8 out of 10 in intensity and radiates down the legs. She underwent a laparoscopic cholecystectomy 4 years ago. She has hypertension, chronic kidney disease, type 2 diabetes mellitus, and major depressive disorder. She lives with her daughter and reports frequent fights with her at home. Her current medications include sertraline, insulin, enalapril, sodium bicarbonate, and sevelamer. She appears uncomfortable. Her temperature is 37.3°C (99.1°F), pulse is 102/min, respirations are 15/min, and blood pressure is 132/94 mm Hg. There is severe tenderness on palpation over the L2 vertebra; range of motion is limited. Neurologic examination shows no focal findings. Laboratory studies show:
Hemoglobin 10.1 g/dL
Leukocyte count 8,700/mm3
Platelet count 130,000/mm3
Serum
Na+ 136 mEq/L
Cl- 101 mEq/L
K+ 5.1 mEq/L
Calcium 8.2 mg/dL
Urea nitrogen 33 mg/dL
Glucose 190 mg/dL
Creatinine 3.8 mg/dL
An x-ray of the spine shows a wedge compression fracture of the L2 vertebra. Which of the following is the most likely explanation for these findings?

Answer Choices:

(A) Tertiary hyperparathyroidism
(B) Secondary hyperparathyroidism
(C) Elder abuse
(D) Primary hyperparathyroidism

> **Correct Answer:**
>
> **(B)**
>
> **OpenEvidence Response:**
>
> **(B)** ✓

OpenEvidence Link: https://openevidence.com/ask/74b3518b-00f2-4ce7-9cae-e281cb7c8003

OpenEvidence Explanation

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The answer is **B. Secondary hyperparathyroidism**.

This patient has **chronic kidney disease (CKD) on dialysis** with a **wedge compression fracture of L2**, which is best explained by **renal osteodystrophy** resulting from secondary hyperparathyroidism. The key laboratory findings supporting this diagnosis include **low serum calcium (8.2 mg/dL)** and **elevated creatinine (3.8 mg/dL)**, which are hallmarks of CKD-mineral and bone disorder (CKD-MBD).[1][2]

Why secondary hyperparathyroidism? In CKD, declining renal function leads to phosphate retention, decreased conversion of vitamin D to its active form (1,25-dihydroxyvitamin D), and resultant hypocalcemia. These changes stimulate compensatory PTH secretion (secondary hyperparathyroidism). Chronically elevated PTH drives excessive osteoclastic bone resorption, leading to high-turnover bone disease (osteitis fibrosa), cortical bone loss, and increased fracture risk.[1][3] Vertebral fractures are highly prevalent in dialysis patients, with one study reporting a 34% prevalence.[4] Elevated PTH is independently associated with fracture risk in CKD.[5]

Why not the other options?

- **Primary hyperparathyroidism** (D) causes **hypercalcemia** due to autonomous PTH secretion from a parathyroid adenoma. This patient has **low** calcium, which is inconsistent with primary disease.[6]
- **Tertiary hyperparathyroidism** (A) occurs when prolonged secondary hyperparathyroidism leads to autonomous parathyroid hyperplasia, resulting in **hypercalcemia** despite the underlying CKD. Again, this patient's calcium is low, ruling out tertiary disease.[6]
- **Elder abuse** (C) is a distractor given the reported family conflict. However, the fracture pattern (vertebral compression fracture at L2) is characteristic of metabolic bone disease rather than trauma, and the clinical context of CKD on dialysis with hypocalcemia provides a clear metabolic explanation.

The following figure illustrates the pathogenesis of secondary hyperparathyroidism and CKD-MBD, showing how declining kidney function triggers the cascade of phosphate retention, vitamin D deficiency, hypocalcemia, and compensatory PTH elevation that ultimately leads to bone disease.

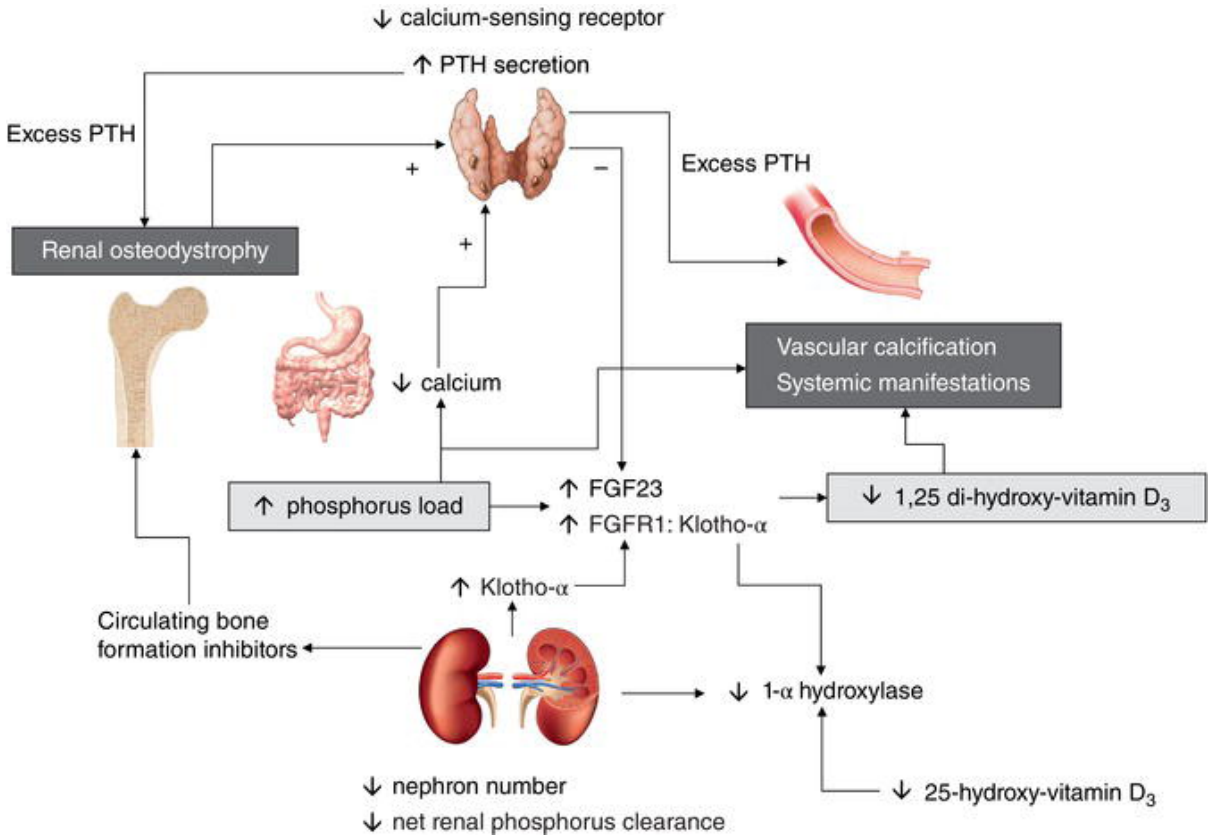


Figure 1. Pathogenesis of secondary hyperparathyroidism and CKD-MBD.

Would you like to explore the management strategies for CKD-MBD, including the role of phosphate binders, vitamin D analogs, and calcimimetics in preventing fractures in dialysis patients?

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Question 718

A 50-year-old man comes to the physician because of swelling of his legs for 2 months. Three months ago, he was diagnosed with hypertension and started on a new medication. His blood pressure is 145/95 mm Hg. Physical examination shows 2+ edema in both lower extremities. Laboratory studies are within the reference ranges. This patient was most likely treated with which of the following drugs?

Answer Choices:

(A) Losartan
(B) Spironolactone
(C) Hydrochlorothiazide
(D) Amlodipine

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/d00b53ce-7bb8-4354-8bab-b61784ce7c12

OpenEvidence Explanation

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The answer is **D. Amlodipine**.

Amlodipine, a dihydropyridine calcium channel blocker (CCB), is the antihypertensive most commonly associated with **bilateral lower extremity**

edema. This is a classic and well-recognized side effect, with an incidence ranging from **2% to 25%** depending on dose and duration of therapy.[1] The timeline in this case — edema developing within 2 months of starting a new antihypertensive — is consistent with the mean onset time of approximately **8.3 weeks** reported in cohort studies.[2]

Key points distinguishing amlodipine from the other options:

- **Losartan** (ARB) — does not cause peripheral edema; in fact, combining an ARB or ACE inhibitor with amlodipine reduces CCB-induced edema.[3][4]
- **Spironolactone** (potassium-sparing diuretic) — promotes diuresis and would not cause peripheral edema.
- **Hydrochlorothiazide** (thiazide diuretic) — also promotes diuresis and would not cause edema.

The mechanism of CCB-induced edema is **not fluid overload** but rather preferential arteriolar dilation that increases capillary hydrostatic pressure, causing fluid extravasation into the interstitial space.[1][5] This is an important clinical distinction because treating this edema with diuretics is generally inappropriate and can lead to overdiuresis, electrolyte imbalances, and acute kidney injury — a well-described **prescribing cascade**.[1] The normal laboratory values in this patient further support a non-systemic cause of edema (no renal, hepatic, or cardiac dysfunction).

A meta-analysis of 22 randomized placebo-controlled trials found the rate of edema was **16.6% with amlodipine vs. 6.2% with placebo** (RR 2.9), with higher rates at the 10 mg dose compared to 2.5–5 mg.[6]

Would you like to explore strategies for managing amlodipine-induced peripheral edema, such as switching to a lipophilic CCB or adding an ACE inhibitor/ARB?

Relevant images

(CONTENT OMITTED)

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Question 722

A 20-day-old child is brought to the emergency department by her parents. They are concerned about lethargy and easy bruising. Her mother reports that she has been eating less for the past few days. Today she was difficult to arouse. She normally nurses four-five times a day, but ate less yesterday and this morning. The girl was born at 39 weeks gestation via spontaneous vaginal delivery at home with minimal prenatal or postnatal care. This is her first visit to a physician of any type. The family is carefully questioned and child abuse is ruled out. The daughter's pulse is 97/min, respirations are 35/min, temperature is 35.8°C (96.4°F), and blood pressure is 71/46 mm Hg. Physical examination shows diffuse petechiae and bruising. Which of the following is the most likely cause?

Answer Choices:

(A) Group B streptococcus (GBS) infection
(B) Hepatitis B infection
(C) Thyroid stimulating hormone deficiency
(D) Vitamin K deficiency

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/9f44e752-69b2-46a7-988a-0be067965e3f

OpenEvidence Explanation

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The correct answer is **D. Vitamin K deficiency**.

This 20-day-old infant presents with **lethargy, poor feeding, diffuse petechiae, and bruising** — classic manifestations of **vitamin K deficiency bleeding (VKDB)**. The critical clue is that she was born at home with **minimal prenatal or postnatal care**, meaning she almost certainly did not receive the standard intramuscular vitamin K prophylaxis administered to all newborns.[1]

Why Vitamin K deficiency fits best:

- At 20 days of life, this presentation falls within the window of **classic-to-late-onset VKDB** (classic: days 2–7; late: 1 week to 6 months). Neonates are inherently vitamin K deficient due to poor placental transfer, immature hepatic synthesis of vitamin K–dependent clotting factors (30–50% of adult levels), and lack of colonic bacterial colonization.[1][2][3]
- Exclusively breastfed infants are at particularly high risk, as human milk contains very low levels of vitamin K.[1]
- Manifestations include cutaneous bruising, petechiae, mucosal bleeding, and in severe cases, intracranial hemorrhage with associated lethargy and poor feeding. The hypothermia (35.8°C) and lethargy may suggest intracranial hemorrhage as a complication.[2][4]
- A case series of infants who did not receive vitamin K at birth demonstrated presentations ranging from overt bleeding to vomiting, poor feeding, and lethargy, with 4 of 7 infants developing intracranial hemorrhage.[4]

Why the other options are less likely:

- **A. GBS infection** — GBS sepsis typically presents with respiratory distress, temperature instability, and signs of infection; diffuse petechiae and bruising without infectious signs is not the classic presentation, and the timing (early-onset GBS is <7 days; late-onset is 7–90 days) could overlap, but the absence of fever and the home birth without vitamin K makes VKDB far more likely.

- **B. Hepatitis B** — Neonatal hepatitis B does not typically present with acute bleeding at 20 days; it causes chronic infection and liver disease over a longer timeline.
- **C. TSH deficiency** — Congenital central hypothyroidism presents with prolonged jaundice, poor feeding, constipation, and hypotonia, not with petechiae and bruising.

The AAP recommends that all newborns receive 1 mg of intramuscular vitamin K within 6 hours of birth to prevent VKDB, and that VKDB should be considered when evaluating bleeding in the first 6 months of life, especially in infants who did not receive prophylaxis.[1]

Would you like to explore the acute management of suspected VKDB, including the role of vitamin K administration, fresh frozen plasma, and emergent imaging for intracranial hemorrhage?

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Question 723

A 10-year-old boy is brought to the physician because of a generalized, non-itchy rash for 2 days. He has also had a fever and sore throat for 4 days. He has not received any routine childhood vaccinations. Examination shows a flushed face except around his mouth. A diffuse, papular, erythematous rash that blanches with pressure is seen over the trunk. Pharyngeal erythema and a red beefy tongue are noted. His leukocyte count is 11,200/mm3 (75% segmented neutrophils, 22% lymphocytes). Without treatment, this patient's current condition puts him at greatest risk for which of the following complications?

Answer Choices:

(A) Coronary artery aneurysms
(B) Encephalitis
(C) Mitral valve regurgitation
(D) Minimal change disease

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/c3789935-7f1d-4183-a665-4cd6a92c7ef2

OpenEvidence Explanation

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The answer is **C. Mitral valve regurgitation**.

The clinical presentation describes **scarlet fever** caused by Group A β-hemolytic streptococcus (GAS): fever, sore throat, pharyngeal erythema, a "red beefy tongue" (strawberry tongue), a diffuse papular erythematous blanching rash over the trunk, **circumoral pallor** (flushed face sparing the area around the mouth), and neutrophil-predominant leukocytosis.[1] This is distinct from measles, which classically presents with the "three Cs" (cough, coryza, conjunctivitis) and Koplik spots rather than circumoral pallor and strawberry tongue.[2][3]

Without treatment, the most significant complication of GAS pharyngitis/scarlet fever is **acute rheumatic fever (ARF)**, which develops 2–4 weeks after infection through molecular mimicry-mediated autoimmune injury to the heart valves.[4][5] Carditis occurs in approximately 50–70% of first ARF episodes, and the **mitral valve is the most commonly affected**, manifesting as mitral regurgitation.[5][6] Approximately 60% of those with rheumatic carditis develop residual valvular damage (rheumatic heart disease).[7]

Why the other options are incorrect:

- **A. Coronary artery aneurysms** — This is the hallmark complication of Kawasaki disease, not scarlet fever.
- **B. Encephalitis** — This is a complication of measles (~1 per 1,000 cases), not GAS pharyngitis/scarlet fever.[3][8]
- **D. Minimal change disease** — Post-streptococcal glomerulonephritis (PSGN) is a recognized renal complication of GAS infection, but it causes a nephritic (not nephrotic) syndrome. Minimal change disease is the most common cause of nephrotic syndrome in children but is not a complication of streptococcal infection.

Would you like to explore the updated Jones Criteria for diagnosing acute rheumatic fever and the recommended approach to secondary prophylaxis?

Relevant images

(CONTENT OMITTED)

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Question 726

A 56-year-old woman is brought to the emergency department because of a 2-day history of fever, chills, nausea, and flank pain. She has multiple sclerosis and a chronic indwelling bladder catheter for neurogenic bladder dysfunction. One week ago, she was discharged from the hospital after treatment for a multiple sclerosis flare. Her temperature is 39.3°C (102.8°C). Physical examination shows marked tenderness in the right costovertebral area. Urine cultures grow a non-lactose fermenting, oxidase-positive, gram-negative rod. The causal organism of this patient's current condition most likely produces which of the following substances?

Answer Choices:

(A) Lipoteichoic acid
(B) K capsule
(C) Toxin B
(D) Pyoverdine

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/8ae6b19f-9d59-42e3-be84-5852ee19d4f2

OpenEvidence Explanation

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The answer is **D. Pyoverdine**.

The clinical scenario describes a catheter-associated urinary tract infection (CAUTI) complicated by pyelonephritis in a patient with multiple sclerosis and a chronic indwelling catheter. The urine culture grows a **non-lactose fermenting, oxidase-positive, gram-negative rod**, which is the classic microbiological description of **Pseudomonas aeruginosa**.[1][2]

Why Pyoverdine: Pyoverdine is a fluorescent yellow-green siderophore produced by *P. aeruginosa* that scavenges iron from host transferrin and lactoferrin under iron-limiting conditions.[3][4] It serves dual roles as both an iron acquisition molecule and a signaling molecule that regulates the production of other virulence factors, including exotoxin A and endoproteases.[3][5] Clinical isolates from catheter-associated UTIs have been shown to produce significant amounts of pyoverdine.[3] Pyoverdine-deficient mutants demonstrate markedly reduced virulence in animal models.[6]

Why not the other options:

- **A. Lipoteichoic acid** — a cell wall component of gram-positive bacteria, not relevant to a gram-negative organism.
- **B. K capsule** — associated with *Klebsiella pneumoniae*, which is a lactose-fermenting, oxidase-negative organism.
- **C. Toxin B** — the major virulence factor of *Clostridioides difficile*, a gram-positive anaerobe.

P. aeruginosa is a common cause of CAUTI, particularly in patients with neurogenic bladder and chronic catheterization, where the spectrum of uropathogens shifts toward organisms like *Pseudomonas*, *Klebsiella*, and *Proteus* compared to uncomplicated UTIs.[7][8]

Would you like to explore the specific virulence mechanisms *P. aeruginosa* uses to establish biofilm on urinary catheters and how this informs prevention strategies?

Relevant images

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Question 728

A 25-year-old woman comes to the physician for the evaluation of nausea for the last two weeks. During this period, she has had increased urinary frequency and fatigue. She also reports two episodes of non-bloody vomiting. There is no personal history of serious illness. Her last menstrual period was 6 weeks ago. Physical examination shows bilateral breast tenderness. The remainder of the examination shows no abnormalities. A urine pregnancy test is positive. Which of the following is the most accurate predictor of the gestational age?

Answer Choices:

(A) Ratio of head to abdominal circumference
(B) Femoral length
(C) Crown-rump length
(D) Biparietal length

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/f8674c7a-751f-4d10-bd81-1838d3d3ab9f

OpenEvidence Explanation

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The answer is **C. Crown-rump length (CRL)**.

Crown-rump length is the most accurate predictor of gestational age, particularly in the first trimester when this patient presents (6 weeks by LMP). According to ACOG, AIUM, and the Society for Maternal-Fetal Medicine, first-trimester CRL measurement has an accuracy of **±5–7 days**, and its precision improves the earlier in the first trimester it is performed.[1][2]

The other answer choices are second- and third-trimester biometric parameters:

- **Biparietal diameter (D)** and **femoral length (B)** are used for dating after 14 weeks when CRL becomes less reliable, but they carry greater variability (±7–10 days in the second trimester, ±21–30 days in the third trimester).[3][4]
- **Head-to-abdominal circumference ratio (A)** is used to assess fetal growth patterns (symmetric vs. asymmetric growth restriction), not primarily for gestational age dating. Notably, abdominal circumference is the least reliable single parameter for estimating gestational age.[5]

At 6 weeks gestation, CRL is the standard and most accurate measurement for establishing gestational age and the estimated due date.[1]

Would you like to explore how ultrasound dating guidelines differ when there is a discrepancy between LMP-based and ultrasound-based gestational age estimates?

Relevant images

(CONTENT OMITTED)

References

1. Committee Opinion No 700: Methods for Estimating the Due Date. . Obstetrics and Gynecology. 2017;129(5):e150-e154. doi:10.1097/AOG.0000000000002046.
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Question 729

A 6-week-old male infant is brought to the physician by his mother because of a 2-day history of recurrent nonbilious vomiting. Vomiting occurs almost immediately after most feeds. Each time, he becomes irritable while feeding and refuses to finish the bottle. He was born at 37 weeks' gestation and weighed 3300 g (7 lb 4 oz); he currently weighs 4000 g (8 lb 13 oz). He has Down syndrome. His vaccinations are up-to-date. He appears agitated and cries during the examination. His temperature is 37.2°C (99°F), pulse is 156/min, respirations are 32/min, and blood pressure is 100/49 mm Hg. Examination shows upward slanting of the eyelids, a broad and flat nasal bridge, and a single transverse palmar crease on both hands. The abdomen is soft and nontender. A 2.5-cm (1-inch) epigastric mass is palpated. Cardiac examination shows no abnormalities. Arterial blood gas analysis is within normal limits. Further diagnostic evaluation of the patient is most likely to show which of the following?

Answer Choices:

(A) Dilated colon segment on abdominal x-ray
(B) Detection of rotavirus antigen on enzyme immunoassay (EIA)
(C) Elongated and thickened pylorus on abdominal ultrasound
(D) Tripple bubble sign on abdominal x-ray

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/250bc29b-d9d8-49c2-9a86-11b48367fcde

OpenEvidence Explanation

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The answer is **C. Elongated and thickened pylorus on abdominal ultrasound**.

This presentation is classic for **infantile hypertrophic pyloric stenosis (IHPS)**. The key clinical features pointing to this diagnosis include:

- **Age**: 6-week-old male — IHPS typically presents between 3 and 8 weeks of age[1][2]
- **Nonbilious, projectile vomiting** occurring shortly after feeds, with hunger and irritability during feeding[3][4]
- **Palpable epigastric mass** (the "olive") — this represents the hypertrophied pyloric muscle and is essentially pathognomonic for IHPS[5]
- **Male sex** — IHPS has a 4:1 male-to-female predominance[1][4]
- **Normal arterial blood gas** — early in the course, before significant electrolyte derangement develops (prolonged vomiting leads to hypochloremic, hypokalemic metabolic alkalosis)[3]

Abdominal ultrasound is the diagnostic study of choice, with sensitivity, specificity, and accuracy approaching **100%** for IHPS.[5] It demonstrates an elongated pyloric canal (≥15–17 mm) and thickened pyloric muscle wall (≥3 mm single wall thickness).[6]

Why the other options are incorrect:

- **A. Dilated colon on abdominal x-ray** — would suggest Hirschsprung disease, which presents with constipation and failure to pass meconium, not projectile vomiting
- **B. Rotavirus antigen on EIA** — gastroenteritis typically presents with diarrhea and fever, not an epigastric mass
- **D. Triple bubble sign on abdominal x-ray** — a "double bubble" sign is associated with duodenal atresia (common in Down syndrome), but this

presents with bilious vomiting in the first days of life, not at 6 weeks with a palpable mass; a "triple bubble" sign is not a standard radiographic finding

The following figure demonstrates the characteristic ultrasound appearance of pyloric stenosis, showing the thickened hypoechoic pyloric muscle and elongated pyloric canal.

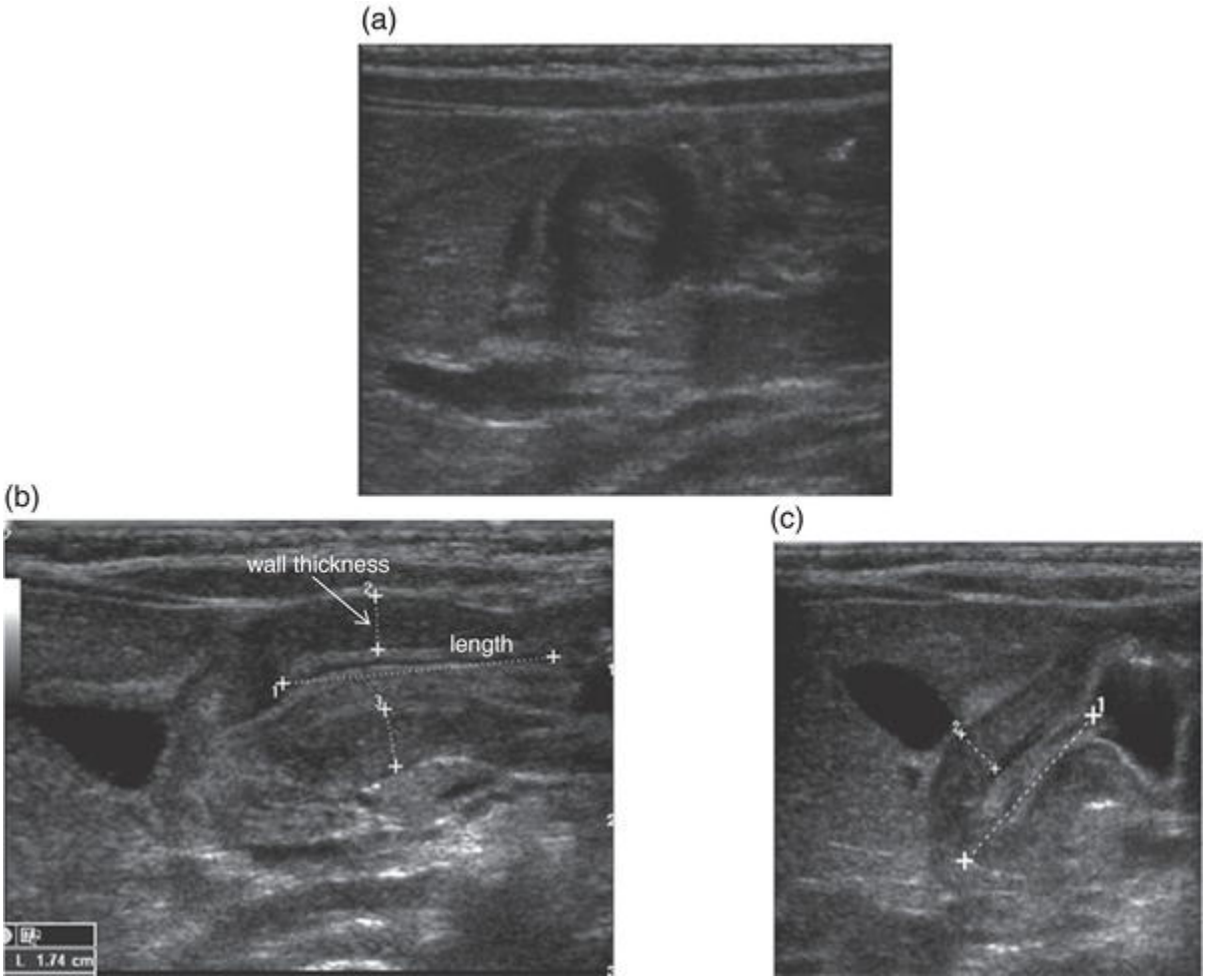


Figure 4. Ultrasound demonstrating pyloric stenosis. (A) Transverse section through pylorus; (B, C) longitudinal section. Measured layer should be <3 mm in thickness (one wall) and <15 mm in length (literature varies on this number – some say 17 mm). This patient had wall thickness of >4.1 mm and length of 17.4 mm.

Would you like to explore the preoperative management and electrolyte correction protocols before pyloromyotomy in infants with IHPS?

References

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6. Vomiting. Samantha White. Chapter 5.2

Question 733

A 1-month-old girl is brought to the emergency department with persistent vomiting, dehydration, and irritability. Over the past week, she has been projectile vomiting after most feedings. Initially, the vomiting would occur just once or twice a day, but now it occurs after every feed. However, her appetite hasn't decreased, and she seeks milk right after each episode of vomiting. She was born at 39 weeks gestation via spontaneous vaginal delivery and is breastfed exclusively. On physical exam, the vital signs include: temperature 37.5°C (99.5°F), blood pressure 85/55 mm Hg, respiratory rate 28/min, and heart rate 150/min. On examination, she appears to be mildly dehydrated, listless, and irritable. Her abdomen is soft and nontender with a palpable olive-shaped mass in the epigastric region. Which of the following acid-base disturbances is most likely associated with this patient's condition?

Answer Choices:

(A) Respiratory alkalosis
(B) Metabolic alkalosis
(C) Respiratory acidosis
(D) Mixed respiratory and metabolic acidosis

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/9eb75456-8bba-4eff-b77c-e5a4e424eda2

OpenEvidence Explanation

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The answer is **B. Metabolic alkalosis**.

This presentation is classic for **hypertrophic pyloric stenosis** (HPS): a 1-month-old with progressive, nonbilious projectile vomiting, a hungry infant who feeds eagerly after emesis, dehydration, and the pathognomonic **olive-shaped mass** in the epigastric region.

Why metabolic alkalosis?

The persistent vomiting in pyloric stenosis causes loss of **gastric hydrochloric acid (HCl)**, leading to:

- **Loss of H^+ ions** → metabolic alkalosis
- **Loss of Cl^- ions** → hypochloremia
- **Renal compensation**: the kidneys attempt to retain Na^+ by exchanging it for K^+ and H^+, worsening both **hypokalemia** and the alkalosis (a "paradoxical aciduria")

The classic electrolyte pattern is a **hypochloremic, hypokalemic metabolic alkalosis**. This is one of the highest-yield associations tested in medical education.

Why not the other options?

- **Respiratory alkalosis (A):** Would require hyperventilation/tachypnea as a primary process; not a feature here.
- **Respiratory acidosis (C):** Would require hypoventilation or CO_2 retention; no pulmonary pathology is described.
- **Mixed respiratory and metabolic acidosis (D):** Could occur in sepsis or severe shock, but the mechanism here is isolated gastric acid loss, which drives alkalosis, not acidosis.

Would you like to explore the fluid resuscitation and electrolyte correction strategy prior to pyloromyotomy in infants with pyloric stenosis?

Question 740

A 42-year-old man presents to his primary care physician for a follow-up visit. He has type 1 diabetes mellitus, for which he takes insulin. He complains of frequent episodes of waking up in the middle of his sleep. When he wakes up, he feels excessive sweating, hand tremors, and weakness. His morning blood glucose is high on repeated measurement. Which of the following is the optimal intervention for this patient condition?

> **Answer Choices:**
>
> (A) Reassurance
> (B) Adding pramlintide
> (C) Increasing daily insulin dose
> (D) Reducing daily insulin dose

> **Correct Answer:**
>
> **(D)**
>
> **OpenEvidence Response:**
>
> **(D)** ✓

OpenEvidence Link: https://openevidence.com/ask/814b3aee-7348-4f88-a8b1-b05a5cb810b2

OpenEvidence Explanation

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The correct answer is **D. Reducing daily insulin dose**.

This patient is experiencing the **Somogyi effect** (posthypoglycemic rebound hyperglycemia). The nocturnal symptoms of sweating, tremors, and weakness are classic adrenergic manifestations of **nocturnal hypoglycemia**, and the elevated morning blood glucose results from a counter-regulatory hormonal response (epinephrine, glucagon, cortisol, growth hormone) to the overnight low. The key distinguishing feature is that the patient is symptomatic during the night, confirming hypoglycemia as the underlying cause of the morning hyperglycemia.

Why reducing the insulin dose is correct: The fundamental problem is inappropriate nocturnal hyperinsulinemia causing hypoglycemia during sleep.[1] Standard management protocols call for dose decreases when symptomatic nocturnal hypoglycemia is present or when fasting blood glucose falls below target.[2] The ADA/EASD consensus report emphasizes that level 2 or 3 hypoglycemic events should trigger reevaluation of the treatment plan with consideration of **deintensification of therapy**.[3] Reducing the basal insulin dose addresses the root cause by preventing the nocturnal hypoglycemia, which in turn eliminates the rebound morning hyperglycemia.

Why the other options are incorrect:

- **A (Reassurance)** — Recurrent nocturnal hypoglycemia is dangerous and requires intervention, not reassurance.
- **B (Adding pramlintide)** — Pramlintide is an amylin analog that slows gastric emptying and suppresses glucagon; it would further increase hypoglycemia risk.
- **C (Increasing insulin dose)** — While the morning glucose is high, increasing insulin would worsen the nocturnal hypoglycemia, perpetuating the cycle. This would be appropriate for the **dawn phenomenon** (morning hyperglycemia without preceding nocturnal hypoglycemia), which is the key differential here.

Would you like to explore how to distinguish the Somogyi effect from the dawn phenomenon in clinical practice, including the role of continuous glucose monitoring?

Relevant images

(CONTENT OMITTED)

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6. Hypoglycaemia. Iskandar Idris, Rudy Bilous, Richard Donnelly. Chapter 13

Question 743

A 63-year-old man presents to the physician with a complaint of back pain for the past 2 months. The pain is present throughout the day, and even at night when he lies down. He also complains of difficulty walking upstairs and says he recently started to wear adult diapers because he seems to have difficulty controlling his bowel movements. His vital signs are within normal limits. The neurological examination revealed bilateral lower limb weakness, diminished temperature sensation, and decreased vibratory sense. The rectal examination revealed a hard nodular mass and a weak rectal sphincter tone. Which of the following is the most likely cause of his symptoms?

Answer Choices:

(A) Syringomyelia
(B) Spinal metastasis
(C) Herniated disc
(D) Spinal hematoma

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/38a8062d-82bc-44ed-aa1e-b2e3a7935612

OpenEvidence Explanation

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The most likely cause of this patient's symptoms is **B. Spinal metastasis**, most probably from prostate cancer.

This 63-year-old man presents with a constellation of findings that point to **metastatic prostate cancer with spinal cord/cauda equina compression**:

- **Hard nodular mass on digital rectal examination** — This is highly suspicious for prostate cancer. A palpable nodular prostate on DRE has a cancer detection rate of approximately 32–53% on biopsy, and a hard, irregular mass is a classic finding of prostate carcinoma.[1][2]
- **Persistent back pain worse at night** — Back pain is the earliest and most common symptom of metastatic epidural spinal cord compression (MESCC), present in over 95% of patients at diagnosis. Characteristically, pain from spinal metastases is **worse when supine and at night**, distinguishing it from mechanical causes. The median time from pain onset to MESCC diagnosis is approximately 2 months, consistent with this patient's timeline.[3][4]
- **Bilateral lower limb weakness, bowel incontinence, and weak rectal sphincter tone** — These findings indicate **cauda equina or conus medullaris compression**. Bowel and bladder dysfunction is noted in nearly half of patients with metastatic spinal cord compression. Prostate cancer accounts for approximately 15–20% of all cases of epidural spinal cord compression.[3][5][6]
- **Diminished temperature sensation and decreased vibratory sense** — These reflect involvement of both the spinothalamic tract (temperature) and dorsal columns (vibration), consistent with spinal cord compression.

Why the other options are less likely:

- **Syringomyelia (A)** — Classically causes a "cape-like" dissociated sensory loss (loss of pain/temperature with preserved proprioception) in the upper extremities due to central cord cavitation, and does not explain the rectal mass.
- **Herniated disc (C)** — While the most common cause of cauda equina syndrome overall, it would not explain the hard nodular rectal mass, the

progressive 2-month course with nocturnal pain, or the bilateral symmetric findings.[7][8]

- **Spinal hematoma (D)** — Typically presents acutely (often in the setting of anticoagulation or trauma), not with a 2-month progressive course, and does not explain the rectal mass.

The combination of a **hard prostatic nodule** with progressive back pain, bilateral neurological deficits, and sphincter dysfunction in a 63-year-old man is the classic presentation of prostate cancer metastatic to the spine with cord compression.

Would you like to explore the urgent workup and management algorithm for suspected metastatic spinal cord compression, including the role of emergent MRI and dexamethasone?

Relevant images

(CONTENT OMITTED)

References

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Question 745

A 63-year-old woman with end-stage renal disease complains of feeling lightheaded after her hemodialysis sessions for the past month. She worries she might eventually lose her balance and fall. She has had diabetes mellitus for 22 years. Her medications include folic acid, vitamin B12, amlodipine, and erythropoietin. At the clinic, her blood pressure is 135/80 mm Hg when lying down before dialysis and 110/55 mm Hg when seated after hemodialysis. Cardiopulmonary examination shows no abnormal findings. Laboratory studies after hemodialysis show a Hb of 10.5 mg/dL, a blood sugar of 189 mg/dL, and a hemoglobin A1C of 7.1%. To reduce the likelihood of falls, the most appropriate management is which of the following?

Answer Choices:

(A) Cooling the dialysate
(B) Eating heavier meals during dialysis
(C) Increasing ultrafiltration
(D) Steroid administration

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/892eecd9-38c6-4e11-91b6-74ac676e36d2

OpenEvidence Explanation

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The correct answer is **A. Cooling the dialysate**.

This patient presents with classic **intradialytic hypotension (IDH)** — lightheadedness after hemodialysis with a significant drop in blood pressure from 135/80 mmHg pre-dialysis to 110/55 mmHg post-dialysis. The concern about falls makes this a clinically important problem to address.

Why cooling the dialysate is correct:

Lowering the dialysate temperature (typically to 35.0–36.0°C from the standard 36.5–37.0°C) is a well-established, simple, and cost-effective intervention for preventing IDH.[1][2] The mechanism involves reducing core body temperature during dialysis, which promotes peripheral vasoconstriction, increases peripheral vascular resistance, and stabilizes blood pressure.[2] A recent systematic review and meta-analysis demonstrated that cool dialysate **reduces IDH occurrence by approximately 65%**.[2] A prospective crossover study showed that cool dialysate (35.5°C) significantly improved the lowest intradialytic systolic BP compared to control (102.6 ± 2.9 vs. 90.6 ± 2.5 mmHg, $P < 0.001$).[3] Multiple guidelines and reviews identify dialysate cooling as a cornerstone of IDH management.[1][4]

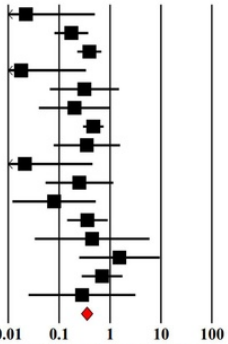
Why the other options are incorrect:

- **B. Eating heavier meals during dialysis** — Eating during dialysis is actually discouraged in patients prone to IDH because it causes splanchnic vasodilation, which drops peripheral vascular resistance and worsens hypotension.[5]
- **C. Increasing ultrafiltration** — Excessive ultrafiltration rate is a primary cause of IDH. Increasing it would worsen the problem; the recommendation is to reduce ultrafiltration rate.[1][6]
- **D. Steroid administration** — Steroids have no established role in the prevention of IDH. Pharmacologic options include midodrine (an alpha-1 agonist), but not corticosteroids.[1][5]

The following meta-analysis figure illustrates the benefits of cool dialysate across multiple outcomes including IDH reduction and blood pressure stabilization:

A. Intradialytic Hypotension

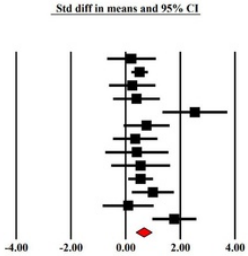
Study name	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
Ayoub 2004	0.022	0.001	0.497	-2.401	0.016
Azar 2009	0.174	0.082	0.368	-4.566	0.000
Bullen 2019	0.392	0.231	0.666	-3.463	0.001
Chesterton 2009	0.018	0.001	0.333	-2.699	0.007
Cruz 1999	0.314	0.066	1.486	-1.460	0.144
Dheenan 2001	0.199	0.041	0.976	-1.990	0.047
Fine 1996	0.470	0.300	0.737	-3.294	0.001
Gritters 2007	0.351	0.079	1.554	-1.379	0.168
Jost 1993	0.021	0.001	0.447	-2.478	0.013
Kaufman 1998	0.250	0.055	1.141	-1.790	0.074
Ramos 2007	0.080	0.012	0.517	-2.651	0.008
Rootjes 2022	0.359	0.145	0.889	-2.214	0.027
Selby 2006	0.444	0.034	5.880	-0.615	0.538
Sherman 1984	1.536	0.250	9.418	0.464	0.643
Teruel 2006	0.698	0.282	1.726	-0.779	0.436
Van der Sande 2009	0.282	0.026	3.113	-1.033	0.302
	0.354	0.275	0.456	-8.057	0.000



Heterogeneity: $Q = 23.361$, $df = 15$ ($p = .077$); $I^2 = 36\%$
Test for overall effect: $Z = -8.057$ ($p < .001$)

B. Mean Arterial Pressure

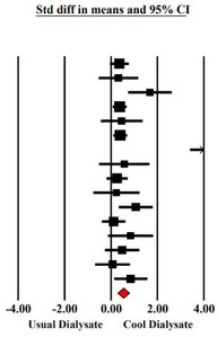
Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Ayoub 2004	0.216	0.449	0.201	-0.663	1.095	0.481	0.631
Bullen 2019	0.515	0.149	0.022	0.223	0.807	3.453	0.001
Cruz 1999	0.241	0.428	0.183	-0.598	1.080	0.563	0.574
Dheenan 2001	0.398	0.431	0.185	-0.446	1.242	0.924	0.355
Hegbrant 1994	2.535	0.601	0.361	1.358	3.712	4.221	0.000
Hoeben 2002	0.763	0.423	0.179	-0.065	1.592	1.805	0.071
Jost 1993	0.351	0.411	0.169	-0.456	1.157	0.852	0.394
Levy 1992	0.409	0.583	0.340	-0.734	1.552	0.701	0.483
Parker 2007	0.550	0.545	0.297	-0.517	1.618	1.011	0.312
Rootjes 2022	0.549	0.228	0.052	0.102	0.995	2.409	0.016
Van der Sande 2000	0.998	0.387	0.150	0.239	1.757	2.577	0.010
Yu 1995	0.094	0.472	0.222	-0.830	1.019	0.200	0.842
Zitt 2008	1.781	0.405	0.164	0.987	2.576	4.395	0.000
	0.674	0.148	0.022	0.384	0.964	4.549	0.000



Heterogeneity: $Q = 23.721$, $df = 12$ ($p = .022$); $I^2 = 49\%$
Test for overall effect: $Z = 4.549$ ($p < .001$)

C. Systolic Blood Pressure

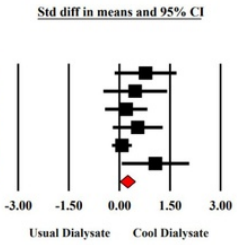
Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Azar 2009	0.358	0.202	0.041	-0.037	0.753	1.775	0.076
D. Beerenhout 2004	0.322	0.429	0.184	-0.519	1.163	0.750	0.453
N. Beerenhout 2004	1.680	0.475	0.225	0.750	2.611	3.539	0.000
Bullen 2019	0.370	0.148	0.022	0.080	0.660	2.504	0.012
Gritters 2007	0.455	0.453	0.205	-0.432	1.343	1.006	0.315
Maggiore 2002	0.391	0.146	0.021	0.104	0.678	2.671	0.008
Marcen 1988	5.590	1.107	1.226	3.419	7.760	5.047	0.000
Parker 2007	0.571	0.545	0.297	-0.498	1.639	1.047	0.295
Rootjes 2022	0.261	0.225	0.050	-0.179	0.701	1.162	0.245
Schneditz 1997	0.229	0.502	0.252	-0.754	1.212	0.456	0.648
Sherman 1984	1.066	0.367	0.134	0.347	1.784	2.907	0.004
Teruel 2006	0.110	0.254	0.065	-0.389	0.608	0.431	0.666
Van der Sande 1999	0.841	0.492	0.242	-0.123	1.805	1.710	0.087
Van der Sande 2000	0.479	0.370	0.137	-0.247	1.205	1.293	0.196
Van der Sande 2009	0.065	0.378	0.143	-0.676	0.806	0.172	0.863
Zitt 2008	0.846	0.358	0.128	0.145	1.548	2.364	0.018
	0.543	0.125	0.016	0.297	0.788	4.337	0.000



Heterogeneity: $Q = 37.445$, $df = 15$ ($p = .001$); $I^2 = 60\%$
Test for overall effect: $Z = 4.337$ ($p < .001$)

D. Urea Clerance-based Dialysis Adequacy

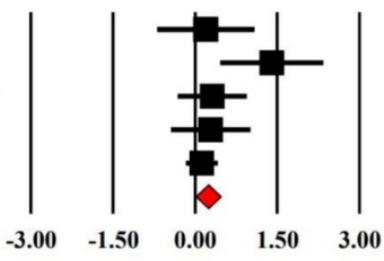
Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Ayoub 2004	0.775	0.464	0.215	-0.133	1.684	1.672	0.094
Chesterton 2009	0.470	0.478	0.228	-0.467	1.406	0.983	0.326
Ghasemi 2008	0.200	0.317	0.101	-0.421	0.821	0.631	0.528
Kaufman 1998	0.543	0.372	0.138	-0.186	1.272	1.461	0.144
Maggiore 2002	0.072	0.145	0.021	-0.213	0.356	0.494	0.621
Yu 1995	1.069	0.504	0.254	0.081	2.056	2.121	0.034
	0.247	0.114	0.013	0.025	0.470	2.178	0.029



Heterogeneity: $Q = 6.290$, $df = 5$ ($p = .279$); $I^2 = 21\%$
Test for overall effect: $Z = 2.178$ ($p = .029$)

E. Urea Reduction Rate

Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Ayoub 2004	0.194	0.448	0.201	-0.685	1.073	0.433	0.665
Dheenan 2001	1.400	0.476	0.226	0.467	2.333	2.943	0.003
Ghasemi 2008	0.313	0.318	0.101	-0.311	0.936	0.982	0.326
Kaufman 1998	0.283	0.367	0.135	-0.436	1.002	0.771	0.441
Maggiore 2002	0.122	0.145	0.021	-0.163	0.406	0.839	0.402
	0.244	0.116	0.013	0.017	0.472	2.104	0.035



Heterogeneity: $Q = 6.681$, $df = 4$ ($p = .154$); $I^2 = 40\%$

Figure 3. Meta-analysis of the effects of cool dialysate on (A) intradialytic hypotension, (B) mean arterial pressure, (C) systolic blood pressure, (D) urea clearance-based dialysis adequacy, (E) urea reduction rate, and (F) body temperature between two groups.

Would you like to explore the specific dialysate temperature targets and protocols for implementing cool dialysate in clinical practice?

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Question 746

A 34-year-old woman presents to the emergency room with a fever. She developed worsening malaise and diaphoresis over the past 48 hours. Her maximum temperature was 102°F (38.9°C) taken the night before presentation. Her past medical history is notable for major depressive disorder, obesity, fibromyalgia, and severe tension headaches. She previously took paroxetine for a 2-month trial but switched to citalopram 6 months ago as she did not feel like paroxetine was adequately helping her symptoms. Her mood has been stable on her current dose of citalopram. She takes ibuprofen for her headaches but previously borrowed a friend's headache medication when her headaches became very severe. Of note, she has been trying to lose weight and recently started taking an amino acid supplement at the suggestion of her nephew who is a nutritionist. She is also trying out a new low-carbohydrate diet. She works as a nurse at a local primary care clinic. Her temperature is 101.5°F (38.6°C), blood pressure is 144/80 mmHg, pulse is 108/min, and respirations are 22/min. She is diaphoretic and shivering. Patellar and brachioradialis reflexes are 3+ bilaterally. Tone is increased in her bilateral upper and lower extremities. Rapid dorsiflexion of her right ankle elicits 3 beats of clonus. Pupils are equally round and reactive to light. A basic metabolic panel is within normal limits. Which of the following is the most likely inciting factor for this patient's condition?

Answer Choices:

(A) Decreased carbohydrate intake
(B) Increased tryptophan intake
(C) Medication change
(D) Surreptitious opiate abuse

Correct Answer:

(B)

OpenEvidence Response:

> **(B)** ✓

OpenEvidence Link: https://openevidence.com/ask/64470b28-bc0c-443d-947c-5fca968b6dec

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OpenEvidence Explanation

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The answer is **B. Increased tryptophan intake**.

This patient is presenting with **serotonin syndrome**, and the most likely inciting factor is the addition of a **tryptophan-containing amino acid supplement** to her existing citalopram (SSRI) regimen.

Clinical Presentation

The findings are classic for moderate serotonin syndrome: fever (38.6°C), tachycardia, hypertension, diaphoresis, shivering, hyperreflexia (3+ patellar and brachioradialis reflexes), increased tone, and inducible clonus — all developing over 48 hours.[1][2] As described in the NEJM review by Boyer and Shannon, moderate cases characteristically show hyperreflexia and clonus that are greater in the lower extremities, along with autonomic findings such as tachycardia, hypertension, and hyperthermia.[2]

Why Tryptophan?

Tryptophan is the amino acid precursor to serotonin. The FDA drug label for citalopram explicitly lists **tryptophan** among the serotonergic agents that increase the risk of serotonin syndrome when used concomitantly with SSRIs.[3][4] Tryptophan is one of the top 10 substances with the highest reporting odds ratio for serotonin syndrome in the FAERS database.[5] The patient recently started an "amino acid supplement" recommended by her nephew — this is the new serotonergic exposure that precipitated the syndrome on top of her stable citalopram dose.

Why Not the Other Answers?

- **A. Decreased carbohydrate intake** — Low-carbohydrate diets do not cause serotonin syndrome.
- **C. Medication change** — She switched from paroxetine to citalopram 6 months ago, and her mood has been stable. Both are SSRIs, and this change occurred too long ago to be the acute precipitant. Paroxetine's half-life (~21 hours) would not produce a relevant interaction 6 months later.[2]
- **D. Surreptitious opiate abuse** — While opioids can contribute to serotonin syndrome, the clinical picture (hyperreflexia, clonus, increased tone) is inconsistent with opiate intoxication, and there is no clinical suggestion of opiate use.

The following diagnostic algorithm from Boyer and Shannon illustrates how inducible clonus with diaphoresis in a patient on a serotonergic agent confirms the diagnosis of serotonin syndrome:

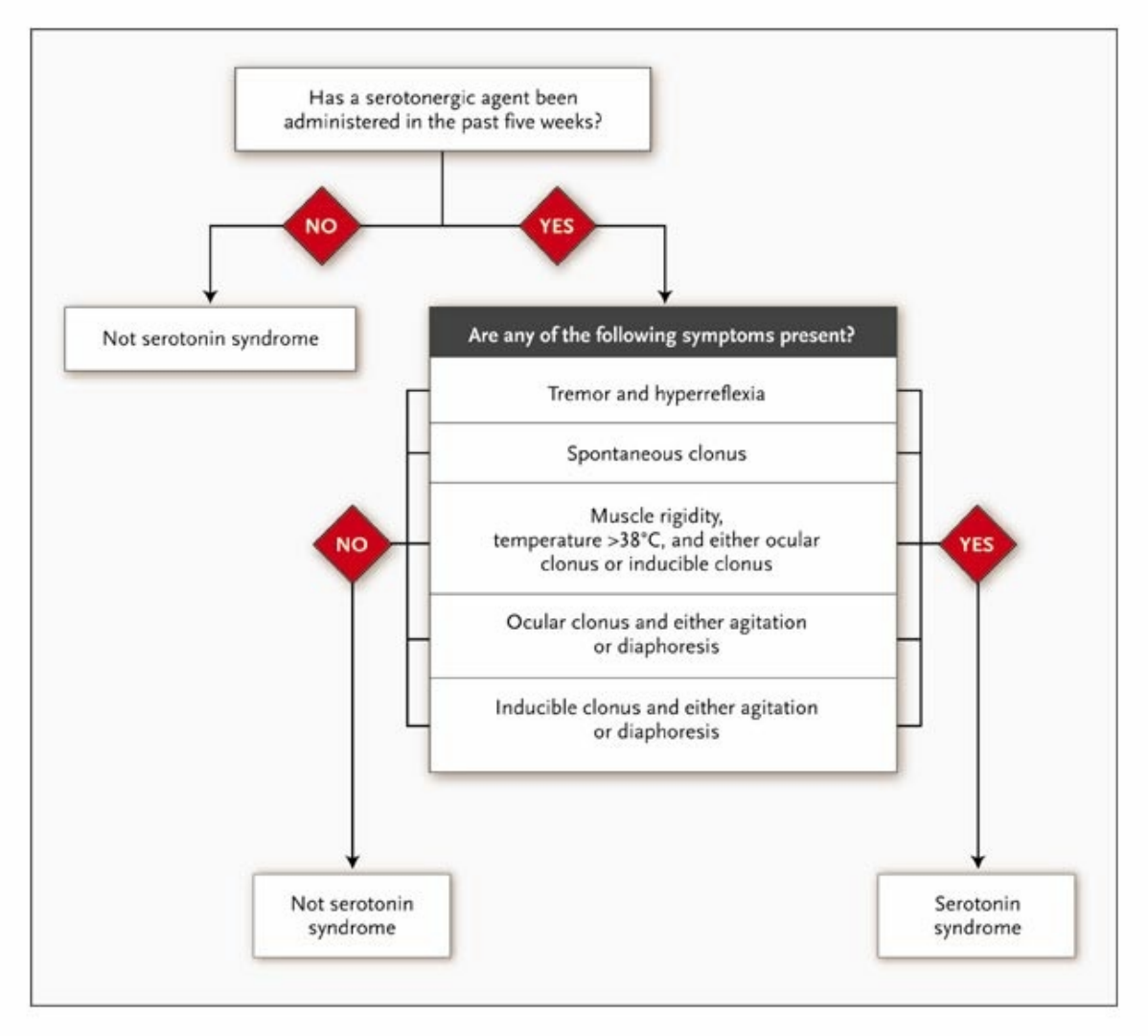


Figure 4. Algorithm for Diagnosis.

Used under license from The New England Journal of Medicine.

Would you like to explore the acute management of serotonin syndrome, including the role of cyproheptadine and supportive care strategies?

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Question 748

A 39-year-old woman presents with headaches, constipation, increased thirst, and increased urinary frequency. Her blood pressure is 160/100 mm Hg and pulse is 67/min. Blood tests reveal high blood glucose and low potassium level. Abdominal CT scan shows a well-circumscribed homogeneous mass in the left adrenal gland. The hormone excess responsible for her symptoms uses which of the following pathways to exert its action?

> **Answer Choices:**
>
> (A) Intracellular receptors
> (B) cAMP pathway
> (C) cGMP pathway
> (D) JAK/STAT pathway

> **Correct Answer:**
>
> **(A)**
>
> **OpenEvidence Response:**
>
> **(A)** ✓

OpenEvidence Link: https://openevidence.com/ask/ef95320e-06ef-4550-a5ca-ea0f2367c14a

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OpenEvidence Explanation

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The correct answer is **A. Intracellular receptors**.

This clinical presentation — hypertension, hypokalemia, hyperglycemia, and a unilateral adrenal mass — is classic for **primary hyperaldosteronism (Conn syndrome)** caused by an aldosterone-producing adenoma.[1][2] Aldosterone is a steroid hormone that exerts its primary biologic effects by binding to an **intracellular mineralocorticoid receptor (MR)**, which belongs to the nuclear steroid receptor superfamily.[3][4]

Mechanism of action: Upon aldosterone binding, the cytoplasmic MR dissociates from chaperone proteins (Hsp70, Hsp90), undergoes conformational change, and translocates to the nucleus where it binds to hormone response elements (HRE) on DNA, regulating transcription of target genes.[4][5] Key downstream effects include increased expression of the epithelial sodium channel (ENaC) and Na^+ / K^+ -ATPase, promoting sodium reabsorption and potassium excretion in the renal collecting duct.[3][6] This genomic pathway accounts for most of aldosterone's biologic actions.[7]

Why the other options are incorrect:

- **B. cAMP pathway** — Used by peptide hormones (e.g., ACTH, PTH, glucagon) that bind G-protein coupled receptors; not the primary signaling mechanism for aldosterone.
- **C. cGMP pathway** — Used by atrial natriuretic peptide (ANP) and nitric oxide signaling; not aldosterone's pathway.
- **D. JAK/STAT pathway** — Used by cytokines (e.g., interferons, interleukins) and growth hormone; not relevant to aldosterone signaling.

While aldosterone does have some rapid nongenomic effects via membrane-associated signaling, the classical and predominant mechanism is through intracellular steroid receptors acting as transcription factors.[3][7][8]

Would you like to explore the diagnostic workup and management of primary hyperaldosteronism, including the aldosterone-to-renin ratio and adrenal vein sampling?

Relevant images

(CONTENT OMITTED)

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Question 750

A 34-year-old man with acute lymphocytic leukemia presents for follow-up in the oncology clinic after his second cycle of chemotherapy. In addition to intermittent nausea, he has mild weakness, tingling, and numbness in his left hand. With his affected hand, he is able to grip, but occasionally drops small objects. His oncologist tells him that one of his chemotherapy agents likely caused his neuropathy given its strong association with neurotoxicity. He was recently treated with cyclophosphamide, vincristine, doxorubicin, dexamethasone, and dasatinib. The culprit medication works by which of the following mechanisms of action?

Answer Choices:

(A) Covalently X-links DNA
(B) Blocks microtubule formation
(C) Intercalates between DNA
(D) Modifies DNA transcription and protein synthesis

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/9249ce0c-8b19-4e8e-8d05-bdb745e274a1

OpenEvidence Explanation

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The answer is **B. Blocks microtubule formation**.

The culprit medication is **vincristine**, which is the agent in this regimen most strongly associated with dose-limiting peripheral neuropathy. Vincristine is a vinca alkaloid that exerts its cytotoxic effects by **interfering with microtubule formation** and mitotic spindle dynamics, leading to mitotic arrest and cell death.[1][2] This same mechanism of disrupting microtubules also underlies its neurotoxicity, as it interferes with axonal transport in peripheral nerves, causing Wallerian degeneration and a length-dependent axonal neuropathy.[3]

The clinical presentation described — numbness, tingling, weakness, and difficulty gripping small objects in the hand — is classic for vincristine-induced peripheral neuropathy (VIPN), which characteristically presents with neuropathic pain, sensory dysfunction, and motor impairment such as impaired manual dexterity.[2][4] VIPN affects approximately 20–30% of patients and is dose-dependent.[2] Among the agents listed in this patient's regimen (cyclophosphamide, vincristine, doxorubicin, dexamethasone, dasatinib), vincristine is identified as the **dominant driver** of peripheral neuropathy and grip strength decline.[5]

The other answer choices correspond to different agents:

- **A (Covalently cross-links DNA)** — cyclophosphamide (alkylating agent)
- **C (Intercalates between DNA)** — doxorubicin (anthracycline)
- **D (Modifies DNA transcription and protein synthesis)** — dexamethasone (corticosteroid)

Would you like to explore the management strategies for vincristine-induced peripheral neuropathy, including dose modification guidelines and neuropathic pain treatment options?

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Question 752

A 47-year-old woman with metastatic breast cancer who is undergoing chemotherapy comes to the physician for a follow-up exam. She reports extreme fatigue since beginning her chemotherapy regimen. Her pulse is 98/min, respirations are 16/min, and blood pressure is 132/84 mm Hg. Her hemoglobin is 10.4 g/dL, leukocyte count is 800/mm3 with 5% monocytes, and platelet count is 50,000/mm3. The patient is started on a new medication. One week later, serum studies show a hemoglobin of 10.6 g/dL, a leukocyte count of 2,000/mm3 with 2% monocytes, and a platelet count of 56,000/mm3. Which of the following drugs is the most likely cause of these findings?

Answer Choices:

(A) Aldesleukin
(B) Interferon beta
(C) Filgrastim
(D) Romiplostim

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/ec7e1b83-60fe-4598-aabe-7c10e28cd066

OpenEvidence Explanation

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The answer is **C. Filgrastim**.

The key to this question is identifying which drug would **selectively increase the leukocyte count** while leaving hemoglobin and platelet counts essentially unchanged. The lab findings show:

- Leukocyte count: 800 → **2,000/mm³** (significant increase)
- Hemoglobin: 10.4 → 10.6 g/dL (essentially unchanged)
- Platelet count: 50,000 → 56,000/mm³ (essentially unchanged)
- Monocyte percentage: 5% → 2% (decreased proportion, consistent with a predominant neutrophil response)

Filgrastim (G-CSF) is a lineage-specific colony-stimulating factor that regulates the production of neutrophils within the bone marrow. Per the FDA label, G-CSF "has been shown to have minimal direct in vivo or in vitro effects on the production or activity of hematopoietic cell types other than the neutrophil lineage".[1][2] It produces a dose-dependent increase in circulating neutrophil counts without significantly affecting erythropoiesis or megakaryopoiesis.[3] This explains the selective rise in WBC count with stable hemoglobin and platelets.

The drop in monocyte percentage from 5% to 2% is also consistent with filgrastim use — while the absolute monocyte count may increase, the percentage decreases because neutrophils increase disproportionately more.[4]

Why not the other options:

- **Aldesleukin (IL-2)** — Used for metastatic renal cell carcinoma and melanoma; causes capillary leak syndrome and would not selectively raise the WBC count in this pattern.
- **Interferon beta** — Used primarily for multiple sclerosis; can cause leukopenia rather than correct it.
- **Romiplostim** — A thrombopoietin receptor agonist that selectively stimulates platelet production; it would be expected to raise the platelet count, not the WBC count.[2]

This patient with chemotherapy-induced pancytopenia and severe neutropenia (WBC 800/mm³) was appropriately started on filgrastim, which is FDA-approved to decrease the incidence of infection (febrile neutropenia) in patients with nonmyeloid malignancies receiving myelosuppressive chemotherapy.[5]

Would you like to explore the NCCN guidelines' risk stratification algorithm for determining when G-CSF prophylaxis is indicated during chemotherapy?

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Question 753

A male newborn born at 27 weeks' gestation is evaluated for rapid breathing and hypoxia shortly after birth. His mother had no prenatal care. Cardiopulmonary examination shows normal heart sounds, intercostal retractions, and nasal flaring. An x-ray of the chest shows low lung volumes, air bronchograms, and diffuse ground-glass opacities. He is started on nasal continuous positive airway pressure. Further evaluation of this patient is most likely to show which of the following findings?

Answer Choices:

(A) Bilateral pleural effusions on lung ultrasound
(B) Corkscrew-shaped organisms on umbilical cord culture
(C) Hyaline membranes lining the alveoli on lung biopsy
(D) Meconium-stained fluid on deep suctioning

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/38c1e6fe-dfc9-4d93-b1c7-86f46ced1d97

OpenEvidence Explanation

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The correct answer is **C. Hyaline membranes lining the alveoli on lung biopsy**.

This presentation is classic for **neonatal respiratory distress syndrome (RDS)**, previously known as **hyaline membrane disease**. The key features pointing to this diagnosis include:

- **Extreme prematurity** (27 weeks' gestation) — RDS occurs in more than 80% of infants born before 28 weeks due to surfactant deficiency, as type II pneumocytes mature in the later stages of fetal development[1][2]
- **Lack of prenatal care** — meaning no antenatal corticosteroids were administered to promote lung maturation
- **Clinical findings** of tachypnea, intercostal retractions, and nasal flaring shortly after birth[2][3]
- **Chest X-ray** showing low lung volumes, air bronchograms, and diffuse ground-glass opacities — the classic reticulogranular pattern of RDS[3][4]

Histologically, RDS is characterized by leakage of proteinaceous fluid into the alveoli and **hyaline membrane formation** — eosinophilic membranes composed of necrotic epithelial cells and fibrinous material lining the alveolar surfaces.[5][6][7] This is the hallmark pathologic finding, which is why the disease was originally named "hyaline membrane disease".[2][8]

Why the other options are incorrect:

- **A. Bilateral pleural effusions** — not a typical feature of RDS; more associated with hydrops fetalis or congenital infections.
- **B. Corkscrew-shaped organisms on umbilical cord culture** — describes Treponema pallidum (congenital syphilis), which presents differently with hepatosplenomegaly, rash, and rhinitis rather than isolated respiratory distress with classic RDS imaging.
- **D. Meconium-stained fluid** — meconium aspiration syndrome occurs in term or post-term infants, not in extremely premature neonates at 27 weeks.[3]

Would you like to explore the current evidence on optimal surfactant replacement strategies (e.g., INSURE vs. LISA techniques) in extremely preterm infants?

References

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Question 756

An otherwise healthy 29-year-old man presents to his family physician with a slowly growing left neck mass for the past 5 weeks. He denies fever or recent upper respiratory tract infections. His temperature is 37.1°C (98.7°F), the blood pressure is 115/72 mm Hg, and the pulse are 82/min. On examination, a 4-cm (1.5 in), firm, non-tender mass is detected on the mid-left neck. Excisional biopsy of the mass reveals Hodgkin's cells. The patient is referred to the oncology department and chemotherapy is started. After the first cycle of chemotherapy, the patient notices that his urine becomes red. The urine tests are positive for blood on further analysis. Which of the following is the most likely cause of this patient condition?

Answer Choices:

(A) Bleomycin
(B) Cyclophosphamide
(C) Doxorubicin
(D) Etoposide

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/b56afd83-b2ce-40de-992d-5249220c5086

OpenEvidence Explanation

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The answer is **B. Cyclophosphamide**.

Cyclophosphamide is the chemotherapy agent most commonly associated with **hemorrhagic cystitis**, which presents with hematuria (red urine that tests positive for blood). This is a well-established and characteristic adverse effect of cyclophosphamide (and its structural isomer ifosfamide).[1][2][3]

Mechanism: Cyclophosphamide is metabolized in the liver to active metabolites including phosphoramide mustard (the therapeutic agent) and **acrolein**, a highly reactive aldehyde that is renally excreted and concentrated in the bladder. Acrolein is directly toxic to the urothelium, causing necrosis, desquamation, edema, ulceration, neovascularization, and hemorrhage.[3][4] The incidence of hemorrhagic cystitis ranges from 5–10% with cyclophosphamide and can be mitigated with aggressive hydration and mesna (2-mercaptoethane sulfonate), which binds and neutralizes acrolein in the bladder.[2][5]

Why not the other options:

- **Bleomycin (A)** — causes pulmonary toxicity (pneumonitis/fibrosis), not hemorrhagic cystitis.[6][7]
- **Doxorubicin (C)** — causes cardiotoxicity (cardiomyopathy, heart failure) and can turn urine red-orange due to the drug's color, but this is not true hematuria and would not test positive for blood on urinalysis.
- **Etoposide (D)** — associated with secondary leukemia and myelosuppression, not hemorrhagic cystitis.

The key clinical distinction here is that the urine tested **positive for blood**, confirming true hematuria rather than simple discoloration, which points specifically to cyclophosphamide-induced hemorrhagic cystitis rather than doxorubicin-related pigment change.

Would you like to explore the prevention strategies for cyclophosphamide-induced hemorrhagic cystitis, including mesna dosing protocols and monitoring recommendations?

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Question 757

An 18-year-old woman is brought to the emergency department because of lightheadedness and a feeling of dizziness. She has had nausea, occasional episodes of vomiting, myalgia, and a generalized rash for the past week. She also reports feeling lethargic. She has no shortness of breath. There is no family history of serious illness. She appears ill. Her temperature is 39.1°C (102.3°F), pulse is 118/min, and blood pressure is 94/60 mm Hg. Cardiac examination shows no abnormalities. There is a widespread erythematous rash on the trunk and extremities with skin peeling on the palms and soles. Laboratory studies show:
Hemoglobin 13.6 g/dL
Leukocyte count 19,300/mm3
Platelet count 98,000/mm3
Serum
Urea nitrogen 47 mg/dL
Glucose 88 mg/dL
Creatinine 1.8 mg/dL
Total bilirubin 2.1 mg/dL
AST 190 U/L
ALT 175 U/L
Urinalysis shows no abnormalities. Further evaluation of this patient's history is most likely to reveal which of the following?

Answer Choices:

(A) Recent hiking trip
(B) Intravenous heroin abuse
(C) Exposure to a patient with mengingococcemia
(D) Currently menstruating

Correct Answer:

(D)

OpenEvidence Response:

> **(D)** ✓

OpenEvidence Link: https://openevidence.com/ask/1e53f427-d76b-46f7-b45f-791a1b8408e6

OpenEvidence Explanation

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The answer is **D. Currently menstruating**.

This presentation is classic for **toxic shock syndrome (TSS)**, and further history would most likely reveal that the patient is **currently menstruating**. The key features pointing to this diagnosis include:

- **Diffuse erythematous rash with desquamation of palms and soles** — this is the hallmark rash of staphylococcal TSS, distinct from the petechial rash of RMSF which starts on wrists/ankles[1]
- **High fever** (≥38.9°C) — her temperature is 39.1°C
- **Hypotension** (systolic BP ≤90 mm Hg) — her BP is 94/60
- **Multisystem involvement** meeting ≥3 organ system criteria:[1]
- Gastrointestinal (nausea, vomiting)
- Muscular (myalgia)
- Renal (BUN 47, creatinine 1.8 — both elevated)
- Hepatic (bilirubin 2.1, AST 190, ALT 175 — elevated)
- Hematologic (platelets 98,000 — ≤100,000)

Why not the other options?

- **A. Recent hiking trip (RMSF):** While RMSF also causes fever, rash involving palms/soles, thrombocytopenia, and elevated transaminases, the rash in RMSF is classically a maculopapular/petechial rash that begins on the wrists and ankles and spreads centripetally — not a diffuse erythroderma with skin peeling. Desquamation of palms and soles is characteristic of TSS, not RMSF.[2][3]
- **B. IV heroin abuse:** Could predispose to endocarditis or sepsis, but the specific constellation of diffuse erythroderma with desquamation and multiorgan involvement without cardiac abnormalities does not fit.
- **C. Meningococcemia:** Typically presents with purpura fulminans and petechial/purpuric rash, not diffuse erythroderma with desquamation.

Menstrual TSS is caused by TSST-1–producing *Staphylococcus aureus* colonizing the vagina, classically associated with tampon use in young menstruating women.[4][5] TSST-1 accounts for **85–100% of menstrual TSS cases**.[6] The disease predominantly affects young women who lack protective antibodies against TSST-1.[6]

Would you like to explore the acute management and antibiotic regimen for staphylococcal toxic shock syndrome?

Relevant images

(CONTENT OMITTED)

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Question 759

A 33-year-old woman presents to the clinic for follow-up of her AIDS treatment with highly active anti-retroviral therapy (HAART). She is in good spirits and has been fully compliant with her medications and clinic visits. Other medications include prophylactic co-trimoxazole. Recent blood studies show the following:
Hemoglobin (Hb%) 11 g/dL
Mean corpuscular volume (MCV) 80 fl
Reticulocyte count 0.5%
Erythrocyte count 2 x 106/mm3
Leucocyte count 700/mm3
Neutrophils 40%
Platelet count 20,000/mm3
Assays also show a decreased viral DNA and mRNA burden, as well as a significantly diminished viral load. To avoid modifying the effective anti-retroviral therapy, she is started on a 'blood improving' medication. Thirty minutes after the first dose, the patient develops difficulty breathing, severe muscle pain, and vomiting. Her pulse rate is 120/min and the blood pressure is 80/50 mm Hg. Which of the following medications was most likely administered to the patient?

Answer Choices:

(A) Interleukin 3
(B) Platelet-derived growth factor
(C) Sargramostim
(D) Thrombopoietin

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/5b996239-a5eb-47b7-b8d4-17ff2c9e6e08

OpenEvidence Explanation

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The answer is **C. Sargramostim** (GM-CSF, granulocyte-macrophage colony-stimulating factor).

This patient has **pancytopenia** (low hemoglobin, leukopenia with absolute neutrophil count of 280/mm³, and thrombocytopenia) likely secondary to HAART and/or co-trimoxazole myelosuppression. Since her antiretroviral therapy is effective (diminished viral load), the clinician chose to add a hematopoietic growth factor rather than modify the regimen. **Sargramostim** is a recombinant GM-CSF that stimulates proliferation and differentiation of myeloid progenitor cells across multiple lineages — including granulocytes, monocytes/macrophages, and to some extent megakaryocytic and erythroid progenitors — making it a rational choice for pancytopenia.[1]

The acute reaction described — dyspnea, severe myalgia, vomiting, tachycardia (120/min), and hypotension (80/50 mmHg) occurring 30 minutes after the first dose — is characteristic of a **first-dose reaction** (infusion-related reaction) to sargramostim. The FDA label for Leukine (sargramostim) specifically lists infusion-related reactions including **dyspnea, hypoxia, hypotension, syncope, and tachycardia** as recognized adverse events.[1] Capillary leak syndrome and severe allergic/hypersensitivity reactions are also documented.[1]

Why not the other options?

- **A. Interleukin 3** — While IL-3 is a multilineage growth factor, it is not an FDA-approved therapeutic agent and would not be used clinically in this setting.
- **B. Platelet-derived growth factor (PDGF)** — PDGF acts on mesenchymal cells (fibroblasts, smooth muscle) and has no role in treating cytopenias.

- **D. Thrombopoietin** — Recombinant thrombopoietin is not used clinically (it was withdrawn due to neutralizing antibody formation against endogenous TPO). TPO receptor agonists (romiplostim, eltrombopag) address only thrombocytopenia and would not treat the concurrent leukopenia and anemia. Their adverse effect profile does not typically include the acute first-dose reaction described here.[2][3]

GM-CSF has been specifically studied in HIV-associated leukopenia, where it produces clinically useful increases in granulocyte counts and permits continued use of myelosuppressive agents like zidovudine and co-trimoxazole.[4][5][6]

Would you like to explore the comparative safety and efficacy of G-CSF versus GM-CSF for managing drug-induced cytopenias in HIV-infected patients?

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Question 760

A 77-year-old woman is brought to the emergency department by her husband because of increasing confusion and unusual behavior for 2 days. She has been mumbling to herself and wandering around the neighborhood. These symptoms are worse in the evenings and she has hardly slept at night. She has not been eating or drinking much for the past 6 days. She has hypertension treated with hydrochlorothiazide. She was diagnosed with breast cancer 12 years ago and was treated with left-sided mastectomy. The patient is oriented to person but not to place or time. Her temperature is 37.1°C (98.8°F), pulse is 78/min, respirations are 18/min, and blood pressure is 122/80 mm Hg. Physical examination shows a supple neck. Neurologic examination shows psychomotor agitation. Attention and concentration are impaired; she makes multiple errors while performing the serial sevens test. Her speech is disorganized. Her fingerstick blood glucose concentration is 122 mg/dL. Which of the following is the most appropriate next step in management?

Answer Choices:

(A) Check serum TSH level
(B) Check serum electrolytes
(C) Perform CT scan of the head
(D) Perform chest x-ray

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/36353f88-1e22-41c2-89a0-377d638d6f59

OpenEvidence Explanation

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The answer is **B. Check serum electrolytes**. This patient presents with classic features of **delirium** — acute onset of confusion with fluctuating course (worse in evenings), inattention (errors on serial sevens), disorganized speech, psychomotor agitation, and sleep-wake cycle disturbance. The most appropriate initial step is to identify the most likely precipitant, which in this case points strongly toward an **electrolyte abnormality**.

Several clinical features converge on this answer:

- **Hydrochlorothiazide use** is one of the most common drug causes of hyponatremia in elderly patients, and thiazide-induced hyponatremia can present with delirium, confusion, and altered consciousness.[1][2]
- **Poor oral intake for 6 days** compounds the risk of both dehydration and electrolyte derangement, particularly hyponatremia (the "tea and toast" pattern) or hypernatremia from volume depletion.[3][4]
- **No focal neurologic findings** and a **supple neck** make intracranial pathology (stroke, meningitis) less likely, reducing the urgency of a CT scan. While brain metastasis from her remote breast cancer history is a consideration, the absence of focal signs and the presence of a clear metabolic precipitant make electrolytes the higher-yield initial test.[5][6]

Guidelines on delirium evaluation consistently list **electrolytes, BUN, and creatinine** among the tests "routinely required" in the initial workup of delirium.[5][7] CT imaging is reserved for patients with head trauma, new focal neurologic findings, or when initial workup is unrevealing.[6] TSH is appropriate in select situations to evaluate reversible causes of cognitive impairment but is not the most urgent first step. A chest X-ray may be part of the workup but does not address the most likely precipitant given the clinical picture.

> "Tests that are routinely required include a complete blood count and measurement of electrolytes, blood urea nitrogen, and creatinine."

—Edward R. Marcantonio, M.D., Beth Israel Deaconess Medical Center and other institutions. Delirium in Hospitalized Older Adults. N Engl J Med. October 12, 2017.

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Would you like to explore the management of thiazide-induced hyponatremia, including safe correction rates and when to consider switching antihypertensive agents?

Relevant images

(CONTENT OMITTED)

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Question 763

A 42-year-old chronic alcoholic man was admitted to the hospital for inappropriate behavior and disturbed memory. He presents with severe retrograde memory loss, confusion, and confabulation. Neurologic examination showed horizontal nystagmus. He also has bilateral pretibial pitting edema and perioral erythema. CT studies of the brain were normal. The duty physician suspects the patient may be vitamin deficient. Which of the following reactions does the deficient vitamin mediate?

Answer Choices:

(A) Alpha-Ketoglutarate + NAD+ + CoA <=> Succinyl-CoA + CO2 + NADH
(B) Succinate + FAD (enzyme bound) <=> Fumarate + FADH2
(C) Isocitrate + NAD+ <=> Alpha-Ketoglutarate + CO2 + NADH
(D) Succinyl-CoA + Pi + GDP <=> Succinate + GTP + CoA

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/62edf53a-5676-4ae5-a7c2-404b2aca8468

OpenEvidence Explanation

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The answer is **A. Alpha-Ketoglutarate + NAD^+ + CoA $\rightleftharpoons$ Succinyl-CoA + CO_2 + NADH**.

This patient presents with classic **Wernicke-Korsakoff syndrome** — confusion, retrograde memory loss, confabulation, and horizontal nystagmus in the setting of chronic alcoholism — caused by **thiamine (vitamin B1) deficiency**.[1][2] The bilateral pretibial pitting edema and perioral erythema further suggest wet beriberi and pellagra-like features of nutritional deficiency.

Why option A is correct:

Thiamine pyrophosphate (TPP) serves as an essential cofactor for three key enzymes:[3][4][5]

- **Alpha-ketoglutarate dehydrogenase** (Krebs cycle) — catalyzes the conversion of α-ketoglutarate + NAD^+ + CoA → succinyl-CoA + CO_2 + NADH (this is option A)
- **Pyruvate dehydrogenase** — converts pyruvate to acetyl-CoA
- **Transketolase** — operates in the pentose phosphate pathway

The α-ketoglutarate dehydrogenase reaction is the earliest enzyme to show decreased activity in thiamine deficiency (within ~4 days), and its impairment is central to the neurological damage seen in Wernicke encephalopathy.[4]

Why the other options are incorrect:

- **B** (Succinate → Fumarate): Catalyzed by succinate dehydrogenase, which requires **FAD** (vitamin B2), not thiamine.
- **C** (Isocitrate → α-Ketoglutarate): Catalyzed by isocitrate dehydrogenase, which requires **NAD^+** but does not use thiamine as a cofactor.
- **D** (Succinyl-CoA → Succinate): Catalyzed by succinyl-CoA synthetase, which does not require thiamine.

The following figure illustrates the three TPP-dependent enzymes and their roles in glucose metabolism:

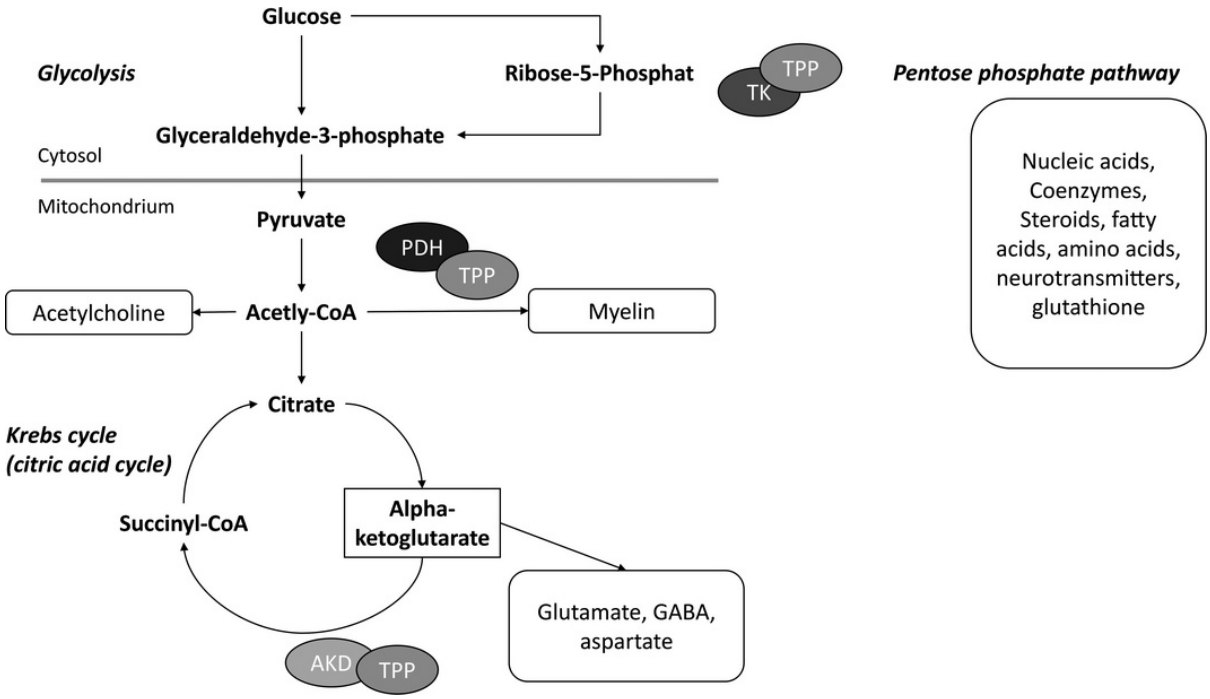


Figure 1. Biochemical mechanism of action of vitamin B1 (thiamine). Modified and simplified illustration based on. TPP, thiamine pyrophosphate; TK, transketolase; PDH, pyruvate dehydrogenase; AKD, alpha-ketoglutarate dehydrogenase; CoA, coenzyme A; GABA, gamma-aminobutyric acid

Would you like to explore the optimal dosing and route of thiamine replacement for preventing progression from Wernicke encephalopathy to Korsakoff syndrome?

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Question 765

A 7-year-old boy is brought to your office with complaints of wheezing and dyspnea. Laboratory work reveals eosinophilia and positive skin tests for allergens. Which of the following types of drugs would be an effective treatment in this patient?

Answer Choices:

(A) Beta-2 antagonist
(B) Histone deacetylase inhibitor
(C) Muscarinic antagonist
(D) Anticoagulant

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/df279c0d-c49e-46a2-a626-32fefbd2b137

OpenEvidence Explanation

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The correct answer is **C. Muscarinic antagonist**.

This clinical scenario describes a child with **allergic asthma** (wheezing, dyspnea, eosinophilia, and positive allergen skin tests). Analyzing each option:

- **A. Beta-2 antagonist** — This is incorrect and would be harmful. Beta-2 **agonists** (e.g., albuterol, salmeterol) are a cornerstone of asthma treatment, causing bronchodilation by relaxing airway smooth muscle. A beta-2 **antagonist** (i.e., a beta-blocker) would cause bronchoconstriction and is contraindicated in asthma.[1][2]
- **B. Histone deacetylase inhibitor** — These are used in oncology (e.g., vorinostat), not in asthma management. This is incorrect.
- **C. Muscarinic antagonist** — This is the correct answer. Muscarinic (anticholinergic) antagonists such as **ipratropium bromide** and **tiotropium** block acetylcholine-mediated bronchoconstriction and are established treatments for asthma. Tiotropium is approved as add-on therapy for poorly controlled asthma, and ipratropium is used as adjunctive bronchodilator therapy in acute exacerbations.[3][4]
- **D. Anticoagulant** — Anticoagulants have no role in asthma treatment. This is incorrect.

The key distinction in this question is between a beta-2 **antagonist** (option A) and a beta-2 **agonist**. While beta-2 agonists are the most commonly used bronchodilators in asthma, the question specifically lists beta-2 *antagonist*, which would worsen bronchoconstriction. Among the remaining options, muscarinic antagonists are the only drug class with an established role in asthma management.[3]

Would you like to explore the specific role of long-acting muscarinic antagonists (e.g., tiotropium) as add-on therapy in pediatric asthma?

Relevant images

(CONTENT OMITTED)

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Question 766

A 16-year-old healthy female presents to her pediatrician concerned that she has not had a menstrual period. She has no past medical history and takes no medications. She plays volleyball and gets good grades in school. Her BMI is 22 kg/m2. Physical examination reveals normal female external genitalia and pubic hair along the mons pubis and superomedial thighs. Her breasts appear normal. Transabdominal ultrasound reveals an absent uterus. Serum testosterone levels is within the normal range for females. What is the most likely cause of this patient's condition?

Answer Choices:

(A) Pituitary tumor
(B) Absence of second X chromosome
(C) Androgen receptor mutation
(D) Failure of paramesonephric duct development

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/dc47ba93-4791-49d7-a4b7-a4a75dc7dc2e

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OpenEvidence Explanation

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The correct answer is **D. Failure of paramesonephric duct development**, which describes **Müllerian agenesis** (Mayer-Rokitansky-Küster-Hauser syndrome).

This patient presents with the classic features of Müllerian agenesis: primary amenorrhea, **absent uterus** on imaging, normal female external genitalia, normal breast development, normal pubic hair distribution, and a **normal female-range testosterone level**.[1][2] Müllerian agenesis results from embryologic underdevelopment of the paramesonephric (Müllerian) ducts, leading to agenesis or atresia of the uterus and upper vagina, with an incidence of approximately 1 in 4,500–5,000 females.[2][3] Because the ovaries derive from a separate embryologic source, ovarian function and secondary sexual characteristics are preserved.[2]

Why the other answers are incorrect:

- **A. Pituitary tumor** — A pituitary tumor causing hypogonadotropic hypogonadism would present with absent or poor breast development and a present (though possibly hypoplastic) uterus, not an absent uterus with normal secondary sexual characteristics.
- **B. Absence of second X chromosome (Turner syndrome, 45,X)** — Turner syndrome presents with short stature, streak gonads, absent breast development (unless mosaic), and a present but infantile uterus. This patient has normal height, normal breasts, and an absent uterus, which is inconsistent.
- **C. Androgen receptor mutation (Complete Androgen Insensitivity Syndrome)** — CAIS can also present with primary amenorrhea and an absent uterus, but it is distinguished by **male-range testosterone levels**, absent or sparse pubic hair, and a 46,XY karyotype. This patient has normal female-range testosterone and normal pubic hair along the mons pubis and superomedial thighs, effectively ruling out CAIS. As the ASRM guideline states, "the simplest means of distinguishing between Müllerian agenesis and complete androgen insensitivity is by measuring serum testosterone, which is in the normal male range or higher in the latter condition".[1][4]

Would you like to explore the evaluation for associated congenital anomalies (renal, skeletal) recommended in patients diagnosed with Müllerian agenesis?

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Question 767

A 61-year-old nulliparous woman comes to the physician for a follow-up examination. Her last Pap smear 3 years ago showed atypical squamous cells of undetermined significance. HPV testing was negative at that time. On questioning, she has had fatigue and an increase in abdominal girth despite a 5-kg (11.0-lb) weight loss over the past 6 months. She has gastroesophageal reflux disease and Hashimoto's thyroiditis. Menarche was at the age of 10 years and her last menstrual period was 2 years ago. Current medications include omeprazole and levothyroxine. Abdominal examination shows shifting dullness. There is tenderness to palpation of the right lower quadrant but no guarding or rebound. Bimanual palpation shows a small uterus and a right adnexal mass. Further evaluation of this patient is most likely to show which of the following findings?

Answer Choices:

(A) Elevated serum CA-125 level
(B) Elevated serum beta-hCG level
(C) Prolonged prothrombin time
(D) Cervical dysplasia on Pap smear

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/bf03759d-cc51-4cc9-8d9e-be31b09ad15e

OpenEvidence Explanation

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The answer is **A. Elevated serum CA-125 level**.

This clinical presentation is classic for **ovarian cancer**: a 61-year-old postmenopausal, nulliparous woman with early menarche (age 10), presenting with fatigue, increasing abdominal girth despite weight loss, ascites (shifting dullness), and a right adnexal mass. Further evaluation would most likely reveal an **elevated serum CA-125 level**, which is the most commonly used tumor marker in the workup of suspected ovarian cancer.

Why CA-125 is the correct answer:

- CA-125 is elevated in approximately **80% of women with epithelial ovarian cancers** and in 75–92% of those with advanced-stage disease. The presence of ascites and an adnexal mass in a postmenopausal woman strongly suggests advanced-stage disease, where CA-125 sensitivity is highest.[1][2]
- NCCN guidelines include CA-125 as part of the standard workup for a suspicious pelvic mass.[3]
- CA-125 testing is particularly useful in **postmenopausal women**, with a meta-analysis showing sensitivity of 69–87% and specificity of 81–93% for diagnosing cancer in this population.[2]

Why this patient is high-risk for ovarian cancer:

- **Nulliparity** confers a ~60% increased risk of epithelial ovarian cancer. Multiparity is protective (OR 0.81 per additional birth).[1][4]
- **Early menarche** (age 10) increases risk through prolonged lifetime ovulatory exposure (HR 1.24–1.37 for menarche ≤12 years vs. >16 years).[5]
- The clinical triad of **adnexal mass, ascites, and weight loss** is highly suggestive of advanced ovarian malignancy.[1][6]

Why the other options are incorrect:

- **B. Elevated beta-hCG** — would suggest a germ cell tumor or gestational trophoblastic disease, both far less likely in a 61-year-old postmenopausal woman. Epithelial ovarian cancer accounts for ~90% of ovarian malignancies.[1]

- **C. Prolonged prothrombin time** — would suggest hepatic dysfunction (e.g., cirrhosis with ascites). However, the adnexal mass and clinical risk factors point to a malignant rather than hepatic etiology for the ascites.
- **D. Cervical dysplasia on Pap smear** — her prior ASC-US with negative HPV testing 3 years ago makes significant cervical dysplasia unlikely. HPV-negative ASC-US carries very low risk of progression.[3]

Would you like to explore the recommended diagnostic workup algorithm and referral criteria for postmenopausal women with a suspicious adnexal mass?

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Question 768

An unresponsive 92-year-old man is brought to the emergency department by ambulance and is quickly followed by his grand-daughter. Approx. 1 month ago, he had a radical prostatectomy, pelvic radiation, and several rounds of chemotherapy for aggressive prostate cancer in Nicaragua and was discharged from the hospital with a suprapelvic catheter and a plan for more chemotherapy. He was coming to the United States to spend time with some extended family. According to the grand-daughter his mental status was altered upon arrival and his health began to decline. She is not aware of his past medical status or medications. At the hospital, his blood pressure is 98/60 mm Hg, the pulse id 110/min, the respiratory rate is 21/min, and the temperature is 35.6°C (96.1°F). On physical exam, the patient appears cachectic, drowsy, and only responds to questions by nodding his head. His heart rate is tachycardic with a regular rhythm and his lungs are clear to auscultation bilaterally. The cystotomy incision for his suprapelvic catheter is red and swollen. The patient admitted to the hospital and stabilized and started on broad-spectrum antibiotics. The catheter tube produces no urine over 24 hours and only thick green-white puss can be expressed. The treatment team concludes this patient has urinary tract obstruction. What is the best method to evaluate urinary tract obstruction in this patient?

Answer Choices:

(A) Renal biopsy
(B) Ultrasound
(C) Abdominal-pelvic CT scan
(D) Blood analysis

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/494d7607-ff7f-429f-aae1-c98096231a5e

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OpenEvidence Explanation

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The best method to evaluate urinary tract obstruction in this patient is **B. Ultrasound**.

Ultrasound is the recommended initial imaging modality for evaluating suspected urinary tract obstruction. It is non-invasive, radiation-free, portable (can be performed at the bedside), and highly accurate for detecting **hydronephrosis**, which is the hallmark finding of urinary obstruction.[1] Point-of-care ultrasound has been shown to accurately detect hydronephrosis and can be performed rapidly in an unstable patient.[1] The European Association of Urology also recommends ultrasound as the initial diagnostic imaging tool for suspected urinary tract pathology due to its safety profile and low cost.[2]

This is particularly appropriate for this patient for several reasons:

- **Hemodynamic instability** — with a blood pressure of 98/60, tachycardia at 110/min, and hypothermia, this patient is septic and hemodynamically fragile. Ultrasound can be performed at the bedside without transporting the patient.
- **Non-invasive and rapid** — unlike CT, ultrasound does not require IV contrast (which could be nephrotoxic in a patient with suspected renal compromise and anuria) and involves no radiation.
- **Clinical context** — the anuria, infected suprapubic catheter site with purulent drainage, and recent pelvic surgery/radiation all raise concern for obstructive uropathy. Ultrasound can quickly confirm or exclude hydronephrosis as the cause.

Regarding the other options: **Renal biopsy (A)** is invasive and not indicated for evaluating obstruction. **Abdominal-pelvic CT (C)**, while more detailed, is a

second-line study typically reserved for when ultrasound is inconclusive or when the etiology of obstruction needs further characterization.[3] **Blood analysis (D)** can reveal elevated creatinine or BUN suggesting renal impairment but cannot directly evaluate or localize urinary tract obstruction.

Would you like to explore the management approach for obstructive uropathy with concurrent sepsis in a post-surgical oncology patient?

Relevant images

(CONTENT OMITTED)

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Question 769

A 51-year-old man presents to his primary care provider for intermittent shaking of his hands. He reports that for the last several years he has noticed this shaking when he brushes his teeth and prepares a cup of coffee in the morning. The shaking then gradually improves over the course of the day. His past medical history is otherwise notable for hypertension and hyperlipidemia. His only home medication is pravastatin. The patient smokes half a pack per day of cigarettes and drinks 2-3 beers throughout the day. His family history is significant for Parkinson disease in his father. On physical exam, his blood pressure is 159/84, pulse is 74/min, and respirations are 12/min. He has a high frequency bilateral hand tremor elicited on finger-to-nose testing. His neurological exam is otherwise unremarkable. This patient should be started on which of the following medications?

Answer Choices:

(A) Alprazolam
(B) Primidone
(C) Propranolol
(D) Trihexyphenidyl

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/9428b30e-003f-44b4-abfd-ccd95516f8d9

OpenEvidence Explanation

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The correct answer is **C. Propranolol**.

This patient presents with a classic case of **essential tremor** — a bilateral, high-frequency action tremor elicited during goal-directed movement (finger-to-nose testing), with a gradual onset over several years and an otherwise unremarkable neurological exam. The improvement over the course of the day (likely related to alcohol consumption, as ethanol is known to transiently suppress essential tremor) further supports this diagnosis. Notably, while the family history of Parkinson disease may raise concern, the bilateral action tremor without resting tremor, bradykinesia, or rigidity makes Parkinson disease unlikely.[1][2]

Propranolol and primidone are both first-line treatments for essential tremor, with Level A evidence (established as effective) per the American Academy of Neurology guidelines.[3] Propranolol is the **only FDA-approved medication** for essential tremor and has demonstrated a mean 55% reduction in tremor amplitude across randomized controlled trials at doses of 120–240 mg/day.[4] In this patient with concurrent **hypertension** (BP 159/84), propranolol offers the additional benefit of blood pressure control, making it the optimal choice.

Why not the other options:

- **Primidone (B)** — Also first-line for essential tremor, but has higher rates of early adverse effects (dizziness, fatigue, malaise in 23–32% vs. 8% with propranolol) and does not offer the added benefit of treating this patient's uncontrolled hypertension.[4]
- **Alprazolam (A)** — A second-line agent (Level B evidence) for essential tremor, but carries risks of dependence, particularly concerning in a patient who already drinks 2–3 beers daily.[3]
- **Trihexyphenidyl (D)** — An anticholinergic used for Parkinson disease tremor, not essential tremor. This patient does not have parkinsonian features.[1]

Would you like to explore the approach to essential tremor that is refractory to first-line pharmacotherapy, including interventional options such as deep brain stimulation and focused ultrasound thalamotomy?

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Question 772

A 25-year-old man presents to his primary care provider complaining of several weeks of intense itching, particularly localized around his anus. Of note, the patient denies any recent travel, sexual contacts, fever, dysuria, or diarrhea. His temperature is 98.1°F (36.7°C), blood pressure is 110/70 mmHg, pulse is 65/min, and respirations are 12/min. On exam, the patient demonstrates severe excoriations in his perianal region with slight erythema over the areas that are torn. He does not have any other dermatologic findings. The scotch tape test is positive. The patient has a previous documented allergy to albendazole. Which of the following is an alternative medication that can be used?

Answer Choices:

(A) Amphotericin B
(B) Ivermectin
(C) Praziquantel
(D) Pyrantel pamoate

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/a3756600-7d43-420a-998b-f9a1f66e3157

OpenEvidence Explanation

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The correct answer is **D. Pyrantel pamoate**.

This clinical presentation — perianal pruritus with excoriations and a positive scotch tape test — is classic for **Enterobius vermicularis (pinworm) infection**. The scotch tape (cellophane tape) test detects pinworm eggs deposited in the perianal region, confirming the diagnosis.[1]

The standard treatment for enterobiasis includes **albendazole, mebendazole, or pyrantel pamoate**, all with cure rates exceeding 90%.[1] Since this patient has a documented allergy to albendazole, **pyrantel pamoate** is an appropriate alternative. It is dosed at 11 mg/kg (maximum 1 g) as a single dose, repeated in two weeks, and is available over the counter.[1]

Why the other options are incorrect:

- **A. Amphotericin B** — An antifungal agent used for systemic fungal infections; it has no antihelminthic activity.
- **B. Ivermectin** — Effective against many helminths (e.g., Strongyloides, Ascaris), but it is not a standard or recommended treatment for Enterobius vermicularis.[2]
- **C. Praziquantel** — Active against trematodes (flukes) and cestodes (tapeworms), not nematodes like pinworm.

Notably, albendazole and pyrantel pamoate have different mechanisms of action — albendazole is a benzimidazole that disrupts microtubule function, while pyrantel pamoate is a nicotinic acetylcholine receptor agonist causing neuromuscular paralysis of the worm.[3] An allergy to one does not preclude use of the other.

Would you like to explore the recommended hygiene measures and household treatment strategies to prevent pinworm reinfection?

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Question 775

A gunshot victim is brought to the Emergency Department and appears to be in shock. You note a penetrating wound at the level of L3. Assuming the bullet remained at this level, which vascular structure might have been injured?

Answer Choices:

(A) Inferior vena cava
(B) Internal iliac vein
(C) Renal artery
(D) Portal vein

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/f441c222-0c82-4b80-a6c3-7a194a2969fa

OpenEvidence Explanation

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The answer is **A. Inferior vena cava**.

At the level of **L3**, the major vascular structures present are the **abdominal aorta** and the **inferior vena cava (IVC)**, both of which lie in direct contact with the anterior vertebral column at this level. The IVC ascends in tight contact with the vertebral column from its formation (which varies from L3 to L5) through the

upper lumbar levels.[1][2] The aorta also descends along the left anterior aspect of the lumbar vertebrae, with its bifurcation typically occurring at L4 (range L3–L5).[1][2][3]

Evaluating the other options:

- **B. Internal iliac vein** — The internal iliac veins are pelvic structures, located well below L3, typically arising from the common iliac veins in the pelvis.
- **C. Renal artery** — The renal arteries originate from the aorta at the level of L1–L2 (range T12–L2), which is above L3.[1][3]
- **D. Portal vein** — The portal vein is located anterior to the IVC at approximately the level of L1–L2, within the hepatoduodenal ligament, and is not a retroperitoneal structure at L3.

Among the choices, the **IVC** is the vascular structure most likely to be injured by a penetrating wound at L3, as it lies directly anterior to the vertebral body at this level.[2][4][5]

Would you like to explore the initial management and resuscitation priorities for penetrating abdominal vascular injuries presenting in hemorrhagic shock?

Relevant images

(CONTENT OMITTED)

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Question 777

A 38-year-old woman is being evaluated by her primary care physician for chronic, widespread pain that started around 5 months ago. This pain has been accompanied by sleeping issues. Her friend recommended that she try yoga to relieve the pain, but she says this has not helped her at all. Se says the symptoms have begun to impact her daily functions and keep her from doing things she used to enjoy. Past medical history includes generalized anxiety disorder, for which she currently takes no medication. The patient had been previously medicated with paroxetine for 5 years. On physical examination, several areas of point tenderness are found on the occipital region, elbows, and medial surface of both knees. Laboratory work up is unremarkable. What is the best treatment option for the most likely diagnosis in this patient?

Answer Choices:

(A) Low-dose prednisolone
(B) High-dose prednisolone
(C) Paroxetine
(D) Allopurinol

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/c029e692-aa12-4317-9c60-363dd758fddc

OpenEvidence Explanation

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The best answer is **C. Paroxetine**.

The clinical presentation — chronic widespread pain for ≥3 months, sleep disturbances, multiple bilateral tender points (occiput, elbows, medial knees), unremarkable labs, and functional impairment — is classic for **fibromyalgia**.

Why paroxetine is the best answer among the options listed:

Among the four choices, paroxetine (an SSRI) is the only medication with evidence of benefit in fibromyalgia. A randomized controlled trial of paroxetine CR in fibromyalgia (excluding patients with current mood/anxiety disorders) demonstrated that 57% of patients achieved ≥25% reduction in Fibromyalgia Impact Questionnaire scores vs. 33% with placebo (P = .016), with significant improvement in overall symptomatology.[1] A meta-analysis in JAMA also found strong evidence for the efficacy of fluoxetine and paroxetine in reducing fibromyalgia pain (SMD −0.39).[2] Additionally, this patient has comorbid generalized anxiety disorder that is currently untreated, and paroxetine would address both conditions.

Why the other options are incorrect:

- **A & B (Low-dose or high-dose prednisolone):** Corticosteroids have no role in fibromyalgia management. Fibromyalgia is not an inflammatory condition, and glucocorticoids are not recommended.[3]
- **D (Allopurinol):** This is a xanthine oxidase inhibitor used for gout/hyperuricemia and has no indication in fibromyalgia.

Important context: In clinical practice, the preferred first-line pharmacologic agents for fibromyalgia are **duloxetine, milnacipran, or pregabalin** (the three FDA-approved medications), along with amitriptyline used off-label.[3][4] A Cochrane review found that SSRIs as a class did not demonstrate robust evidence for treating pain, fatigue, or sleep problems in fibromyalgia, though they may help with depression.[3][5] However, given the answer choices presented, paroxetine is clearly the most appropriate option, particularly since this patient also has untreated anxiety.

Would you like to explore the comparative effectiveness of FDA-approved fibromyalgia medications (duloxetine, milnacipran, pregabalin) and how to tailor selection based on the patient's predominant symptom profile?

Relevant images

(CONTENT OMITTED)

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Question 779

A 29-year-old man presents to the emergency department after a motor vehicle accident. On presentation, he is found to have scalp and trunk lacerations that are still actively bleeding. He has no past medical history and does not take any medications. On presentation, his temperature is 98.6°F (37°C), blood pressure is 110/74 mmHg, pulse is 82/min, and respirations are 17/min. On physical exam, he is found to be anxious but does not have any visible injuries other than the lacerations. Which of the following processes would most likely be seen in this patient?

Answer Choices:

(A) Baroreceptor-mediated vasodilation
(B) Increased acetylcholine at the sinoatrial node
(C) Increased atrial natriuretic peptide release
(D) Increased norepinephrine at the sinoatrial node

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/504ffc71-9aad-4812-a76a-f85fdda3f3e5

OpenEvidence Explanation

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The correct answer is **D. Increased norepinephrine at the sinoatrial node**.

This patient is presenting with active hemorrhage from scalp and trunk lacerations following a motor vehicle accident. Although his vital signs are currently relatively stable (BP 110/74, HR 82), his body is in the **compensatory phase of hemorrhage**, during which the sympathetic nervous system is the predominant mechanism activated to maintain hemodynamic stability.

Physiologic rationale:

Acute blood loss triggers a decrease in cardiac output and pulse pressure, which is sensed by **baroreceptors** in the aortic arch and carotid sinus. The reduced stretch on these baroreceptors leads to decreased afferent signaling to the brainstem, resulting in **increased sympathetic outflow** and decreased parasympathetic tone.[1][2] This sympathetic activation releases **norepinephrine** at target organs, including the sinoatrial (SA) node, to increase heart rate and contractility, and at peripheral vasculature to increase systemic vascular resistance.[3] Plasma norepinephrine has been shown to increase significantly (~35–43% above baseline) even after modest, non-hypotensive blood loss.[3]

Why the other options are incorrect:

- **A. Baroreceptor-mediated vasodilation** — Baroreceptor unloading during hemorrhage leads to vasoconstriction, not vasodilation. Vasodilation would only occur in the decompensatory phase after severe blood loss (>30% of blood volume).[1]
- **B. Increased acetylcholine at the SA node** — Acetylcholine is the parasympathetic neurotransmitter that would slow heart rate. During hemorrhage, parasympathetic tone is withdrawn, not increased.
- **C. Increased atrial natriuretic peptide (ANP) release** — ANP is released in response to atrial stretch from volume overload. In hemorrhage, atrial volume and pressure are decreased, so ANP release would be reduced, not increased.

The patient's anxiety is also consistent with the sympathoadrenal response to hemorrhage, with circulating catecholamines contributing to this symptom.[2]

Would you like to explore the classification of hemorrhagic shock stages and how vital sign changes correlate with estimated blood loss volume?

Relevant images

(CONTENT OMITTED)

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Question 780

A 14-year-old teenager presents to his pediatrician complaining of frequent headaches and excessive fatigue during soccer practice. His mother notes that he seems to have gained a lot of weight despite the fact that he eats a healthy, well-balanced diet. His teachers have also become concerned because he leaves class to use the restroom frequently throughout the day. He has no medical problems and family history is insignificant. A physical exam is significant for a short, overweight child with nonpitting edema and decreased reflexes. His systolic blood pressure drops by 20 mm Hg when he stands. Fundoscopic exam is significant for papilledema and visual field exam is significant for bitemporal hemianopsia. Laboratory findings include:
BUN 22 mg/dL N: 7–20 mg/dL
pCO2 32 mm Hg N: 35–45 mm Hg
Creatinine 0.8 mg/dL N: 0.8–1.4 mg/dL
Glucose 50 mg/dL N: 64–128 mg/dL
Serum chloride 95 mmol/L N: 101–111 mmol/L
Serum potassium 3.3 mEq/L N: 3.7–5.2 mEq/L
Serum sodium 120 mEq/L N: 136–144 mEq/L
Bicarbonate (HCO3) 15 mmol/L N: 18–22 mmol/L
Thyroid-stimulating hormone (TSH) 0.1 mIU/L N: 0.5–5 mIU/L
Free T4 6 pmol/L N: 10–20 pmol/L
What is the necessary treatment?

Answer Choices:

(A) Chemotherapy, surgical resection and radiation
(B) Chemotherapy and radiation
(C) Surgical resection
(D) Hormone replacement therapy

Correct Answer:

(C)

OpenEvidence Response:

> (C) ✓

OpenEvidence Link: https://openevidence.com/ask/259070ac-8ec4-4bf1-bf98-ceefae3acd34

OpenEvidence Explanation

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The correct answer is **C. Surgical resection**.

This clinical presentation is consistent with a **craniopharyngioma**, a benign (WHO grade I) sellar/suprasellar tumor arising from embryonic remnants of Rathke's pouch. The key findings pointing to this diagnosis include:

- **Bitemporal hemianopsia and papilledema**: indicating optic chiasm compression and raised intracranial pressure from a suprasellar mass[1][2]
- **Short stature, weight gain, and hypothyroidism** (low TSH with low free T4 = central hypothyroidism): reflecting panhypopituitarism from hypothalamic-pituitary axis compression[1][3]
- **Hyponatremia, hypoglycemia, and orthostatic hypotension**: consistent with ACTH deficiency (secondary adrenal insufficiency) and possibly SIADH from hypothalamic involvement[4]
- **Polyuria** (frequent bathroom use): likely from diabetes insipidus due to posterior pituitary/hypothalamic involvement
- **Age 14**: falls within the peak incidence of the adamantinomatous subtype (5–15 years)[1][5]

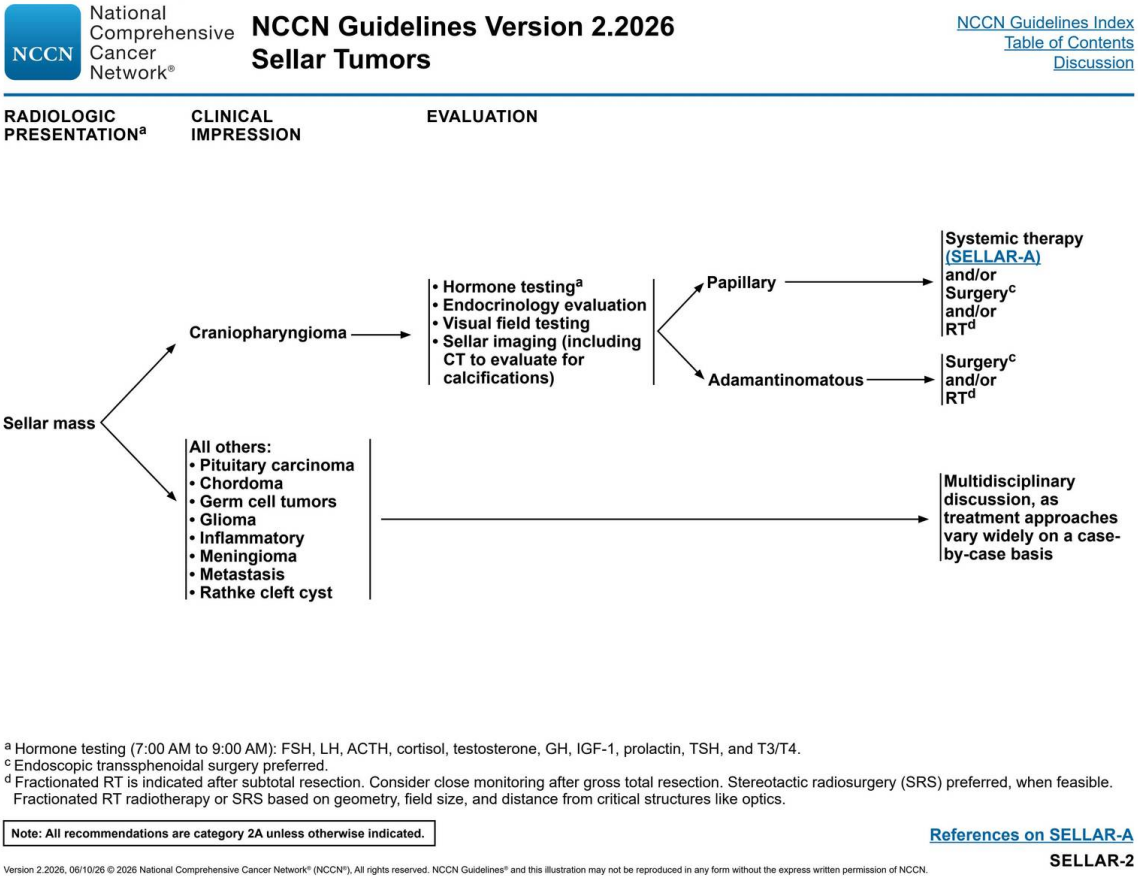
Why surgical resection is the primary treatment:

Surgical resection is the treatment of choice for craniopharyngioma.[1][3][6] When the tumor is favorably located (without significant hypothalamic involvement), complete resection is the preferred approach, with care taken to

preserve optic and hypothalamic function.[6][7] Gross total resection achieves 5-year progression-free survival of approximately 67–77%.[8][9] The NCCN guidelines for adamantinomatous craniopharyngioma list surgery and/or radiation therapy as treatment options, with radiation indicated primarily after subtotal resection.[10]

Why the other options are incorrect:

- **A (Chemotherapy, surgical resection, and radiation)** and **B (Chemotherapy and radiation)**: Craniopharyngiomas are not chemosensitive tumors. Systemic chemotherapy has no established role in the treatment of adamantinomatous craniopharyngioma. Targeted therapy (e.g., BRAF-MEK inhibition) has shown promise only in the papillary subtype, which occurs exclusively in adults.[5][11]
- **D (Hormone replacement therapy)**: While hormone replacement is essential for managing the endocrine deficiencies (and will almost certainly be needed lifelong after treatment), it does not address the underlying tumor causing mass effect on the optic chiasm and hypothalamus.[1][12]



Would you like to explore the long-term endocrine management and monitoring strategies required after craniopharyngioma resection in pediatric patients?

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Question 781

Hypoxia-inducible factor 1-alpha (HIF-1a) is a transcription factor with increased activity under conditions of cellular hypoxia. In normoxia, von Hippel-Lindau (VHL) protein hydroxylates prolyl residues on oxygen-dependent degradation domains of HIF-1a, targeting it for proteasomal degradation. Hydroxylation by VHL is inhibited under hypoxic conditions, allowing HIF-1a to escape degradation, dimerize with HIF-1ß, and translocate to the nucleus. This results in the upregulation of hypoxic response elements, leading to angiogenesis. Renal cell carcinoma (RCC) can mimic the hypoxic state to promote angiogenesis by inhibiting HIF-1a hydroxylation, even in the absence of hypoxia. A researcher wants to perform an experiment to detect HIF-1a in RCC under normoxic conditions with blotting techniques. Which of the following statements are most likely to be true regarding her experiment?

Answer Choices:

(A) A Northern blot will show increased HIF-1α, compared to a hypoxic control cell.
(B) A Northern blot will show increased HIF-1α, compared to a normoxic control cell.
(C) A Southern blot will show increased HIF-1α, compared to a normoxic control cell.
(D) A Western blot will show increased HIF-1α compared to a normoxic control.

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/806bbc30-2edb-4c4e-8e31-e2e1bd59b47f

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OpenEvidence Explanation

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The correct answer is **D. A Western blot will show increased HIF-1α compared to a normoxic control.**

The key to this question lies in understanding two concepts: (1) the type of regulation involved in HIF-1α accumulation in RCC, and (2) what each blotting technique detects.

HIF-1α regulation in RCC is post-translational, not transcriptional. In RCC with VHL loss-of-function, the VHL protein can no longer ubiquitinate HIF-1α for proteasomal degradation under normoxic conditions. This means HIF-1α **protein** accumulates constitutively, even in normoxia.[1][2][3] Critically, this is a defect in protein degradation — the HIF-1α mRNA (gene transcription) is not necessarily increased; rather, the protein is simply stabilized because it escapes ubiquitin-mediated destruction.[4][5]

Blotting technique review:

- **Southern blot** detects **DNA** — the HIF-1α gene itself is not amplified or altered in copy number in this scenario, so a Southern blot would not show a difference.[6][7]
- **Northern blot** detects **mRNA** — while some studies have noted modest changes in HIF-1α mRNA in VHL-deficient cells, the primary mechanism of HIF-1α upregulation in RCC is post-translational stabilization, not increased transcription. Importantly, HIF-1α mRNA levels would not be expected to differ significantly between RCC cells and a normoxic control cell based on the mechanism described in the question stem.[1][8][9]

- **Western blot** detects **protein** — this is the appropriate technique to detect the increased HIF-1α protein that accumulates due to impaired proteasomal degradation.[7][10]

Option A is incorrect because a Northern blot would not show increased HIF-1α mRNA compared to a hypoxic control (hypoxic cells also have stabilized HIF-1α, but again at the protein level). Option B is incorrect because the mechanism is post-translational, not transcriptional. Option C is incorrect because Southern blots detect DNA, which is unchanged. **Option D is correct** because the Western blot detects the accumulated HIF-1α protein that escapes VHL-mediated degradation in RCC cells under normoxic conditions, whereas in a normal normoxic control cell, HIF-1α protein would be rapidly degraded.[2][3]

Would you like to explore how this understanding of the VHL-HIF pathway has led to the development of targeted therapies for clear cell renal cell carcinoma, including HIF-2α inhibitors like belzutifan?

Relevant images

(CONTENT OMITTED)

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Question 782

A 25-year-old primigravida is admitted to the hospital at 36 weeks gestation after a generalized tonic-clonic seizure. She is conscious, but lethargic and complains of a headache that started 2 hours prior to the seizure. She denies alcohol intake or drug use. She has no history of convulsive disorders and the antepartum course has been unremarkable. She was compliant with the recommended prenatal care and her last prenatal visit was 2 weeks ago. She has gained 2 kg (4.4 lb) since her last visit. The blood pressure was 160/90 mm Hg, the heart rate was 79/min, the respiratory rate was 14/min, and the temperature was 37.0°C (98.6°F). The physical examination shows leg and perineal edema. The neurologic examination is significant for symmetric upper and lower extremity hyperreflexia and ankle clonus. Which of the following laboratory findings would be most common in this patient?

Answer Choices:

(A) Elevated transaminases
(B) Leukocytosis
(C) Hyponatremia
(D) Proteinuria

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/1bafaaca-9002-4234-92c9-0fe67802aa21

OpenEvidence Explanation

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The answer is **D. Proteinuria**.

This patient presents with classic **eclampsia** — new-onset tonic-clonic seizures in the setting of hypertension (160/90 mmHg), headache, edema, hyperreflexia, and ankle clonus at 36 weeks gestation in a primigravida. **Proteinuria is the most common laboratory finding** in preeclampsia/eclampsia, as renal involvement is the most frequent organ manifestation of the disease.

Why proteinuria is the most common finding:

Renal involvement in preeclampsia is most commonly manifested as proteinuria due to the pathognomonic lesion of **glomerular endotheliosis** and associated loss of podocyte integrity.[1] Proteinuria (≥300 mg per 24-hour collection or protein/creatinine ratio ≥0.3) is a core diagnostic criterion for preeclampsia, alongside hypertension.[2][3] While proteinuria is not absolutely required for diagnosis if other severe features are present, it remains the most frequently observed laboratory abnormality.

Why the other options are less likely:

- **A. Elevated transaminases** — Hepatic involvement occurs in only about **20–30% of patients** with preeclampsia, and elevated aminotransferases are seen in approximately one-third of cases. While elevated transaminases are a recognized severe feature, they are far less common than proteinuria.[4][5]
- **B. Leukocytosis** — Relative neutrophilia can occur as part of the hematologic manifestations of preeclampsia, but it is not a defining or commonly tested laboratory finding.[1]
- **C. Hyponatremia** — Hyponatremia is not a characteristic laboratory finding of preeclampsia/eclampsia and is not included in any diagnostic criteria.[2][3]

Per ACOG, preeclampsia is defined by hypertension after 20 weeks gestation with proteinuria or other evidence of end-organ dysfunction.[2] The presence of

seizures elevates this to eclampsia, which occurs in the setting of these same findings.[2]

Would you like to explore the acute management of eclampsia, including magnesium sulfate dosing and delivery timing considerations?

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Question 783

A 3-year-old male is brought by his mother to the pediatrician's office. The mother and child are refugees from Somalia and arrived in the United States one week ago. They were recently placed in temporary housing. The mother reports that the child has been chronically tired and subdued since before their arrival in the United States. The child was born at 38 weeks gestation with the help of a local midwife. The child's temperature is 98.2°F (36.8°C), blood pressure is 105/60 mmHg, pulse is 90/min, and respirations are 18/min. Physical examination reveals a listless child with a rotund abdomen and positive fluid wave. Notable lower extremity edema is present. This patient's condition is most likely caused by a deficiency in which of the following?

Answer Choices:

(A) Total caloric intake
(B) Relative protein intake
(C) Relative carbohydrate intake
(D) Relative fat intake

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/31f47ca5-a584-483f-99c1-2f85e2173b3c

OpenEvidence Explanation

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The answer is **B. Relative protein intake**. This presentation is classic for **kwashiorkor**, a form of severe protein-energy malnutrition caused by a **relative deficiency of dietary protein** with relatively preserved caloric (energy) intake.

Key clinical features supporting this diagnosis:

- **Edema** (lower extremity edema and ascites with positive fluid wave) — the hallmark of kwashiorkor, resulting from hypoalbuminemia due to insufficient protein for hepatic albumin synthesis[1][2]
- **Abdominal distension** ("rotund abdomen") — caused by ascites and hepatomegaly from fatty liver infiltration, as well as loss of abdominal wall musculature[3]
- **Listlessness and chronic fatigue** — consistent with the neurodevelopmental impairment and apathy seen in kwashiorkor[4]
- **Epidemiologic context** — a young child from a developing country (Somalia), the demographic most affected by kwashiorkor[5]

Distinguishing kwashiorkor from marasmus is critical here. Marasmus results from total caloric deficiency (option A) and presents with severe muscle wasting and emaciation without significant edema. In contrast, kwashiorkor classically occurs when children are weaned onto carbohydrate-rich but protein-poor diets (e.g., maize or cassava gruel), maintaining caloric intake while becoming profoundly protein-deficient.[1][6] As described in the NEJM, kwashiorkor manifests when "the principal cause of malnutrition is a dietary protein deficiency with a still substantial intake of energy".[1] Waterlow's seminal work confirmed that "the development of oedema depends on a relative deficiency of protein with a relative excess of energy".[2]

Would you like to explore the recommended refeeding protocols and monitoring strategies for children with kwashiorkor, including the risks of refeeding syndrome?

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Question 786

A 14-year-old boy is brought to the emergency department by his mother after falling from the jungle gym and developing severe left knee pain and swelling. On presentation, he is found to be in pain with a hot, swollen, erythematous left knee. His past medical history is significant for abnormal coagulation lab tests before an appendectomy, but his mother cannot recall the exact details. Coagulation tests are conducted with the following results:

Bleeding time: 3 minutes
Prothrombin time: 11 seconds
Partial thromboplastin time: 53 seconds
Bradykinin formation: decreased

Which of the following factors is most likely defective in this patient?

Answer Choices:

(A) Factor VII
(B) Factor VIII
(C) Factor IX
(D) Factor XII

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/4e267bf2-c5a9-4765-b3ca-a665c76e24f0

OpenEvidence Explanation

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The answer is **D. Factor XII**.

The key to this question is the combination of an **isolated prolonged PTT** (53 seconds) with a **normal PT** (11 seconds), **normal bleeding time** (3 minutes), and critically, **decreased bradykinin formation**. This pattern uniquely identifies **Factor XII (Hageman factor) deficiency**.

Why Factor XII fits all the findings:

- **Isolated prolonged PTT with normal PT:** Factor XII is part of the intrinsic coagulation pathway. Its deficiency prolongs the PTT without affecting the PT (extrinsic pathway). While Factors VIII, IX, and XI deficiencies also cause this pattern, the decreased bradykinin is the distinguishing clue.[1][2]
- **Decreased bradykinin formation:** Factor XII activates prekallikrein to kallikrein, which cleaves high-molecular-weight kininogen (HMWK) to release bradykinin. Factor XII deficiency therefore directly impairs bradykinin generation. This finding is not seen with deficiencies of Factors VIII or IX.[3][4][5]
- **Normal bleeding time:** Factor XII deficiency does not cause clinical bleeding. The knee swelling in this patient is from the traumatic injury itself, not a coagulopathy. This is consistent with the well-established observation that FXII deficiency prolongs the aPTT but is dispensable for hemostasis in vivo.[1][2][4][6]
- **Abnormal preoperative coagulation labs without bleeding history:** The mother recalls abnormal labs before appendectomy — this is a classic presentation of incidentally discovered FXII deficiency, which causes a markedly prolonged aPTT but no bleeding tendency.[2]

Why the other options are incorrect:

- **A. Factor VII** — Would cause a prolonged PT with normal PTT (extrinsic pathway factor).[1]

- **B. Factor VIII** — Would cause prolonged PTT but does not affect bradykinin formation; also, hemophilia A typically presents with significant bleeding episodes, not just incidental lab abnormalities.
- **C. Factor IX** — Same reasoning as Factor VIII; hemophilia B does not impair bradykinin generation.

Would you like to explore the clinical significance of Factor XII deficiency in the context of thrombotic risk, given emerging evidence that FXII plays a role in pathological thrombosis despite being dispensable for hemostasis?

Relevant images

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Question 787

A 52-year-old man with Crohn disease comes to the physician because of a 1-week history of dysuria and urinary urgency. He had been treated for urinary tract infections twice in the past 6 months. He is currently taking infliximab. Cystoscopy shows pearl-like plaques on the bladder wall. Biopsy of these lesions shows a focal layer of stratified squamous epithelium with hyperkeratosis. If the patient's bladder finding is caused by a vitamin deficiency, which of the following features is also most likely to be seen?

Answer Choices:

(A) Carpopedal spasm
(B) Photodermatitis
(C) Night blindness
(D) Intracranial hypertension

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/b342c4e2-8484-4b5d-b85b-fd6bb3a2d410

OpenEvidence Explanation

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The answer is **C. Night blindness**.

The pearl-like plaques on the bladder wall with keratinizing squamous metaplasia and hyperkeratosis on biopsy are characteristic of **vitamin A deficiency**. Vitamin A (retinol) is essential for maintaining normal differentiation of epithelial tissues, including the transitional epithelium (urothelium) of the urinary bladder. In vitamin A deficiency, the normal urothelium undergoes squamous metaplasia with keratinization, which appears cystoscopically as white, pearl-like plaques (leucoplakia).[1][2][3]

This patient with Crohn disease is at risk for fat-soluble vitamin deficiencies (A, D, E, K) due to malabsorption, particularly if the terminal ileum is involved.

Night blindness (nyctalopia) is the earliest and most classic clinical manifestation of vitamin A deficiency.[4][5] Vitamin A is required for the synthesis of rhodopsin (visual purple), the photopigment in rod cells responsible for scotopic (dim-light) vision. Progressive vitamin A deficiency leads to xerophthalmia, including conjunctival xerosis, Bitot's spots, corneal xerosis, and ultimately keratomalacia and blindness.[4]

The other options correspond to different vitamin deficiencies:

- **Carpopedal spasm** — hypocalcemia, associated with vitamin D deficiency
- **Photodermatitis** — niacin (vitamin B3) deficiency (pellagra)
- **Intracranial hypertension** — paradoxically associated with vitamin A excess (hypervitaminosis A), not deficiency

Would you like to explore the full spectrum of fat-soluble vitamin deficiencies seen in Crohn disease and their clinical manifestations?

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Question 788

A 26-year-old gravida 2 para 1 at 24 weeks gestation is admitted to the labor and delivery suite with mild abdominal cramps, uterine contractions, and a watery vaginal discharge. She has a history of preterm birth. The vital signs are as follows: blood pressure 125/80 mm Hg; heart rate 100/min; respiratory rate 13/min; and temperature 36.6°C (97.9°F). The pelvic examination reveals cervical softening and shortening. Transvaginal ultrasound shows a cervical length of 12 mm, which is consistent with preterm labor. A tocolytic and a single dose of betamethasone are administered. Betamethasone stimulates which fetal cells?

Answer Choices:

(A) Goblet cells
(B) Bronchial epithelial cells
(C) Type II pneumocytes
(D) Vascular smooth myocytes

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/3476c690-32b6-4a31-9f9a-f9dbc74371f8

OpenEvidence Explanation

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The correct answer is **C. Type II pneumocytes**.

Antenatal betamethasone primarily stimulates **type II pneumocytes** (alveolar type II cells) in the fetal lung to accelerate surfactant production, which is essential for reducing surface tension at the air-liquid interface of the alveoli and preventing respiratory distress syndrome (RDS) in preterm neonates.[1][2]

The mechanism involves glucocorticoids crossing the placenta and acting on fetal lung tissue to enhance the production of surfactant-associated proteins (SP-A, SP-B, SP-C, SP-D) and increase phospholipid synthesis — particularly phosphatidylcholine — by type II pneumocytes.[2][3] Interestingly, the pathway is partly indirect: glucocorticoids stimulate fetal lung fibroblasts to produce fibroblast-pneumonocyte factor, which in turn stimulates surfactant synthesis by type II pneumocytes.[4] Additional effects include maturation of lung parenchymal structure, decreased vascular permeability, and increased clearance of lung water.[1]

The clinical benefit is well established — the ACOG recommends a single course of antenatal corticosteroids for pregnant women between 24 0/7 and 33 6/7 weeks of gestation at risk of preterm delivery within 7 days, with demonstrated reductions in RDS, intraventricular hemorrhage, necrotizing enterocolitis, and neonatal mortality.[5]

The other answer choices are incorrect because:

- **Goblet cells** produce mucus in the airways and are not the target of betamethasone for lung maturation.
- **Bronchial epithelial cells** line the airways but are not the primary cells responsible for surfactant production.
- **Vascular smooth myocytes** are not the cellular target for betamethasone's lung maturation effects.

Would you like to explore the optimal dosing regimens and timing of antenatal corticosteroids, including the evidence for repeat courses versus single courses?

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Question 796

While traveling abroad a physician is asked to attend a meeting regarding healthcare in the region. The rate of chlamydial infection is exceptionally high in the area, and the local government is wanting to test a new treatment for these infections. To test the new therapy, the physician is asked to oversee the operations of testing this new treatment. When asking what this would entail, the officials tell the physician that they plan to infect the local prison population with chlamydia and then test the new treatment on these individuals. Which of the following is the best response from the physician?

Answer Choices:

(A) “I can not help you due to the ethical principle of autonomy.”
(B) “I can not help you due to the ethical principle of justice.”
(C) “I can not help you due to the ethical principle of nonmaleficence.”
(D) “I can not help you due to the ethical principle of beneficence.”

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/3c9168a8-d847-452a-b7ed-f385601a4e45

OpenEvidence Explanation

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The best response is **C. "I can not help you due to the ethical principle of nonmaleficence."**

Nonmaleficence — the obligation to "first, do no harm" — is the principle most directly violated by this proposal. The plan involves **deliberately infecting** healthy prisoners with chlamydia, which constitutes intentional infliction of harm on individuals who are not currently ill.[1][2]

While multiple ethical principles are violated in this scenario, the question asks for the *best* response:

- **Nonmaleficence** is the most fitting answer because the core ethical violation is the act of intentionally causing disease in healthy individuals. This directly contravenes the duty not to inflict harm.[1][2][3]
- **Autonomy** is also violated (prisoners cannot freely consent due to their coercive environment), but the primary wrong here is not the lack of consent — it is the deliberate infection itself.[4][5]
- **Justice** is implicated because prisoners are a vulnerable population being unfairly targeted for research, but again, the most fundamental issue is the intentional harm.[5][6]
- **Beneficence** (the duty to promote good) is less directly applicable than nonmaleficence in this context, as the proposal actively causes harm rather than merely failing to promote benefit.

The distinction between nonmaleficence and the other principles is important: even if the prisoners consented (autonomy satisfied), even if the population was fairly selected (justice satisfied), and even if the treatment ultimately worked (beneficence achieved), deliberately infecting people with a pathogen remains a violation of the duty to do no harm.[2][7]

Would you like to explore how human challenge studies (deliberate infection trials) are ethically regulated and under what narrow circumstances they may be permissible?

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Question 797

A 48-year-old woman comes to the physician because of a 7-day history of progressively worsening shortness of breath. She has a history of asthma and has frequent exacerbations despite receiving maximal medical therapy. Physical examination shows scattered expiratory wheezing. Laboratory studies show a leukocyte count of 9,800/mm3 (13% eosinophils) and elevated serum concentration of immunoglobulin E. An x-ray of the chest shows thickened bronchial walls and perihilar opacities. Sputum culture shows scattered septate hyphae that branch at 45 degrees. Which of the following is most likely to be increased in this patient?

Answer Choices:

(A) IL-28
(B) TGF-β
(C) IFN-α
(D) IL-4

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/b6b5e918-2c5e-4425-9ac1-bbbb114d3ed2

OpenEvidence Explanation

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The answer is **D. IL-4**.

This clinical vignette describes **allergic bronchopulmonary aspergillosis (ABPA)**, characterized by an asthmatic patient with peripheral eosinophilia (13%), elevated serum IgE, perihilar opacities with bronchial wall thickening, and sputum showing **septate hyphae branching at 45 degrees** (classic for *Aspergillus fumigatus*).

ABPA is driven by an exaggerated **Th2 immune response** to *Aspergillus* antigens. The hallmark cytokines are **IL-4**, IL-5, and IL-13.[1][2] IL-4 plays a central role in this pathogenesis:

- It drives **IgE class switching** in B cells, directly explaining the elevated serum IgE[2]
- It promotes **Th2 differentiation** while suppressing Th1 responses and IFN-γ production[2]
- It enhances **eosinophil recruitment** by upregulating VCAM-1 on endothelial cells[2]
- T cell-derived IL-4/IL-13 is essential for *Aspergillus*-induced lung eosinophilia and inflammation[3]

BAL fluid analysis in ABPA patients demonstrates significantly increased levels of IL-4 and IL-5, consistent with a Th2 cytokine pattern.[4]

The following figure illustrates the immunopathogenesis of ABPA, showing how Aspergillus antigens drive a Th2-skewed response with IL-4 as a central mediator of IgE production and eosinophilic inflammation.

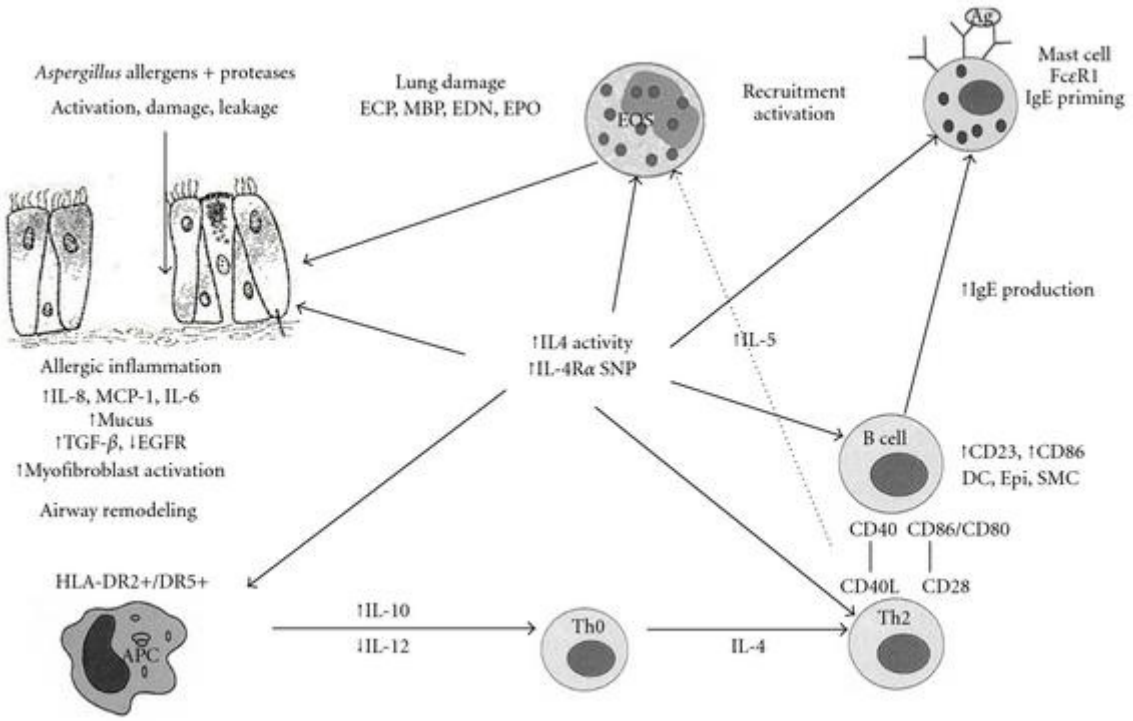


Figure 1. Proposed immunopathogenesis of ABPA. In the pathogenesis of ABPA, A. fumigatus proteases have a direct effect on bronchial epithelia causing epithelial cell damage with subsequent stimulation of cytokines and chemokines. Aspergillus proteins are processed via HLA-DR2/DR5 bearing dendritic cells that skew the Th0 response to a Th2 response. Th2 cytokines stimulate IgE synthesis and eosinophil activation. This leads to an eosinophilic inflammatory in the bronchial airways. Abbreviations: Af: Aspergillus fumigates, Asp fx: Aspergillus fumigatus proteins, APC: antigen presenting cell, MBP: major basic protein, ECP: eosinophil cationic protein, EDN: eosinophil derived neurotoxin, VLA: very late activation antigen, VCAM: vascular cell adhesion molecule, CxCR and CCR: chemokines receptors, MCO: monocyte chemotactic protein, sCD23: soluble CD23, cyst-LT: cysteinyl leukotriene.

Regarding the other options: **IFN-α** (choice C) and **IL-28** (choice A, also known as IFN-λ) are type I and type III interferons involved in antiviral responses, not Th2-mediated allergic disease. **TGF-β** (choice B) is an immunoregulatory cytokine; in ABPA, dendritic cells actually show lower TGF-β secretion, which contributes to the Th2-biased response.[5]

Would you like to explore the diagnostic criteria and staging of ABPA, or the role of anti-IgE therapy (omalizumab) in its management?

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Question 798

A 29-year-old G1P0 female presents at 22 weeks gestation for her first prenatal care appointment. Physical exam demonstrates a uterine size greater than expected for her gestational age and taut, shiny skin with scattered striae on her abdomen. Ultrasound examination of the fetus reveals 2.5 L of amniotic fluid (normal 1.5-2.0 L) with an amniotic fluid index (AFI) of 34 (normal AFI 20-25). Which of the following fetal abnormalities or dysfunctions could have contributed to these abnormal ultrasound findings?

Answer Choices:

(A) Renal agenesis
(B) Pulmonary hypoplasia
(C) Duodenal atresia
(D) Posterior urethral valve

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/b6c17fac-feb5-4d52-be30-f6c39493b40b

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OpenEvidence Explanation

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The answer is **C. Duodenal atresia**.

The ultrasound findings describe **polyhydramnios** (amniotic fluid volume of 2.5 L with AFI of 34, both above normal). **Duodenal atresia** is a gastrointestinal tract obstruction that impairs fetal swallowing and absorption of amniotic fluid, which is a well-established cause of polyhydramnios.[1]

Here is why each other option is incorrect:

- **A. Renal agenesis** — Bilateral renal agenesis causes **oligohydramnios** (decreased amniotic fluid), not polyhydramnios, because the fetal kidneys are the primary source of amniotic fluid production after 16–17 weeks of gestation. Absence of kidneys leads to anuria and anhydramnios.[2][3][4]
- **B. Pulmonary hypoplasia** — Pulmonary hypoplasia is a **consequence** of oligohydramnios, not a cause of polyhydramnios. It results from inadequate amniotic fluid during the critical period of lung development (16–24 weeks), leading to depressurization of fetal airways and impaired pulmonary growth.[3][5]
- **D. Posterior urethral valves** — This condition causes lower urinary tract obstruction (LUTO), which leads to **oligohydramnios** due to impaired fetal urine output. Severe cases are associated with oligohydramnios or anhydramnios, bilateral hydronephrosis, and megacystis.[5][6][7]

The key physiologic principle is that amniotic fluid volume in the second and third trimesters is maintained by a balance between fetal urine production (the major source) and fetal swallowing/absorption (the major removal pathway). Conditions that impair swallowing or GI absorption (like duodenal atresia) lead to polyhydramnios, while conditions that impair urine production (like renal agenesis or urethral obstruction) lead to oligohydramnios.[1][2]

Would you like to explore the prenatal ultrasound findings that help distinguish between different causes of GI obstruction associated with polyhydramnios, such as the "double bubble" sign in duodenal atresia?

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Question 799

A 68-year-old woman presents to the emergency room with chest pain. She reports sudden severe and crushing substernal chest pain that started 1 hour ago. Her past medical history is notable for hypertension, hyperlipidemia, diabetes mellitus, obesity, and a prior myocardial infarction requiring a coronary artery bypass graft 2 years ago. She takes aspirin, metoprolol, lisinopril, spironolactone, atorvastatin, and insulin. She is retired and lives a sedentary lifestyle at home. Her temperature is 98.8°F (37.1°C), blood pressure is 109/68 mmHg, pulse is 118/min, and respirations are 24/min. Before being able to start the physical examination, the patient loses consciousness. Her pulse is palpable but weak. Her blood pressure is now 88/50 mmHg and pulse is 130/min. Her skin is pale, cold, and clammy. An electrocardiogram demonstrates ST elevations in leads I, aVL, V3, V4, V5, and V6. A medication that primarily stimulates which of the following receptors would be most appropriate to improve the hemodynamic status of this patient?

Answer Choices:

(A) Alpha-2 adrenergic receptor
(B) Beta-1 adrenergic receptor
(C) Beta-2 adrenergic receptor
(D) D2 receptor

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/c16e76b6-a6e9-40c3-ad52-95c86c819ab5

OpenEvidence Explanation

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The answer is **B. Beta-1 adrenergic receptor**.

This patient is presenting with an acute **STEMI** (ST elevations in leads I, aVL, V3–V6 indicating anterolateral MI) complicated by **cardiogenic shock** — evidenced by sudden hemodynamic collapse with hypotension (BP 88/50 mmHg), tachycardia (130/min), and signs of poor perfusion (pale, cold, clammy skin). The primary hemodynamic problem is severely reduced cardiac output due to acute myocardial pump failure.

Why Beta-1 stimulation is correct: The immediate goal is to improve cardiac contractility (inotropy) and cardiac output. **Beta-1 adrenergic receptors** are the primary mediators of increased myocardial contractility and heart rate. Agents such as **dobutamine** (a predominantly beta-1 agonist) are the most commonly used inodilators in cardiogenic shock to augment cardiac output.[1][2] Norepinephrine, which also has significant beta-1 activity alongside alpha-1 effects, is recommended as a first-line vasopressor when hypotension is present.[3][4]

Why the other options are incorrect:

- **A. Alpha-2 adrenergic receptor** — Alpha-2 agonists (e.g., clonidine) reduce sympathetic outflow, causing decreased heart rate and blood pressure — the opposite of what is needed in cardiogenic shock.
- **C. Beta-2 adrenergic receptor** — Beta-2 stimulation primarily causes bronchodilation and peripheral vasodilation, which would worsen hypotension without meaningfully improving cardiac contractility.
- **D. D2 receptor** — Dopamine D2 receptor activation at low doses causes vasodilation in renal and mesenteric beds but does not improve cardiac contractility or blood pressure. The inotropic effects of dopamine at intermediate doses are mediated through beta-1 receptors, not D2 receptors.[5][6]

Would you like to explore the current evidence comparing mechanical circulatory support devices versus pharmacotherapy in AMI-related cardiogenic shock?

Relevant images

(CONTENT OMITTED)

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Question 800

A 4-year-old child is rushed to the emergency department after developing sudden abdominal pain followed by nausea, vomiting, and dark, almost black-colored stool. Prior to the onset of symptoms, he was seen playing with his mother's purse containing a bottle of vitamin supplements, which she takes for chronic microcytic anemia. Which of the following medications is the treatment for this patient's intoxication?

Answer Choices:

(A) Dimercaprol
(B) Deferoxamine
(C) Protamine
(D) Succimer

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/fdd9df33-ca8b-44bc-b0de-5b02126ea156

OpenEvidence Explanation

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The correct answer is **B. Deferoxamine**.

This clinical scenario describes **acute iron poisoning** in a child. The key clues are: a 4-year-old playing with vitamin supplements taken by the mother for

chronic microcytic anemia (iron deficiency anemia treated with iron supplements), presenting with sudden abdominal pain, nausea, vomiting, and **melena** (dark/black stool from GI mucosal injury caused by iron's direct corrosive effect).

Deferoxamine mesylate is the specific iron-chelating agent FDA-approved for the treatment of acute iron intoxication.[1] It works by chelating free iron to form a stable complex (ferrioxamine), which is water-soluble and excreted renally, producing a characteristic "vin rosé" (reddish-orange) discoloration of the urine.[1] For patients not in shock, the initial dose is 1,000 mg IM, with subsequent doses of 500 mg every 4–12 hours (maximum 6,000 mg/day); IV administration is reserved for patients in cardiovascular collapse.[1]

Why the other options are incorrect:

- **A. Dimercaprol (BAL)** — A chelator used for arsenic, mercury, gold, and lead poisoning. It does not effectively chelate iron.
- **C. Protamine** — The antidote for heparin overdose, not relevant to iron toxicity.
- **D. Succimer (DMSA)** — An oral chelator used primarily for lead poisoning in children. It is not indicated for iron intoxication.

Would you like to explore the clinical stages of acute iron toxicity and the indications for initiating deferoxamine based on serum iron levels?

References

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Question 804

A 45-year-old man presents to the emergency department with weakness. He states that it started yesterday and has been progressively worsening. Initially, he noticed blurry vision and some trouble speaking and swallowing but thought he was just coming down with a cold. He then noticed weakness of his facial muscles and shortness of breath. The patient works as a farmer and harvests and cans his own foods. He has had diarrhea recently and a cough prior to these symptoms of weakness. His temperature is 97.9°F (36.6°C), blood pressure is 144/94 mmHg, pulse is 87/min, respirations are 18/min, and oxygen saturation is 94% on room air. Physical exam is notable for a man who seems unable to smile with dysarthric speech. He takes shallow and weak breaths on pulmonary exam. The patient demonstrates 3/5 strength with diminished reflexes in his upper extremities. The patient is subsequently intubated. Which of the following is the best treatment for this patient?

Answer Choices:

(A) Antitoxin
(B) Neostigmine
(C) Plasmapheresis
(D) Riluzole

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/8e69980e-64bf-4e5a-8092-3909d305af19

OpenEvidence Explanation

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The correct answer is **A. Antitoxin**.

This presentation is classic for **foodborne botulism**, not Guillain-Barré syndrome, and the best treatment is **botulism antitoxin**. Several key features point to this diagnosis:

- **Descending paralysis pattern**: Symptoms began with cranial nerve involvement (blurry vision, dysarthria, dysphagia, facial weakness) and progressed to limb weakness and respiratory failure — the hallmark descending pattern of botulism, as opposed to the ascending paralysis of GBS.[1][2]
- **Home-canned foods**: The patient is a farmer who harvests and cans his own foods, providing the classic exposure to improperly preserved anaerobic food products where *Clostridium botulinum* spores germinate and produce toxin.[1][3]
- **Preceding GI symptoms**: Diarrhea is consistent with early foodborne botulism, where gastrointestinal symptoms precede or accompany the neurological syndrome.[3][4]
- **Diminished reflexes with motor weakness**: Botulinum toxin irreversibly blocks acetylcholine release at presynaptic motor nerve terminals, causing flaccid paralysis with hyporeflexia.[1]

Why antitoxin is correct: Botulism antitoxin (heptavalent botulism antitoxin, or H-BAT) is the only specific therapy for botulism in patients older than 1 year. A systematic review demonstrated that antitoxin treatment significantly reduced mortality (OR 0.16; 95% CI 0.09–0.30), with even greater benefit when administered within 48 hours of symptom onset (OR 0.12; 95% CI 0.03–0.41).[5] Antitoxin prevents progression of paralysis by neutralizing circulating toxin but cannot reverse already-bound toxin.[2][6]

Why the other options are incorrect:

- **B. Neostigmine** — an acetylcholinesterase inhibitor used for myasthenia gravis, which involves postsynaptic antibody-mediated destruction of acetylcholine receptors. Botulism is a presynaptic disorder, so neostigmine is ineffective.
- **C. Plasmapheresis** — a treatment for GBS and myasthenia gravis. GBS typically presents with ascending paralysis, paresthesias, and areflexia following an infection, distinct from the descending cranial-nerve-first pattern seen here.[7][8]
- **D. Riluzole** — used for amyotrophic lateral sclerosis (ALS), a chronic neurodegenerative disease with upper and lower motor neuron signs, not an acute paralytic illness.

Would you like to explore the electrodiagnostic findings that help distinguish botulism from Guillain-Barré syndrome and myasthenia gravis in the acute setting?

Relevant images

(CONTENT OMITTED)

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1. Clinical Reasoning: A Teenager With Shortness of Breath and Difficulty Walking. Liu SC, Poon JT, Candee MS.. Neurology. 2021;96(18):e2346-e2350. doi:10.1212/WNL.0000000000011544.
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Question 805

A 79-year-old woman comes to the physician because of a 1-month history of difficulty starting urination and a vague sensation of fullness in the pelvis. Pelvic speculum examination in the lithotomy position shows a pink structure at the vaginal introitus that protrudes from the anterior vaginal wall when the patient is asked to cough. Which of the following is the most likely cause of this patient's symptoms?

Answer Choices:

(A) Vaginal rhabdomyosarcoma
(B) Cystocele
(C) Rectocele
(D) Uterine leiomyomata

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/b4bcd675-89e1-451a-8519-b3442d5fba42

OpenEvidence Explanation

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The most likely cause is **B. Cystocele**.

This presentation is classic for a **cystocele (anterior vaginal wall prolapse)**. The key findings pointing to this diagnosis include:

- **Anterior vaginal wall protrusion** visible at the introitus, which increases with Valsalva (coughing) — this is the hallmark physical exam finding of a cystocele, where the bladder herniates into the anterior vaginal wall.
- **Difficulty initiating urination** — a cystocele can kink or compress the urethra, leading to obstructive voiding symptoms.
- **Pelvic fullness** — a common symptom of pelvic organ prolapse, reflecting the descent of the bladder into the vaginal canal.
- **79-year-old woman** — advanced age, with associated pelvic floor weakening from estrogen deficiency and connective tissue attenuation, is a major risk factor.

Why not the other options?

- **A. Vaginal rhabdomyosarcoma** — This is a malignancy seen predominantly in young children (sarcoma botryoides), presenting as a grape-like mass. It would be exceedingly rare in a 79-year-old and would not characteristically protrude from the anterior wall with coughing.
- **C. Rectocele** — A rectocele involves herniation of the rectum into the **posterior** vaginal wall, not the anterior wall. It typically causes symptoms of incomplete defecation rather than urinary difficulty.
- **D. Uterine leiomyomata** — Fibroids are estrogen-dependent and typically regress after menopause. They would not present as an anterior vaginal wall protrusion that increases with Valsalva.

Would you like to explore the current guideline recommendations for management of pelvic organ prolapse, including when to pursue pessary versus surgical repair?

Question 806

A 30-year-old woman presents to the physician because of ongoing diarrhea for the past 1 month. She reports that diarrhea has been intermittently present for the past month. The stool is often loose and associated with blood and lower abdominal pain. She denies any recent travel history, and she works at a nursing home as a caretaker. She is not currently on any medications. Clinical examination shows mild tenderness in the suprapubic region, and there is no organomegaly. Findings on colonoscopy include patchy erythema and ulceration in the cecum, ascending, descending, and sigmoid colon. Mucosal biopsy shows colonic crypts with lymphocytic and neutrophilic infiltrates. What is the most likely diagnosis?

Answer Choices:

(A) Crohn's disease
(B) Acute infective colitis
(C) Pseudomembranous colitis
(D) Irritable bowel syndrome

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/b3e39e0b-3c69-44a3-8c18-584c83c99509

OpenEvidence Explanation

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The most likely diagnosis is **A. Crohn's disease**.

The key features pointing to Crohn's disease in this case are:

- **Patchy (skip) lesions on colonoscopy**: The colonoscopy shows patchy erythema and ulceration involving the cecum, ascending colon, descending colon, and sigmoid colon — with areas of normal mucosa in between. This pattern of **skip lesions** (areas of inflammation alternating with normal mucosa) is the hallmark endoscopic finding of Crohn's disease. Ulcerative colitis, by contrast, produces continuous, confluent inflammation starting from the rectum.[1][2][3]

- **Chronic duration (1 month)**: The intermittent bloody diarrhea over 1 month with abdominal pain is consistent with the relapsing-remitting course of IBD rather than a self-limited infectious colitis, which typically resolves within 1–2 weeks.[4][5]

- **Histology with crypt inflammation**: Colonic crypts with lymphocytic and neutrophilic infiltrates (cryptitis) are consistent with IBD. While granulomas are found in only ~50–60% of Crohn's disease biopsies, their absence does not exclude the diagnosis.[1]

Why the other options are less likely:

- **B. Acute infective colitis** — Although the patient works at a nursing home (a risk factor for pathogen exposure, including C. difficile), the 1-month duration, patchy skip lesions, and absence of antibiotic use or other typical risk factors make this less likely. Infectious colitis is usually acute and self-limited, and histologically tends to preserve crypt architecture.[5][6]

- **C. Pseudomembranous colitis** — C. difficile colitis is strongly associated with recent antibiotic use, hospitalization, or immunosuppression. This patient is on no medications, and the colonoscopy does not describe pseudomembranes.[7]

- **D. Irritable bowel syndrome** — IBS does not cause bloody diarrhea, mucosal ulceration, or inflammatory infiltrates on biopsy. It is a functional disorder without structural abnormalities.[2]

Would you like to discuss the workup for confirming Crohn's disease in this patient, such as imaging or serologic markers?

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Question 807

A 45-year-old man presents to the emergency department after being stabbed 12 times in various parts of his body. Paramedics report extensive blood loss at the scene where he was found. Due to his Glasgow Coma Scale score of 3, an endotracheal airway and large-bore access are secured prior to arrival. He is aggressively resuscitated with a massive transfusion protocol as the operating room is prepared for an exploratory laparotomy. An arterial line and central access are obtained. His temperature is 95°F (35°C), blood pressure is 50/40 mmHg, and pulse is 80/min, and respirations are controlled at 20/min on lung-protective volume control. After a 6:6:1 ratio of red blood cells, plasma, and platelets and the use of continuous phenylephrine infusion, the patient's vital signs remain the same. The surgical team reports no active blood loss. A stat ScvO2 results as 39% with a SaO2 of 100% on 100% oxygen. His extremities remain cold despite having the ambient room temperature increased to 80°F (26.7°C). What is the most likely cause of his presentation?

Answer Choices:

(A) Cardiac tamponade
(B) Cervical spinal cord transection
(C) Pulmonary embolism
(D) Undiagnosed pneumonia

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/395f02bd-ee12-4b0c-a189-ab3df415c8cf

OpenEvidence Explanation

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The most likely cause is **A. Cardiac tamponade**.

The clinical picture — persistent profound hypotension (50/40 mmHg) despite aggressive resuscitation with no ongoing surgical bleeding, a **critically low ScvO2 of 39%** with normal SaO2, **inappropriately normal heart rate (80/min)** for the degree of shock, and **cold extremities** — points to an obstructive shock physiology most consistent with cardiac tamponade in this penetrating trauma patient.

Why cardiac tamponade fits best:

- A ScvO2 of 39% with SaO2 of 100% indicates severely impaired oxygen delivery due to **low cardiac output**, as tissues are extracting a markedly increased fraction of delivered oxygen. This is the hallmark of cardiogenic or obstructive shock, not distributive shock.[1][2]
- Cardiac tamponade causes impaired ventricular filling, reduced stroke volume, and low cardiac output — directly explaining the critically low ScvO2 and cold extremities (peripheral vasoconstriction from sympathetic compensation).[1]
- In penetrating trauma with multiple stab wounds, pericardial injury with accumulating hemopericardium is a well-recognized surgical emergency. FAST examination has near 100% sensitivity for pericardial effusion in penetrating thoracic trauma.[3]
- The heart rate of 80/min, while seemingly "normal," reflects the reflex tachycardia limitation imposed by tamponade physiology (stroke volume becomes fixed and rate-dependent, but pulsus paradoxus and equalization of diastolic pressures limit effective output).

Why the other options are less likely:

- **B. Cervical spinal cord transection** — Neurogenic shock causes hypotension with **bradycardia** due to loss of sympathetic tone, but it produces **warm, vasodilated** extremities (distributive physiology) and

would be expected to have a **normal or elevated** ScvO2 (since oxygen delivery is redistributed, not reduced in absolute cardiac output terms). The cold extremities and profoundly low ScvO2 argue strongly against this. [4][5]

- **C. Pulmonary embolism** — While PE can cause obstructive shock with low ScvO2, it is far less likely in this acute trauma setting compared to tamponade. There is no described risk factor (prolonged immobility, DVT history), and the penetrating mechanism makes pericardial injury much more probable.

- **D. Undiagnosed pneumonia** — Septic shock from pneumonia would cause distributive physiology with **warm** extremities and a **normal-to-high** ScvO2, which is the opposite of this presentation.[1]

Recommended next steps would include immediate bedside echocardiography or FAST to evaluate for pericardial effusion, with preparation for emergent pericardiotomy or sternotomy if tamponade is confirmed.[3][6]

Has bedside ultrasound or FAST already been performed in this case, and were any of the stab wounds in the precordial or thoracic region?

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Question 808

A 71-year-old woman presents to her physician accompanied by her son. She has no complaints, but her son states that the patient has impaired memory and poor orientation in space. She is ambulatory and is capable of self-care, but she tends to forget newly introduced information. Also, she got lost on the way from the home to the local market several times for the past 6 months, and her family is now afraid to let her go anywhere on her own. She does not have any concomitant chronic conditions nor did she have major cardiovascular events or head trauma. It is known that her father had dementia. The vital signs include: blood pressure is 130/80 mm Hg, heart rate is 62/min, respiratory rate is 11/min, and the temperature is 36.5°C (97.7°F). The respiratory, cardiologic, and abdominal examinations are unremarkable. The neurological examination shows equal, round pupils with a normal reaction to light. The eye movements are normal with no nystagmus and normal oculocephalic reflex. There is no facial droop, the facial sensation is preserved, and there is no tongue deviation noted. There is no motor or sensory deficits on the upper and lower extremities. The patient scores 18 on the Montreal Cognitive Assessment. Which of the following medications is indicated in the patient?

Answer Choices:

(A) Imipramine
(B) Lithium
(C) Donepezil
(D) Sulpiride

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/6a5870e6-9f09-44be-bc08-d539309b6fa7

OpenEvidence Explanation

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The correct answer is **C. Donepezil**.

This patient presents with a clinical picture consistent with **Alzheimer disease (AD) dementia**: progressive memory impairment (forgetting newly introduced information), spatial disorientation (getting lost on familiar routes), a positive family history of dementia, and a MoCA score of 18 — well below the cutoff of ~21 that indicates dementia.[1][2][3] Importantly, there are no focal neurological deficits, no history of stroke or head trauma, and no features suggesting an alternative etiology.

Donepezil, an acetylcholinesterase inhibitor, is the first-line pharmacologic treatment for mild to moderate AD dementia. It is FDA-approved for all stages of AD (mild, moderate, and severe).[4][5][6] Donepezil works by inhibiting acetylcholinesterase, increasing acetylcholine availability at the synaptic cleft to support cholinergic neurotransmission critical for memory function.[7] In meta-analyses, donepezil 10 mg/day improved cognitive function by approximately 2.7 points on the ADAS-Cog and 1.1 points on the MMSE over 24–26 weeks compared with placebo, with modest improvements in activities of daily living and clinician-rated global clinical state.[8]

The other options are incorrect:

- **Imipramine** is a tricyclic antidepressant — not indicated here, and its anticholinergic properties would worsen cognitive function in dementia.
- **Lithium** is a mood stabilizer used for bipolar disorder — no indication in this scenario.

- **Sulpiride** is an atypical antipsychotic — not indicated for primary treatment of AD, and antipsychotics carry increased mortality risk in elderly patients with dementia.

Standard initial dosing of donepezil is **5 mg once daily**, titrated to 10 mg after 4–6 weeks as tolerated, with gastrointestinal side effects (nausea, diarrhea, vomiting) being the most common adverse effects.[6][7]

Would you like to explore the evidence for combining donepezil with memantine in patients who progress to moderate-to-severe Alzheimer disease?

Relevant images

(CONTENT OMITTED)

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Question 809

A 16-year-old teenager presents to the emergency department with a sudden onset of severe pain in his right knee. He describes the pain as the worst pain he has ever felt. He denies any recent trauma or injury to the knee. The joint appears red and swollen and is hot to the touch. He denies any lower extremity numbness. There is no family history of joint or connective tissue disorders. The teenager is otherwise healthy. On physical examination, his blood pressure is 124/82 mm Hg, respirations are 17/min, pulse is 104/min, and temperature is 39.1°C (102.4°F). On palpation of the affected joint, there is evidence of tenderness and capsular swelling; the joint is red and warm. Laboratory studies show increased serum CRP and procalcitonin levels. Which of the following will most likely found with analysis of his synovial fluid?

Answer Choices:

(A) WBC/mm3 1,600; % PMN > 25%; Viscosity N
(B) WBC/mm3 53,000; % PMN > 75%; Viscosity low
(C) WBC/mm3 160; % PMN < 20%; Viscosity high
(D) WBC/mm3 2,400; % PMN < 20%; Viscosity low

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/6920746f-1508-43ee-a091-c4c5a9544706

OpenEvidence Explanation

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The answer is **B. WBC/mm³ 53,000; % PMN > 75%; Viscosity low**.

This clinical presentation — acute monoarticular arthritis with fever (39.1°C), joint erythema, warmth, capsular swelling, and elevated CRP and procalcitonin — is classic for **septic arthritis**, a musculoskeletal emergency. In a previously healthy 16-year-old without trauma or family history of joint disease, the combination of systemic inflammatory markers and a hot, swollen joint strongly points to a bacterial etiology.

Synovial fluid in septic arthritis characteristically shows:[1][2][3]

- **WBC count typically >50,000/mm³** (often exceeding 100,000/mm³), though lower counts do not exclude the diagnosis
- **Neutrophil (PMN) predominance >75%**, often >90%
- **Low viscosity** due to enzymatic degradation of hyaluronic acid by bacterial and inflammatory cell products
- Fluid is typically yellow-green and opaque

The following table summarizes the synovial fluid characteristics across different types of arthritis:

TABLE 4

Synovial Fluid Analysis in Patients with Suspected Septic Arthritis

Arthritis diagnosis	Color	Transparency	Viscosity	WBC count (per µL [x 10^9 per L])	PMN cell count (%)	Gram stain	Culture	PCR test	Crystals	Multiplex PCR test*
Normal	Clear	Transparent	High/thick	< 200 (0.20)	< 25	Negative	Negative	Negative	Negative	Negative
Noninflammatory	Straw	Translucent	High/thick	200 to 2,000 (0.20 to 2)	< 25	Negative	Negative	Negative	Negative	Negative
Inflammatory										
Crystalline disease	Yellow	Cloudy	Low/thin	2,000 to 100,000 (2 to 100)	> 50	Negative	Negative	Negative	Positive	Negative
Noncrystalline disease	Yellow	Cloudy	Low/thin	2,000 to 100,000	> 50	Negative	Negative	Negative	Negative	Negative
Infectious										
Lyme disease	Yellow	Cloudy	Low	3,000 to 100,000 (3 to 100)	> 75	Negative	Negative	Positive	Negative	Positive
Gonococcal	Yellow	Cloudy-opaque	Low	34,000 to 68,000 (34 to 68)	> 75	Variable (< 50%)	Positive (25% to 70%)	Positive (> 75%)	Negative	Positive
Nongonococcal	Yellow-green	Opaque	Very low	> 50,000 (50); > 100,000 is more specific, < 50,000 is common in atypical infection and periprosthetic joint infection	> 75	Positive (60% to 80%)	Positive (> 90%)	—	Negative†	Positive

Note: These are general guidelines in the interpretation of synovial fluid. Many parameters vary widely and must be interpreted in the clinical context. Three bedside observations (color, transparency, and viscosity) are quick and easy to assess. With normal transparent fluid, words can be read clearly through the fluid. The words become less crisp and gradually obscured with increasing turbidity. Viscosity is assessed by observing the fluid dropping from the syringe. Normal viscosity has a long, stringy tail.

PCR = polymerase chain reaction; PMN = polymorphonuclear; WBC = white blood cell.

*—This information is based on limited data. Multiplex PCR is not as readily available as many other tests, and its use is still being investigated.
†—Crystalline disease can coexist with septic arthritis. A positive result does not exclude infection.

Adapted with permission from Horowitz DL, Katzap E, Horowitz S, et al. Approach to septic arthritis. Am Fam Physician. *2011;84(6):656-657, with additional information from references 14-16.*

Table 4. Synovial Fluid Analysis in Patients with Suspected Septic Arthritis

Why the other options are incorrect:

- **A (WBC 1,600; PMN >25%; normal viscosity)** — Consistent with a noninflammatory process (e.g., osteoarthritis), which does not match this febrile, acutely inflamed presentation.
- **C (WBC 160; PMN <20%; high viscosity)** — Consistent with normal synovial fluid, incompatible with the clinical picture.
- **D (WBC 2,400; PMN <20%; low viscosity)** — A mildly inflammatory pattern with mononuclear predominance, more suggestive of a non-infectious inflammatory process, and inconsistent with the high fever and elevated procalcitonin seen here.

Elevated procalcitonin further supports a bacterial etiology, as it has high specificity (87–98%) for bacterial septic arthritis at a cutoff of ≥0.5 ng/mL, though sensitivity is moderate.[3][4]

Would you like to explore the empiric antibiotic regimens and management approach for suspected septic arthritis in the pediatric population?

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Question 812

A 45-year-old African-American woman comes to the physician after an episode of hemoptysis. Over the past 8 months, she has had a nonproductive cough, fatigue, and a 9-kg (20-lb) weight loss. She drinks a glass of wine every night and does not smoke. She has a history of hypertension and osteoarthritis. She does not take any medications. She has never traveled out of the country. She works as an accountant. Her temperature is 37.0°C (98.6°F), pulse is 94/min, and blood pressure is 130/90 mm Hg. Lungs are clear to auscultation. An x-ray of the chest shows a 2.5-cm nodule with irregular borders at the apex of the left lung with no mediastinal or hilar enlargement. Which of the following is the most likely diagnosis?

Answer Choices:

(A) Carcinoid tumor
(B) Sarcoidosis
(C) Squamous cell carcinoma of the lung
(D) Adenocarcinoma of the lung

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/71d64263-7056-4696-a5e9-ca160937b68b

OpenEvidence Explanation

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The most likely diagnosis is **D. Adenocarcinoma of the lung**.

Several key features in this presentation point to adenocarcinoma rather than the other options:

Non-smoking status strongly favors adenocarcinoma. Among nonsmoking individuals with lung cancer, **60%–80%** of cases are histologically adenocarcinomas.[1][2] Adenocarcinoma is the predominant subtype in never-smokers, particularly in women.[2][3] In contrast, squamous cell carcinoma is most strongly associated with cigarette smoking, with relative risks of 25.4 for current smokers versus 6.2 for adenocarcinoma.[4] Squamous cell carcinoma classically presents as a central/hilar mass, whereas adenocarcinoma typically presents as a **peripheral lesion** — consistent with this patient's apical nodule.[5][6][7]

Why not the other options?

- **Squamous cell carcinoma (C):** Most strongly linked to smoking and typically presents as a central, endobronchial mass, often with cavitation. This patient is a nonsmoker with a peripheral nodule.[6][7]
- **Sarcoidosis (B):** While sarcoidosis is more common in African-American women, it typically presents with bilateral hilar lymphadenopathy rather than a solitary peripheral nodule with irregular borders. The absence of hilar/mediastinal enlargement on chest X-ray argues against this diagnosis.
- **Carcinoid tumor (A):** Carcinoid tumors are typically central, endobronchial lesions that are not strongly associated with the constitutional symptoms (significant weight loss, fatigue) seen here, and they are uncommon relative to adenocarcinoma.

The clinical picture — a **nonsmoking woman** with hemoptysis, chronic cough, significant weight loss, and a **peripheral solitary pulmonary nodule with irregular borders** — is most consistent with lung adenocarcinoma.[1][5]

Would you like to explore the recommended diagnostic workup and molecular testing approach for a suspected lung adenocarcinoma in a never-smoker?

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Question 814

An 11-month-old boy is brought to the physician for a well-child examination. He is growing along with the 75th percentile and meeting all milestones. Physical examination shows a poorly rugated scrotum. The palpation of the scrotum shows only 1 testicle. A 2nd testicle is palpated in the inguinal canal. The examination of the penis shows a normal urethral meatus. The remainder of the physical examination shows no abnormalities. Which of the following is the most appropriate next step in management?

Answer Choices:

(A) Chorionic gonadotropin therapy
(B) Exploratory laparoscopy
(C) Orchiectomy
(D) Orchiopexy

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/da7d1593-1b4c-4373-ae4b-d451a68068d3

OpenEvidence Explanation

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The correct answer is **D. Orchiopexy**. This 11-month-old boy has a **palpable undescended testis** (cryptorchidism) located in the inguinal canal, and

orchiopexy — surgical repositioning of the testis into the scrotum — is the standard of care.

Key considerations supporting this answer:

- **Spontaneous descent is unlikely after 6 months of age.** The AUA guideline states that in a 10-year retrospective study of 1,235 boys with cryptorchidism, no patient presenting beyond 6 months of age had spontaneous testicular descent.[1][2]
- **Timing:** Surgery is recommended between **6 and 18 months of age**, with evidence showing that testicular growth and fertility potential improve significantly when orchiopexy is performed before 12 months of age. At 11 months, this child is within the ideal surgical window.[2][3]
- **For a palpable testis**, the AUA guideline recommends scrotal or inguinal orchiopexy as a standard recommendation (Evidence Strength: Grade B).[1]

Why the other options are incorrect:

- **A. Chorionic gonadotropin therapy** — Hormonal therapy is generally **not recommended** for cryptorchidism. Multiple guidelines (AUA, EAU, Nordic consensus) advise against it, as orchiopexy is the most successful therapy.[1][2][4]
- **B. Exploratory laparoscopy** — This is reserved for **nonpalpable** testes to determine their location. Since this testis is palpable in the inguinal canal, laparoscopy is unnecessary.[1]
- **C. Orchiectomy** — Removal of the testis is reserved for **postpubertal** patients with cryptorchidism or when a testis is nonviable. In a prepubertal child, the goal is to preserve the testis.[1][2]

The following figure from the AAFP guidelines illustrates the evaluation and management algorithm for cryptorchidism:

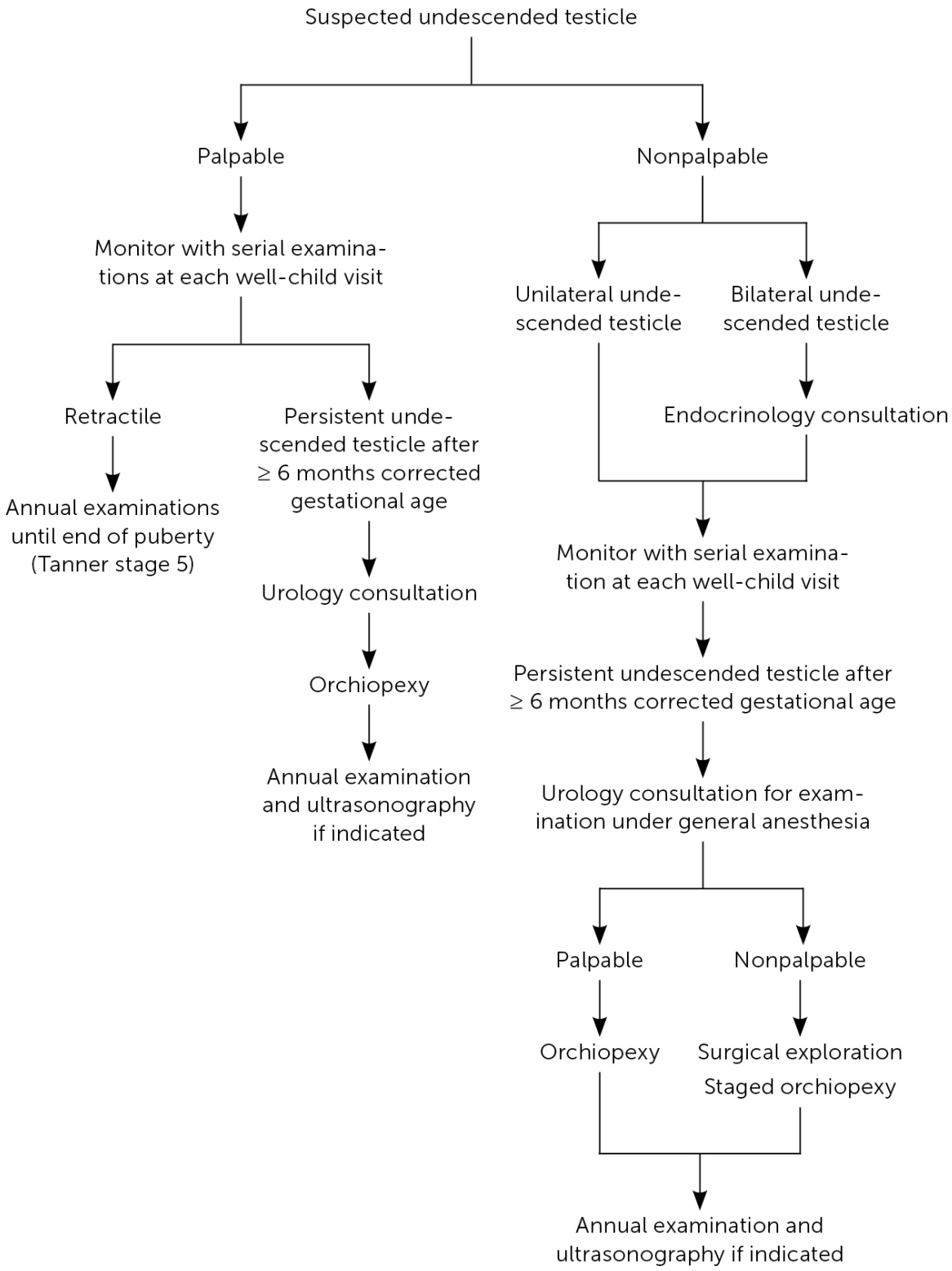


Figure 1. Evaluation and management of cryptorchidism. Information from references 1, 9, 12, and 16–18.

Would you like to explore the long-term outcomes of orchiopexy regarding fertility preservation and testicular cancer risk reduction?

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Question 815

A 24-year-old woman comes to the physician because of 1-day history of nausea and weakness. She has no history of serious illness. She is sexually active with 2 male partners and uses an oral contraceptive; she uses condoms inconsistently. Her last menstrual period was 4 days ago. Her temperature is 37.8°C (100°F), pulse is 88/min, respirations are 18/min, and blood pressure is 115/70 mm Hg. Physical examination shows right costovertebral angle tenderness. The abdomen is soft and nontender. Cardiopulmonary examination shows no abnormalities. Laboratory studies show:
Hemoglobin 14 g/dL
Leukocyte count 13,000/mm3
Platelet count 250,000/mm3
Serum
Urea nitrogen 18 mg/dL
Creatinine 0.8 mg/dL
Glucose 95 mg/dL
C-reactive protein 16.4 mg/L (N=0.08–3.1)
Which of the following is the most appropriate next step in management?

Answer Choices:

(A) Urinalysis
(B) Cervical swab
(C) Blood culture
(D) CT scan of the abdomen

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/c5b00727-7c7c-4519-8049-6cb470e8603c

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OpenEvidence Explanation

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The most appropriate next step is **A. Urinalysis**.

This young woman presents with nausea, weakness, low-grade fever, right costovertebral angle (CVA) tenderness, leukocytosis, and elevated CRP — a clinical picture highly suggestive of **acute pyelonephritis**. The initial diagnostic step is a **urinalysis** (with urine culture), which serves as the foundational test to confirm urinary tract infection by demonstrating pyuria and bacteriuria.[1][2]

Key reasoning for each option:

- **Urinalysis (correct):** In a patient with flank/CVA tenderness and fever, a urinalysis showing pyuria and/or bacteriuria confirms the presumptive diagnosis of pyelonephritis. The IDSA recommends that urine culture with susceptibility testing should always be performed in suspected pyelonephritis to guide antibiotic therapy. Urinalysis is the essential first step before any other workup.[1][3]
- **Cervical swab:** While this patient has risk factors for STIs (multiple partners, inconsistent condom use), the presentation with CVA tenderness and systemic inflammatory markers points to an upper urinary tract process rather than cervical infection. A cervical swab would be appropriate if pelvic inflammatory disease were suspected, but the absence of abdominal/pelvic tenderness makes this less likely.
- **Blood culture:** Blood cultures are not routinely indicated in uncomplicated pyelonephritis. They rarely change management, as bacteriology is typically concordant with urine cultures. Blood cultures are reserved for patients with sepsis, septic shock, or diagnostic uncertainty.[4][5]

- **CT abdomen:** Imaging is not indicated as an initial step in uncomplicated pyelonephritis. CT is reserved for patients who fail to improve within 48–72 hours, have suspected complications (abscess, obstruction), or present with sepsis.[1][6]

Would you like to explore the empiric antibiotic regimen recommendations for uncomplicated pyelonephritis in young women?

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Question 816

A 65-year-old woman comes to the physician for a routine bone mineral density screening. She does not have any children. Menopause was at age 55. Her mother died of breast cancer at the age of 48 years. She has hypertension for which she takes ramipril. Dual-energy x-ray absorptiometry at the femoral neck shows a T-score of -2.7 SD. The physician considers treatment with raloxifene. This medication would put her at increased risk of developing which of the following conditions?

Answer Choices:

(A) Pulmonary embolism
(B) Cellulitis
(C) Breast cancer
(D) Hypercholesterolemia

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/fe479b78-8226-4ebd-8bcd-46387f4b12c5

OpenEvidence Explanation

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The answer is **A. Pulmonary embolism**.

Drug Label

According to the FDA-approved drug label, raloxifene (Evista) carries a **boxed warning for increased risk of venous thromboembolism**, including both deep vein thrombosis and **pulmonary embolism**.[1] In clinical trials, raloxifene-treated women had an increased risk of VTE, with a hazard ratio of **2.4** (95% CI, 1.2–4.5) compared to placebo, and the highest risk occurred during the initial months of treatment.[1] The drug is contraindicated in women with active or past history of venous thromboembolism.[1]

Notably, raloxifene does **not** increase breast cancer risk — it actually **reduces** the risk of invasive breast cancer and is FDA-approved for this indication in postmenopausal women at high risk.[1] It also does not increase the risk of endometrial cancer, cataracts, or gallbladder disease.[1]

Raloxifene is a selective estrogen receptor modulator (SERM) that acts as an estrogen **agonist** in bone and lipid metabolism but as an **antagonist** in breast and uterine tissue.[2][3] This tissue selectivity explains its distinct risk profile:

- **Venous thromboembolism (including pulmonary embolism)** is the most serious adverse effect. High-quality evidence from the ACP guideline shows an OR of **1.82** (95% CI, 1.16–2.92) specifically for pulmonary embolism, and an OR of **1.63** (95% CI, 1.36–1.98) for thromboembolic events overall. The MORE trial confirmed a relative risk of 2.1 for VTE.[4][5]
- **Breast cancer risk is reduced, not increased** — raloxifene reduced invasive breast cancer by approximately 44–65% in clinical trials. This is why option C is incorrect and why raloxifene is particularly appealing for this patient, who has a family history of breast cancer.[6][7][8]
- **Hypercholesterolemia** is not a recognized adverse effect; raloxifene actually has favorable effects on lipid metabolism.[3]
- **Cellulitis** has no established association with raloxifene use.

Other adverse effects include hot flashes (~10%), leg cramps, peripheral edema, and an increased risk of death from stroke in women with coronary heart disease or major coronary risk factors.[1][2]

Would you like to explore the comparative safety profiles of different osteoporosis treatments for postmenopausal women at elevated breast cancer risk?

Relevant images

(CONTENT OMITTED)

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Question 817

A multi-specialty physician practice is meeting to determine which compensation scheme would best serve the practice and its patient population. Which of the following are true in regards to physician compensation?

Answer Choices:

(A) Capitation poses the least financial risk to physicians
(B) Fee-for-service pays physicians a set amount of money per unit time for every patient under their care
(C) Fee-for-service may incentivize physicians to increase healthcare utilization irrespective of quality
(D) Fee-for-service poses the most amount of financial risk to physicians

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/2973b009-fb62-4356-b2a6-22855aa4ca25

OpenEvidence Explanation

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The correct answer is **C. Fee-for-service may incentivize physicians to increase healthcare utilization irrespective of quality**.

Under fee-for-service (FFS), physicians are reimbursed for each individual service provided, creating an inherent incentive to deliver more services — potentially including unnecessary ones — to increase income, regardless of whether those services improve quality or outcomes.[1][2] A Cochrane review found that FFS physicians may see more "well patients" and deliver more unnecessary services compared to salaried physicians.[1] A systematic review in oncology similarly noted that FFS reimbursement "may provide financial incentives for physicians to increase health care use, potentially leading to low-value and/or unnecessary care".[3]

Why the other options are incorrect:

- **A. Capitation poses the least financial risk to physicians** — This is false. Capitation actually poses **more** financial risk to physicians than FFS because physicians receive a fixed payment per patient regardless of the volume or cost of services delivered. If a patient requires expensive or extensive care, the physician absorbs that cost. FFS is perceived as representing more guaranteed income, as physicians are paid for each service rendered.[1][3][4]

- **B. Fee-for-service pays physicians a set amount of money per unit time for every patient under their care** — This describes **capitation**, not FFS. Capitation pays a fixed amount per patient per unit time. FFS pays physicians per service or procedure performed, not per patient enrolled.[4][5]

- **D. Fee-for-service poses the most amount of financial risk to physicians** — This is also false. FFS poses relatively **low** financial risk because income is directly tied to volume of services delivered. Capitation and other risk-bearing arrangements expose physicians to greater financial risk from unanticipated utilization.[3][6]

Would you like to explore how blended payment models (combining elements of FFS, capitation, and pay-for-performance) compare in terms of balancing quality incentives with financial sustainability?

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Question 818

A 29-year-old woman presents to her primary care doctor for a prenatal visit. She has just learned that she is pregnant and estimates she is approximately 6 weeks pregnant given the timing of her last menstrual cycle. She has a history of recurrent fetal loss. In total, she has had 4 miscarriages between the gestational ages of 8 and 15 weeks. She has a history of systemic lupus erythematosus and has had several DVTs in the past and a clot in her lung once. Her vitals today are unremarkable. She is asking if there are any treatments she should receive to prevent fetal loss. Which of the following is the most appropriate management of this patient?

Answer Choices:

(A) Aspirin and heparin
(B) Aspirin and warfarin
(C) No treatment indicated
(D) Rivaroxaban

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/8de2c2d5-a0e5-4069-9489-4c8765dfa2a3

OpenEvidence Explanation

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The correct answer is **A. Aspirin and heparin**.

This patient's clinical picture — SLE, recurrent pregnancy loss (4 miscarriages between 8–15 weeks), multiple DVTs, and a pulmonary embolism — is classic for **antiphospholipid syndrome (APS)** with both obstetric and thrombotic manifestations. The standard of care for preventing recurrent pregnancy loss in this setting is combination therapy with **low-dose aspirin and heparin** (typically low-molecular-weight heparin [LMWH]).

Why aspirin and heparin?

The 2020 American College of Rheumatology (ACR) guidelines strongly recommend combined low-dose aspirin and heparin for patients meeting criteria for obstetric APS. For patients with thrombotic APS (as in this case, with prior DVTs and PE), the recommendation is specifically for low-dose aspirin plus **therapeutic-dose** heparin throughout pregnancy and postpartum.[1] A Cochrane review of five trials (1,295 women) found that heparin plus aspirin increased live birth rates compared to aspirin alone (RR 1.27; 95% CI 1.09–1.49) and reduced pregnancy loss (RR 0.48; 95% CI 0.32–0.71).[2][3] The SMFM similarly recommends therapeutic heparin for pregnant patients with a history of thrombosis and antiphospholipid antibodies.[4]

Why not the other options?

- **B. Aspirin and warfarin** — Warfarin is **teratogenic** and contraindicated in pregnancy, particularly during the first trimester (causes warfarin embryopathy) and throughout pregnancy due to fetal CNS hemorrhage risk.
- **C. No treatment** — Withholding treatment in a patient with APS and recurrent pregnancy loss would be inappropriate given strong guideline recommendations for anticoagulation.[1][4]
- **D. Rivaroxaban** — Direct oral anticoagulants (DOACs) are **contraindicated in pregnancy** due to lack of safety data and potential teratogenicity. They also cross the placenta and are contraindicated in APS patients based on evidence of inferior outcomes compared to warfarin.[5]

Would you like to explore the specific dosing protocols for LMWH in pregnant patients with thrombotic APS, including the transition to postpartum anticoagulation?

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Question 819

A 17-year-old girl is brought to the physician because she has not attained menarche. There is no personal or family history of serious illness. She is 168 cm (5 ft 5 in) tall and weighs 63 kg (139 lb); BMI is 22.3 kg/m2. Examination shows normal breast development. Scant axillary hair is present. Abdominal examination shows a firm, nontender left inguinal mass. Pelvic examination shows a blind vaginal pouch. Ultrasonography does not show a uterus or ovaries. Which of the following is the most likely underlying cause of this patient's symptoms?

> **Answer Choices:**
>
> (A) 5-α reductase deficiency
> (B) Sex chromosome mosaicism
> (C) Sex chromosome monosomy
> (D) Androgen insensitivity

> **Correct Answer:**
>
> **(D)**
>
> **OpenEvidence Response:**
>
> **(D)** ✓

OpenEvidence Link: https://openevidence.com/ask/5e0f0514-f68c-4759-9402-fd70bfb50286

OpenEvidence Explanation

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The answer is **D. Androgen insensitivity**.

This presentation is classic for **complete androgen insensitivity syndrome (CAIS)**, formerly known as testicular feminization. The key features pointing to this diagnosis include:

- **Primary amenorrhea** in a phenotypically female adolescent
- **Normal breast development** (estrogen effect from peripheral aromatization of testosterone)
- **Scant axillary (and pubic) hair** — androgen-dependent hair growth is impaired
- **Blind vaginal pouch** — no müllerian structures developed due to anti-müllerian hormone (AMH) secreted by testes
- **Absent uterus and ovaries** on ultrasonography
- **Inguinal mass** — representing an undescended testis (46,XY karyotype)

CAIS results from a **loss-of-function mutation in the androgen receptor gene** (X-linked). These individuals are 46,XY with functional testes that produce testosterone and AMH. AMH causes regression of müllerian structures (uterus, fallopian tubes, upper vagina), while the inability to respond to androgens prevents virilization and wolffian duct development. Breast development occurs because testosterone is aromatized to estrogen peripherally.

Why not the other options?

- **A. 5-α reductase deficiency** — presents with ambiguous genitalia at birth and virilization at puberty, not a phenotypically female appearance with breast development.
- **B. Sex chromosome mosaicism (e.g., 45,X/46,XY)** — typically presents with ambiguous genitalia or features of Turner syndrome; would not produce this classic phenotype.
- **C. Sex chromosome monosomy (Turner syndrome, 45,X)** — presents with short stature, streak gonads, absent breast development (without exogenous estrogen), and webbed neck; this patient has normal height and breast development.

Would you like to explore the recommended timing and approach for gonadectomy in patients with complete androgen insensitivity syndrome?

Question 820

A 68-year-old man presents with a 6-month history of worsening fatigue and weight loss. He is especially concerned about a recent episode in which he noticed a blurring of his vision and headache; he also notes that his "memory is not as good as it used to be," which his wife confirms. Physical exam is notable only for pallor and general weakness. Laboratory studies reveal anemia as well as an elevated erythrocyte sedimentation rate. Serum protein electrophoresis (SPEP) reveals a sharp, narrow spike of monoclonal IgM; serum IgM concentration is 6.3 g/dL. What is the most likely diagnosis in this case?

Answer Choices:

(A) IgM monoclonal gammopathy of undetermined significance (MGUS)
(B) Multiple myeloma
(C) Waldenstrom's macroglobulinemia
(D) Non-Hodgkin's lymphoma

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/22746f75-72bd-45fa-8a13-407979ca2305

OpenEvidence Explanation

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The correct answer is **C. Waldenström's macroglobulinemia (WM)**.

This presentation is classic for WM: a 68-year-old man with fatigue, weight loss, anemia, elevated ESR, a **monoclonal IgM spike on SPEP**, a markedly elevated **serum IgM of 6.3 g/dL**, and symptoms of **hyperviscosity syndrome** (blurred vision, headache, and cognitive changes). WM is defined as a lymphoplasmacytic lymphoma with bone marrow involvement and an IgM monoclonal gammopathy. [1][2]

Why the other options are incorrect:

- **A. IgM MGUS** — By definition, MGUS requires a serum M protein <3 g/dL, <10% clonal cells in the bone marrow, and the absence of end-organ damage or symptoms attributable to the clonal process. This patient's IgM level of 6.3 g/dL far exceeds the MGUS threshold, and the presence of symptomatic anemia and hyperviscosity features rules out MGUS.[3]
- **B. Multiple myeloma** — While IgM multiple myeloma exists, it constitutes only ~1% of all myeloma cases. Key distinguishing features of IgM myeloma include lytic bone lesions, t(11;14) translocation, high CD138 expression, and absence of MYD88 mutations — none of which are described here. The monoclonal IgM spike with hyperviscosity symptoms is far more characteristic of WM.[2][4]
- **D. Non-Hodgkin's lymphoma** — While WM is technically classified as a subtype of B-cell NHL (lymphoplasmacytic lymphoma), the specific combination of monoclonal IgM paraprotein with hyperviscosity syndrome makes WM the most precise and clinically appropriate diagnosis rather than the broader category of NHL.[5]

The hyperviscosity symptoms in this case — blurred vision, headache, and cognitive impairment — are characteristic of WM and occur in approximately 10–15% of patients, typically when IgM levels are highly elevated (generally >4 g/dL). [2][5] The most common presenting symptom of WM is fatigue related to normocytic anemia, with a median hemoglobin at diagnosis of 10 g/dL.[2]

Would you like to explore the recommended initial workup and treatment approach for a symptomatic WM patient presenting with hyperviscosity?

Relevant images

(CONTENT OMITTED)

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Question 823

A 40-year-old woman presents to the emergency department with severe left upper quadrant pain (duration 3 hours, stabbing quality, 10/10 on the pain scale). Past medical history is significant for sickle cell anemia. Physical examination is significant for severe tenderness to palpation in the left upper quadrant. Significant splenomegaly is also noted. The patient is admitted to the hospital for close observation and placed on deep vein thrombosis (DVT) prophylaxis as part of a routine protocol. Laboratory findings drawn sometime after admission demonstrate a normal prothrombin time (PT) and elevated partial thromboplastin time (PTT). Which of the following factors is most directly affected by the DVT prophylaxis?

Answer Choices:

(A) VII
(B) VIIa
(C) X
(D) XII

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/5bf5f41e-b943-4824-86d1-a8b649dd38b0

OpenEvidence Explanation

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The answer is **C. X**.

The clinical scenario describes a hospitalized sickle cell disease patient with splenic sequestration crisis who is placed on **DVT prophylaxis**, most commonly with **unfractionated heparin (UFH)** or **low-molecular-weight heparin (LMWH)** in the inpatient setting.[1][2] The laboratory findings show a **normal PT with an elevated PTT**, which is the classic pattern seen with heparin therapy.[3][4]

Why Factor X is the answer:

Heparin-based DVT prophylaxis works by binding to **antithrombin III**, which accelerates the inhibition of activated coagulation factors — most importantly **Factor Xa** and **thrombin (Factor IIa)**.[5][6][7] The question asks which factor is "most directly affected," and **Factor X (via its activated form, Factor Xa)** is the primary target shared by both UFH and LMWH:

- **Unfractionated heparin** inhibits both Factor Xa and thrombin (IIa), but small amounts preferentially inhibit Factor Xa.[6]
- **Low-molecular-weight heparin** has even greater selectivity for **Factor Xa** over thrombin, due to its shorter polysaccharide chains that cannot form the ternary complex needed for thrombin inhibition.[5][7]

Why not the other options:

- **Factor VII (A) and Factor VIIa (B)** belong to the extrinsic pathway, which is measured by the PT/INR — the PT is normal here, so these are not affected.[3]
- **Factor XII (D)** initiates the intrinsic (contact activation) pathway and is measured by the PTT, but heparin does not target Factor XII. Factor XII deficiency can prolong the PTT, but it is not the mechanism of heparin's anticoagulant effect.[8][9][10]

The following figure illustrates the coagulation cascade and the factors assessed by the APTT, providing context for why Factor X inhibition by heparin prolongs the PTT while leaving the PT unaffected.

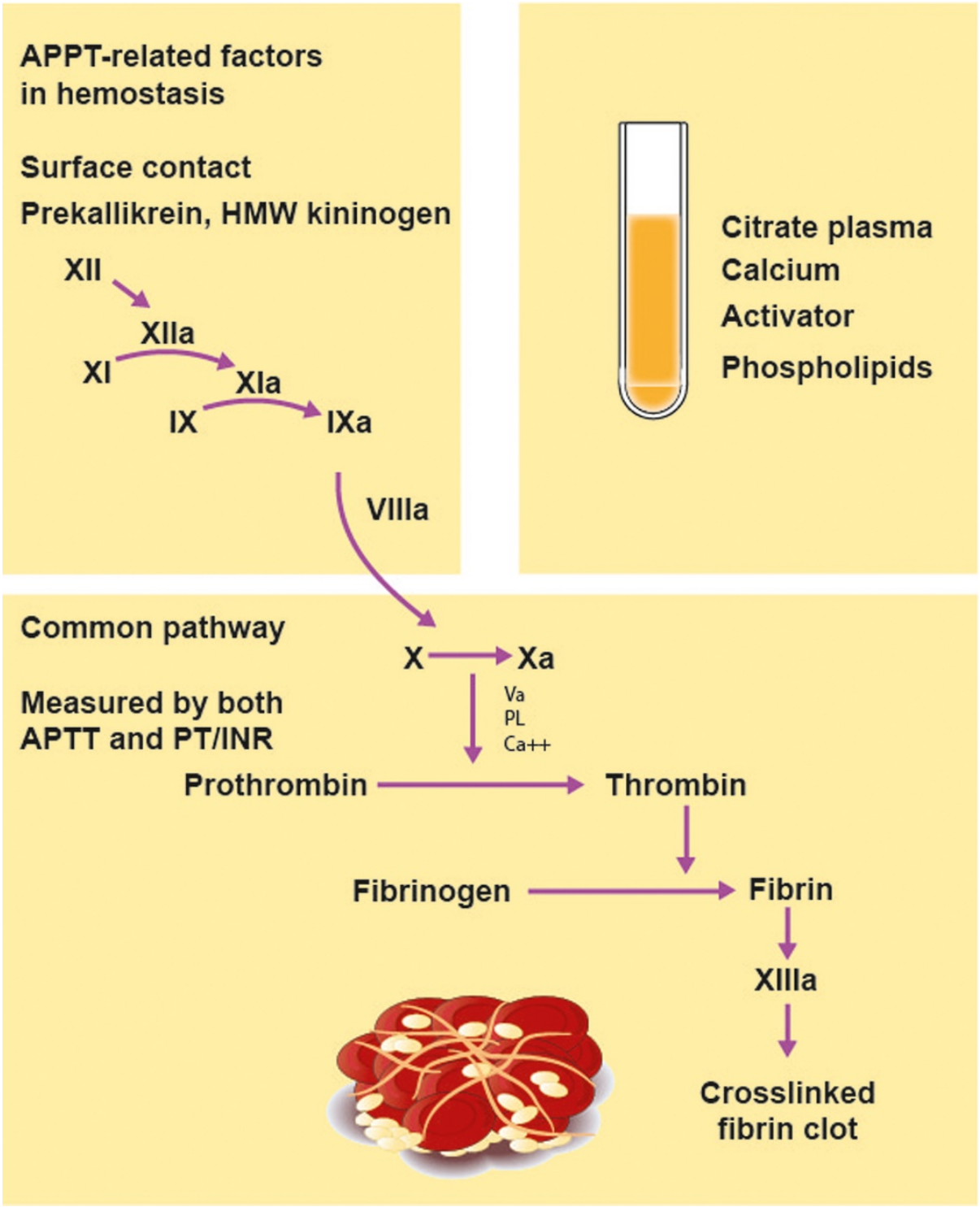


Figure 1. Overview of the APTT related in vitro factor activation. Activation involves the coagulation factors of the intrinsic and the common pathway of the coagulation cascade. Initially, activation of contact factors (high-molecular-weight [HMW] kininogen, prekallikrein, factor XII, and factor XI) is achieved by addition of an activator, such as ellagic acid or silica. 3 Deficiency of coagulation factors in the in vitro activation of the intrinsic and the common pathways leads to a prolongation of APTT. For an isolated prolonged APTT, the normal PT, however, indicates that the activation of the common pathway is intact. Prothrombin is factor II and thrombin is factor IIa. HMW, high molecular weight

Would you like to explore the differences in monitoring strategies and anti-Xa assays versus aPTT for heparin-based DVT prophylaxis in hospitalized patients?

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Question 824

A 47-year-old man with a history of HIV1 infection presents to his HIV clinic to discuss his antiretroviral medications. He is interested in including maraviroc in his maintenance regimen after seeing advertisements about the medication. On exam, his temperature is 98.8°F (37.1°C), blood pressure is 116/74 mmHg, pulse is 64/min, and respirations are 12/min. His viral load is undetectable on his current regimen, and his blood count, electrolytes, and liver function tests have all been within normal limits. In order to consider maraviroc for therapy, a tropism assay needs to be performed. Which of the following receptors is affected by the use of maraviroc?

Answer Choices:

(A) gp120
(B) gp160
(C) p24
(D) Reverse transcriptase

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/35faf673-7dce-4a5a-9356-20d70658ed08

OpenEvidence Explanation

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The answer is **A. gp120**. Maraviroc is a **CCR5 co-receptor antagonist** that works by binding to the CCR5 chemokine receptor on the host cell surface, thereby preventing the interaction between HIV-1 **gp120** and CCR5 that is necessary for viral entry into CD4+ T cells.[1][2][3]

Mechanism of action: During HIV-1 entry, the viral envelope glycoprotein gp120 first binds with low affinity to the CD4 receptor, triggering a conformational change in gp120 that then allows it to bind the CCR5 co-receptor. Maraviroc occupies the CCR5 binding site allosterically, so that CCR5 complexed with maraviroc cannot be recognized by gp120, blocking the entry process.[4][5] Importantly, maraviroc targets a **host protein** (CCR5) rather than a viral protein, making it unique among antiretroviral classes.[2]

The following figure illustrates the stages of HIV-1 entry and where maraviroc acts to block gp120–CCR5 interaction:

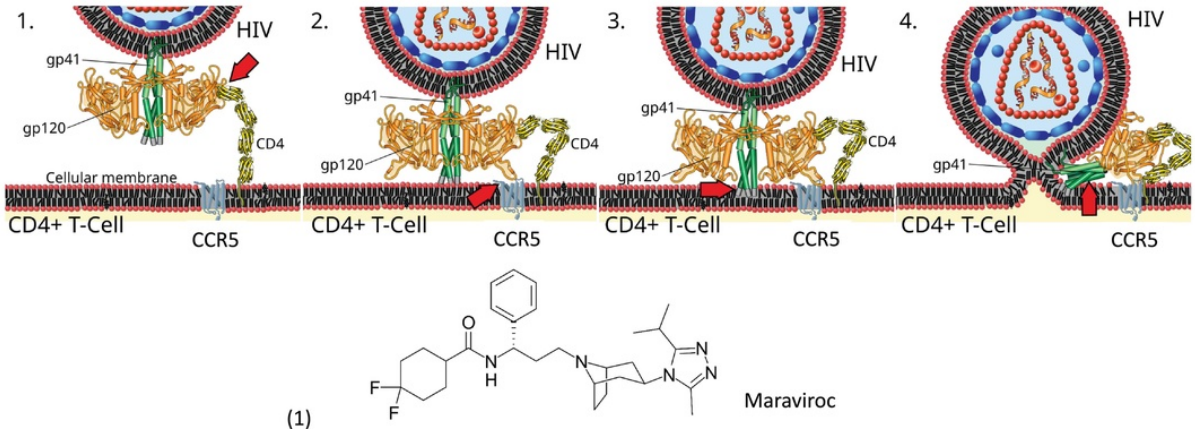


Figure 5. Entry of HIV-1 into the host cell. 1. Initial interaction between gp120 SU and CD4. 2. Conformational change in gp120 allows for secondary interaction with the co-receptor CCR5. 3. The distal tips of gp41 TM are inserted in to the cellular membrane. 4. gp41 undergoes significant conformational change; folding in half and forming coiled-coils. This process pulls the viral and cellular membranes together, fusing them. The antiviral Maraviroc (1) can bind to the extracellular face of CCR5 (red arrow in step 2) and prevent the binding of gp120 which inhibits the subsequent entry steps. Figure credit: Mike Jones from Wikipedia.

Why the other options are incorrect:

- **gp160** (answer B) is the precursor polyprotein that is cleaved into gp120 and gp41; it is not the direct target of maraviroc's mechanism. Fostemsavir (temsavir) binds directly to the gp120 subunit of gp160 to prevent CD4 attachment.[6]

- **p24** (answer C) is the HIV capsid protein used primarily as a diagnostic marker; it is not involved in viral entry.
- **Reverse transcriptase** (answer D) is targeted by NRTIs and NNRTIs, not by entry inhibitors like maraviroc.

Because maraviroc is only effective against **CCR5-tropic (R5) virus**, a co-receptor tropism assay must be performed before initiating therapy, as recommended by the HHS guidelines.[7] CXCR4-tropic or dual/mixed-tropic viruses are not inhibited by maraviroc.[1][8]

Would you like to explore the different types of tropism assays (phenotypic vs. genotypic) and how they guide clinical decision-making for CCR5 antagonist use?

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Question 826

A 22-year-old woman presents to the emergency department with a headache. She has had episodic headaches like this in the past and states that her headache today is severe, worse when laying down, and not responding to ibuprofen. She also reports a transient episode of vision loss and current blurry vision. She states she has a ringing in her ears as well. The patient has a past medical history of headaches, obesity, polycystic ovarian syndrome, and constipation. Her temperature is 98.7°F (37.1°C), blood pressure is 149/92 mmHg, pulse is 83/min, respirations are 15/min, and oxygen saturation is 99% on room air. Physical exam is not remarkable and an initial head CT is within normal limits. Which of the following is the best next step in management for the most likely diagnosis?

Answer Choices:

(A) Ibuprofen
(B) Lumbar puncture
(C) MRI
(D) Tissue plasminogen activator

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/3f97a8ab-cf65-4bf3-b921-17f70abbdd64

OpenEvidence Explanation

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The best next step in management is **B. Lumbar puncture**. The clinical presentation is classic for **idiopathic intracranial hypertension (IIH)**, and lumbar puncture is required to confirm the diagnosis by demonstrating elevated CSF opening pressure (≥25 cm H_2O) with normal CSF composition.[1][2]

This 22-year-old obese woman with PCOS presents with the hallmark features of IIH: severe headache worsened by recumbency, transient visual obscurations, blurry vision, and pulsatile tinnitus.[3] More than 95% of patients with IIH are women of childbearing age with obesity, and PCOS has been identified as an associated condition.[3][4] The normal head CT has already excluded a mass lesion or acute hemorrhage.

Why the other options are incorrect:

- **A. Ibuprofen** — The patient has already failed ibuprofen, and this would not address the underlying elevated intracranial pressure.
- **C. MRI** — While MRI with MR venography is part of the full diagnostic workup to exclude venous sinus thrombosis and identify secondary signs of raised ICP (empty sella, flattening of the posterior globe, transverse sinus stenosis), the CT has already excluded a mass lesion. The lumbar puncture is the critical diagnostic step to confirm elevated opening pressure and analyze CSF composition.[2][5]
- **D. Tissue plasminogen activator (tPA)** — This is used for acute ischemic stroke, which is not consistent with this presentation. There is no focal neurological deficit, and the CT is normal.

The diagnostic lumbar puncture also serves a therapeutic role — removal of CSF (typically 30–40 mL) transiently lowers ICP and often provides immediate symptom relief, with lasting remission after a single puncture not uncommon.[1][3]

Would you like to explore the long-term management of IIH, including the evidence for acetazolamide from the IIH Treatment Trial and the role of weight loss strategies?

Relevant images

(CONTENT OMITTED)

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Question 827

A 28-year-old woman presents to her primary care physician for evaluation of amenorrhea. Her last period occurred 4 months ago but she has not had sex in the last year and home pregnancy tests have come back negative. She first started having periods at age 13 and her periods have been unremarkable up until they stopped 4 months ago. Her past medical history is significant for radius and ulnar forearm fractures that she sustained in a car crash 3 months ago. She didn't see the car coming and has had increasing difficulty noticing objects in her peripheral vision. She also notes having recurrent headaches 5 months ago. Otherwise she has been healthy with no previous pregnancies. Physical exam reveals galactorrhea and temporal field visual defects. Which of the following mechanisms is most likely responsible for this patient's amenorrhea?

Answer Choices:

(A) Inhibition of gonadotropin-releasing hormone release
(B) Intrauterine scar tissue accumulation
(C) Nondisjunction of chromosomes
(D) Nutritional imbalance

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/5f4054ef-6866-4c48-987a-2903e4bd2ddd

OpenEvidence Explanation

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The answer is **A. Inhibition of gonadotropin-releasing hormone release**.

This patient's presentation — secondary amenorrhea, galactorrhea, headaches, and **bitemporal hemianopia** (temporal field visual defects) — is classic for a **prolactinoma** (likely a macroprolactinoma given the visual field defects from optic chiasm compression). The mechanism by which hyperprolactinemia causes amenorrhea is through **suppression of GnRH pulsatile secretion** from the hypothalamus.

Excess prolactin suppresses GnRH by reducing kisspeptin secretion from arcuate nucleus neurons, which are major excitatory inputs to GnRH neurons.[1][2] Increased opioid tone induced by elevated prolactin concentrations also contributes to GnRH suppression.[1] This results in decreased LH and FSH release (hypogonadotropic hypogonadism), leading to anovulation and amenorrhea.[3][4] Restoration of ovulatory menstrual periods with pulsatile GnRH administration in hyperprolactinemic women confirms that the defect lies at the level of GnRH secretion.[4]

Why the other options are incorrect:

- **B. Intrauterine scar tissue accumulation** — This describes Asherman syndrome, which causes amenorrhea due to endometrial adhesions, typically following uterine instrumentation (e.g., D&C). This patient has no history of uterine procedures.
- **C. Nondisjunction of chromosomes** — This would describe Turner syndrome (45,X), which causes primary amenorrhea and ovarian failure. This patient had normal menarche at age 13 and regular periods until recently, making a chromosomal abnormality unlikely.
- **D. Nutritional imbalance** — Functional hypothalamic amenorrhea from caloric restriction or excessive exercise can suppress GnRH, but it would not explain the galactorrhea, bitemporal hemianopia, or headaches seen in this patient.

Would you like to explore the diagnostic workup and management of prolactinomas, including the role of dopamine agonist therapy?

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Question 830

A 72-year-old man in a nursing home was brought to the emergency department with right hand and leg weakness for 1 hour. There has been a gradual increase in the degree of weakness. The patient is disoriented. The medical history includes ischemic heart disease diagnosed 2 months ago, and long histories of diabetes and hypertension (30 and 25 years, respectively). On examination, the reflexes are hypertonic and the Babinski reflex is positive. The CT scan is shown. What is the most likely pathologic change?

> **Answer Choices:**
>
> (A) Gangrenous necrosis
> (B) Liquefactive necrosis
> (C) Caseous necrosis
> (D) Fibrinoid necrosis

> **Correct Answer:**
>
> **(B)**
>
> **OpenEvidence Response:**
>
> **(B)** ✓

OpenEvidence Link: https://openevidence.com/ask/6fae6da9-b1f7-4864-848f-bf50c65f5556

OpenEvidence Explanation

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The answer is **B. Liquefactive necrosis**.

This clinical presentation — acute onset right-sided hemiparesis, upper motor neuron signs (hypertonic reflexes, positive Babinski), and risk factors including ischemic heart disease, diabetes, and hypertension — is consistent with an **ischemic stroke** (cerebral infarction). The CT scan in this context would be expected to show a hypodense area corresponding to the infarct territory.

Why liquefactive necrosis?

The brain characteristically undergoes **liquefactive necrosis** following ischemic infarction, unlike most other organs which undergo coagulative necrosis. This is because brain tissue has relatively low protein content and high lipid content, along with abundant hydrolytic enzymes released from dying neurons and infiltrating inflammatory cells (microglia and macrophages). Infarcted brain tissue softens, undergoes enzymatic degradation, and eventually forms a fluid-filled cystic cavity.[1][2][3] Histopathologically, the infarcted tissue progresses through liquefactive necrosis and then cavitation, with infiltration by fat-laden macrophages.[1][4]

Why not the other options?

- **Gangrenous necrosis (A):** Occurs in ischemic limbs or bowel — not characteristic of brain infarction.
- **Caseous necrosis (C):** A hallmark of tuberculosis and certain granulomatous diseases, characterized by a cheese-like, amorphous appearance.
- **Fibrinoid necrosis (D):** Seen in vessel walls in conditions such as malignant hypertension or vasculitis — not the predominant tissue-level pathologic change in cerebral infarction.

Would you like to explore the pathophysiologic mechanisms that make brain tissue uniquely susceptible to liquefactive rather than coagulative necrosis?

Relevant images

(CONTENT OMITTED)

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Question 831

An 11-year-old boy was brought in by his mother with red tender bumps on his legs. The patient's mother says that his symptoms started 3 days ago with a low-grade fever, malaise, and joint pain. He began to improve over the next 2 days, but this morning, when he woke up, she noticed multiple painful red bumps on his shins. Past medical history is significant for a recent severe sore throat and fever 1 week ago which resolved without treatment. The vital signs include: temperature 38.0°C (100.4°F), blood pressure 120/70 mm Hg, pulse 85/min, and respiratory rate 15/min. Physical examination reveals multiple, firm and tender erythematous nodules with indistinct borders, averaging 4 cm in diameter. Lesions are localized to the anterior surface of the lower legs. No evidence of drainage, bleeding, abscess formation or ulceration. Which of the following is the next best diagnostic step in this patient?

Answer Choices:

(A) Throat culture
(B) Chest radiograph
(C) Bone marrow biopsy
(D) Colonoscopy

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/a05fb447-09b0-4c66-ac78-6a09fa4eaa3a

OpenEvidence Explanation

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The answer is **A. Throat culture**.

This presentation is classic for **erythema nodosum (EN)** — tender, firm, erythematous nodules on the anterior shins without ulceration or drainage, preceded by a prodrome of fever, malaise, and arthralgias.[1][2] The history of a severe sore throat and fever one week prior strongly suggests **streptococcal pharyngitis** as the triggering etiology, which is the most common identifiable cause of EN in both children and adults.[2][3]

Why throat culture is the best next step: The diagnostic workup for EN should be directed at identifying the underlying cause. Given the preceding pharyngitis, testing for streptococcal infection is the highest-yield initial investigation. A throat culture can confirm group A streptococcal (GAS) infection, which is critical because untreated GAS pharyngitis carries risk for complications such as acute rheumatic fever.[2][4] Throat culture is part of the recommended initial workup for EN alongside CBC, ESR/CRP, and ASO titers.[2][5] Notably, EN eruptions typically appear 2–3 weeks after streptococcal pharyngitis, so pharyngeal swabs may still be positive at this stage (1 week post-pharyngitis).[5]

Why the other options are less appropriate:

- **Chest radiograph (B)** — Useful when evaluating for sarcoidosis or tuberculosis as causes of EN, but these are not suggested by this clinical scenario. Chest X-ray would be considered if the initial streptococcal workup is negative or if respiratory symptoms are present.[2][6]
- **Bone marrow biopsy (C)** — Would be considered only if malignancy (e.g., lymphoma, leukemia) were suspected, which is not supported by this presentation.
- **Colonoscopy (D)** — Relevant if inflammatory bowel disease were suspected (e.g., chronic diarrhea, weight loss, abdominal pain), but there are no GI symptoms here.[7]

Would you like to explore the complete diagnostic algorithm and workup for erythema nodosum when the initial streptococcal testing is negative?

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Question 832

Two hours after admission to the hospital for rupture of membranes, a 35-year-old woman, gravida 3, para 2, at 40 weeks' gestation is evaluated for the sudden onset of chills, dyspnea, confusion, and hypotension. The patient successfully underwent combined spinal-epidural anesthesia 1 hour ago. Her pregnancy was uncomplicated with the exception of a positive vaginal swab for group B streptococci 3 weeks ago, for which she received one dose of intravenous penicillin. Her temperature is 37.6°C (99.8°F), pulse is 130/min, respirations are 30/min, and blood pressure is 70/30 mm Hg. Pulse oximetry on room air shows an oxygen saturation of 82%. Physical examination shows labored breathing and thready pulses. Crackles are heard at both lung bases. The abdomen is nontender. Speculum examination shows pooling of bright red blood in the cervical canal. Laboratory studies show a hemoglobin concentration of 7.6 mg/dL and an undetectable fibrinogen concentration. Which of the following is the most likely underlying cause of this patient's current condition?

Answer Choices:

(A) Apical ballooning of the left ventricle
(B) Amniotic fluid entering the endocervical veins
(C) Anesthetic agent entering the subarachnoid space
(D) Systemic bacterial infection

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/90928dca-f309-411d-b2fc-c62a5f0d6be0

OpenEvidence Explanation

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The answer is **B. Amniotic fluid entering the endocervical veins**.

This presentation is classic for **amniotic fluid embolism (AFE)**, a catastrophic obstetric emergency characterized by the sudden entry of amniotic fluid or fetal debris into the maternal circulation. The clinical triad of sudden **cardiovascular collapse** (hypotension, tachycardia), **respiratory distress** (dyspnea, hypoxia with SpO_2 82%), and **disseminated intravascular coagulation** (undetectable fibrinogen, vaginal hemorrhage) in a laboring patient after rupture of membranes is the hallmark presentation.[1][2][3]

Key features supporting AFE in this case:

- **Sudden onset** of chills, dyspnea, confusion, and hypotension during labor — AFE typically presents intrapartum or immediately postpartum with abrupt hemodynamic and respiratory compromise.[1][4]
- **Undetectable fibrinogen** — precipitous drops in fibrinogen levels due to consumptive coagulopathy and hyperfibrinolysis are characteristic of AFE, distinguishing it from other causes of peripartum collapse.[5][6]
- **Vaginal hemorrhage** (bright red blood pooling in the cervical canal) — resultant from the severe DIC.[1][5]
- **Altered mental status** (confusion) — neurologic impairment is a recognized component of the syndrome.[7]

The pathophysiology involves amniotic fluid and fetal antigens (including tissue factor and endothelin) entering the maternal circulation through endocervical veins, triggering an anaphylactoid-like immune response with massive activation of the coagulation cascade and cardiopulmonary collapse.[1][4][5]

Why the other options are incorrect:

- **A (Apical ballooning / Takotsubo)** — would not explain the DIC with undetectable fibrinogen or vaginal hemorrhage.

- **C (High spinal anesthesia)** — could cause hypotension and respiratory compromise, but would not cause DIC, undetectable fibrinogen, or hemorrhage.
- **D (Systemic bacterial infection / sepsis)** — although GBS-positive, the patient received prophylactic penicillin, has only a low-grade temperature (37.6°C), and the abrupt onset with immediate severe coagulopathy is far more consistent with AFE than sepsis, which typically evolves over hours.

The following figure illustrates the proposed pathophysiological cascade of amniotic fluid embolism, showing how amniotic fluid and fetal debris breach the maternal-fetal barrier and trigger cardiovascular collapse and DIC.

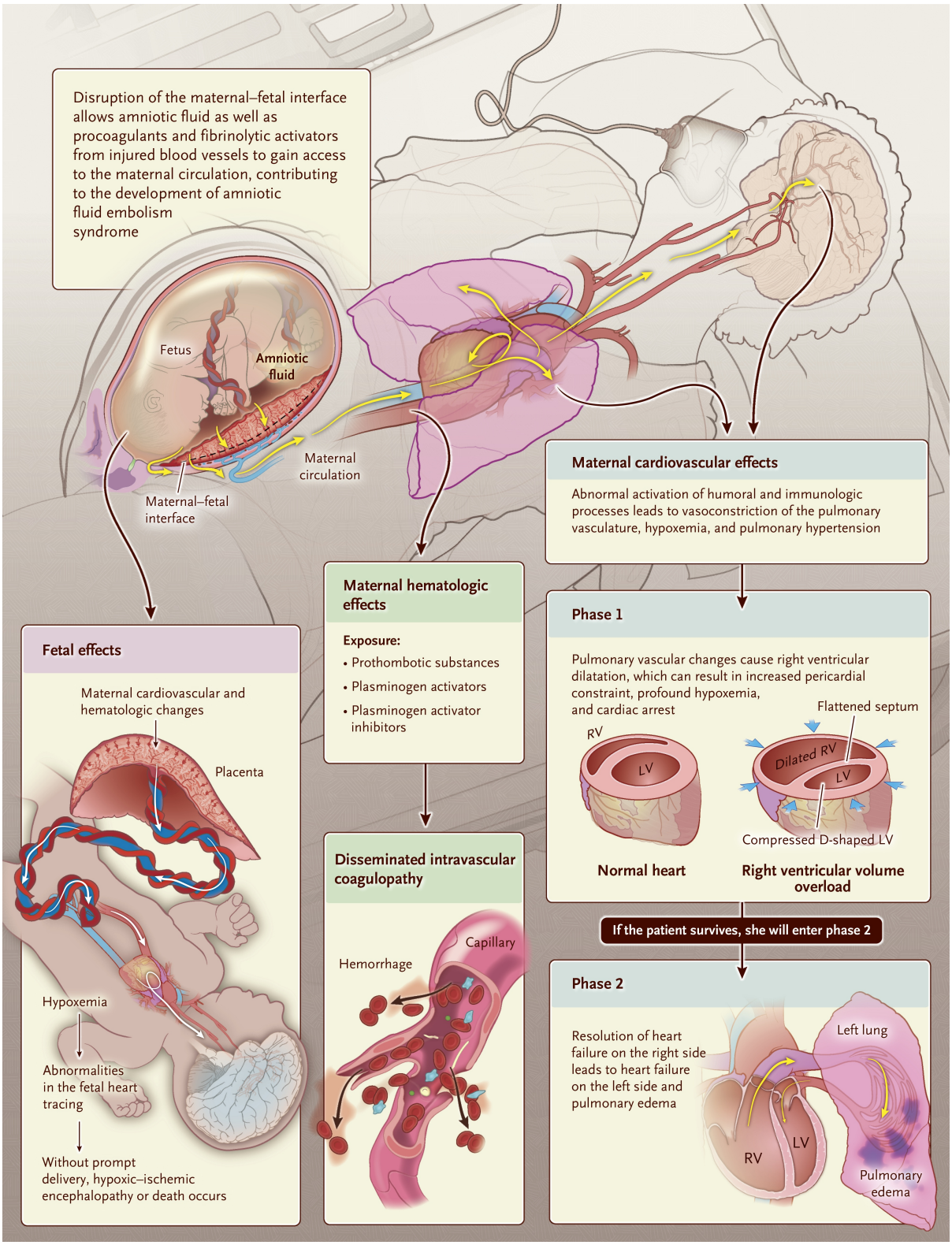


Figure 1. Hypothesis for the Pathophysiological Process of Amniotic Fluid Syndrome.

Used under license from The New England Journal of Medicine.

Would you like to explore the current evidence on initial resuscitation strategies and the emerging A-OK regimen (Atropine, Ondansetron, Ketorolac) for managing amniotic fluid embolism?

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Question 834

While on a teaching sabbatical in Uruguay, a pathologist examined the excised liver of an 18-year-old otherwise healthy female who passed away due to massive hepatic necrosis 5 days after she underwent general anesthesia to repair a fractured femur. Which of the following is a general anesthetic most likely responsible for her death?

Answer Choices:

(A) Lidocaine
(B) Midazolam
(C) Halothane
(D) Desflurane

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/cfb0efda-fa45-4645-8f04-68717300134f

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OpenEvidence Explanation

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The answer is **C. Halothane**.

Halothane is the general anesthetic most classically associated with fatal massive hepatic necrosis, a condition known as "**halothane hepatitis.**" This

presentation — an otherwise healthy young patient developing fulminant hepatic failure days after general anesthesia — is the hallmark clinical scenario.

Why halothane? Halothane undergoes approximately 20% hepatic metabolism via CYP2E1, producing trifluoroacetyl chloride metabolites that covalently bind to liver proteins, forming neoantigens.[1][2] This triggers an immune-mediated idiosyncratic reaction leading to massive hepatocellular necrosis, typically presenting **2–14 days postoperatively**.[3] The condition carries a high mortality rate, with the morphologic spectrum ranging from spotty necrosis to massive necrosis.[4]

Why not the other options?

- **Lidocaine (A)** is a local anesthetic, not a general anesthetic used for inhalational anesthesia.
- **Midazolam (B)** is a benzodiazepine used for sedation/anxiolysis; it is not associated with massive hepatic necrosis.
- **Desflurane (D)** undergoes only ~0.02% hepatic metabolism and has **not been reported to cause hepatic dysfunction** or fatal hepatic necrosis. Sera from halothane hepatitis patients show no antibody reactivity against hepatic proteins from desflurane-exposed animals.[2][3][5]

The geographic detail (Uruguay) is a clue — halothane has been largely replaced in developed countries by newer agents (sevoflurane, desflurane) but remains in use in some lower-resource settings due to its low cost.[6]

Would you like to explore the mechanism of cross-sensitization between halogenated volatile anesthetics and the risk of hepatotoxicity with re-exposure?

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Question 836

A 72-year-old anthropologist with long-standing hypertension visits your office for a routine exam. You notice an abnormality on his laboratory results caused by his regimen of captopril and triamterene. What abnormality did you most likely find?

Answer Choices:

(A) Hyperkalemia
(B) Hypernatremia
(C) Thrombocytopenia
(D) Anemia

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/ac8c6059-e984-4a07-bf00-696a4443c0d0

OpenEvidence Explanation

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The answer is **A. Hyperkalemia**.

Both **captopril** (an ACE inhibitor) and **triamterene** (a potassium-sparing diuretic) independently raise serum potassium, and their combination carries a well-established, synergistic risk of **hyperkalemia**.

- **Captopril** decreases aldosterone production by inhibiting the renin–angiotensin–aldosterone system, reducing renal potassium excretion.[1]
- **Triamterene** blocks the epithelial sodium channel (ENaC) in the cortical collecting duct, abolishing the lumen-negative potential that drives potassium secretion.[2]

The FDA label for triamterene explicitly warns that potassium-sparing agents "should be used with caution in conjunction with ACE inhibitors due to an increased risk of hyperkalemia".[3] Similarly, the captopril label states that potassium-sparing diuretics including triamterene "should be given only for documented hypokalemia, and then with caution, since they may lead to a significant increase of serum potassium".[1] A study of elderly patients on ACE inhibitors found that those hospitalized for hyperkalemia were **27 times more likely** to have recently received a potassium-sparing diuretic.[2]

The 2025 AHA/ACC hypertension guidelines reinforce that hyperkalemia may be caused by ACE inhibitors and potassium-sparing diuretics, "especially when used in combination or in the setting of CKD".[4] This risk is particularly relevant in a 72-year-old patient, as age-related decline in renal function further impairs potassium excretion.

The other options — hypernatremia, thrombocytopenia, and anemia — are not characteristic adverse effects of this drug combination.

Would you like to explore the management strategies for drug-induced hyperkalemia, including the role of newer potassium binders like patiromer and sodium zirconium cyclosilicate?

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Question 837

A 56-year-old woman is brought to the emergency department by her husband because of increasing confusion, generalized fatigue, and irritability for the past week. She has been unable to recall her husband's name or their address. She has had insomnia and daytime sleepiness during this period. Her last bowel movement was 3 days ago. One month ago, she underwent a transjugular intrahepatic portal shunt (TIPS) placement. She has alcoholic liver cirrhosis. Current medications include spironolactone and furosemide. She used to drink over a pint of vodka daily but quit 2 months ago. She is oriented to place and person. Her temperature is 37.3°C (99.1°F), pulse is 88/min, and blood pressure is 102/64 mm Hg. Examination shows scleral icterus and jaundice. There are several telangiectasias over the chest and back. Palmar erythema is present. The abdomen is mildly distended and nontender. Shifting dullness is present. There is a flapping tremor of both hands when outstretched and dorsiflexed. Neurologic examination shows no other focal findings. She completes the number connection test slower than the age-normalized standard. Which of the following is the most appropriate next step in management?

Answer Choices:

(A) Reversal of TIPS
(B) Paracentesis
(C) Administer IV ceftriaxone
(D) Administer lactulose

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/4ee8456c-87e4-4c92-a117-a091dfe94daf

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OpenEvidence Explanation

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The most appropriate next step is **D. Administer lactulose**.

This patient presents with classic **overt hepatic encephalopathy (OHE)** following TIPS placement — confusion, inability to recall names/address, sleep-wake cycle inversion, constipation, and **asterixis** (flapping tremor), with a prolonged number connection test. TIPS is a well-known precipitant of HE, occurring in 30–50% of patients post-procedure.[1][2]

Lactulose is the first-line treatment for overt hepatic encephalopathy, recommended as a strong recommendation with moderate certainty of evidence by the ACG.[1] The recommended approach is lactulose 10–20 g (15–30 mL) every 1–2 hours until a bowel movement occurs, then titrated to achieve 2–3 soft bowel movements daily.[1] Constipation (last bowel movement 3 days ago) is itself a precipitating factor for HE, further supporting lactulose as the immediate intervention.

Why not the other options:

- **A. Reversal of TIPS** — TIPS reduction or occlusion is reserved for **refractory** post-TIPS HE (3–7% of cases) that fails to respond to medical therapy with lactulose and rifaximin. It is not a first-line measure and carries procedural risks including mesenteric infarction and recurrence of the original indication (variceal bleeding or ascites).[1][3]
- **B. Paracentesis** — While ascites is present (shifting dullness), there is no clinical suggestion of spontaneous bacterial peritonitis (no fever, no abdominal tenderness). Diagnostic paracentesis may be reasonable as part of the workup for precipitating factors, but it is not the most appropriate *next step* over initiating lactulose.

- **C. IV ceftriaxone** — Empiric antibiotics are not indicated without clinical or laboratory evidence of active infection. The patient is afebrile (37.3°C) with a nontender abdomen.[1]

Would you like to explore the role of rifaximin as adjunctive therapy to lactulose for secondary prophylaxis of hepatic encephalopathy after the acute episode resolves?

Relevant images

(CONTENT OMITTED)

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Question 838

A 50-year-old woman is brought to the office by her daughter with a chief complaint of finger pain in her left hand. She is slightly confused and can't remember when the pain started. Her daughter states that the pain has been present for approximately one month. She expresses concern that her mother has been progressively more confused during the past week. She reports that her mother also has had worsening nausea for several months. The patient's vital signs are heart rate 92/min, respiratory rate 13/min, temperature 37.1°C (98.8°F), and blood pressure 120/86 mm Hg. Upon physical examination, the patient reports pain when the fingers of the left hand are palpated, and small palpable tumors are visible on the fingers. An X-ray image of the left-hand shows thin bones with brown tumors and osteolysis of the distal phalanges. What is the most likely cause for this patient's condition?

Answer Choices:

(A) Hyperparathyroidism
(B) Hypocalcemia
(C) Osteosarcoma
(D) Multiple myeloma

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/7f5ffb15-b27a-4cdf-989c-0f8762ffd142

OpenEvidence Explanation

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The correct answer is **A. Hyperparathyroidism**.

This presentation is classic for **primary hyperparathyroidism** with osteitis fibrosa cystica. The key findings that point to this diagnosis include:

Skeletal findings: The X-ray showing **brown tumors**, thin bones (cortical thinning), and **osteolysis of the distal phalanges** (acro-osteolysis/subperiosteal resorption) is pathognomonic for osteitis fibrosa cystica caused by hyperparathyroidism. Brown tumors result from prolonged PTH-driven osteoclastic bone resorption, leading to multinucleated giant cell conglomerates with hemosiderin deposits that give the characteristic brown color.[1][2] The hands are among the most common sites for brown tumors in primary hyperparathyroidism.[2]

Neuropsychiatric symptoms: The progressive confusion is explained by **hypercalcemia**, which causes neuropsychiatric manifestations including altered mental status, lethargy, decreased concentration, and cognitive decline.[3][4] Severe hypercalcemia can progress to confusion, stupor, and coma.[3]

Gastrointestinal symptoms: The worsening nausea over several months is consistent with hypercalcemia-induced slowed peristalsis and gastrointestinal dysfunction.[3]

This constellation of symptoms is captured by the classic mnemonic "**stones, bones, groans, and psychiatric overtones**" — referring to renal stones, bone disease (osteitis fibrosa cystica), gastrointestinal complaints (nausea, constipation), and neuropsychiatric manifestations.[5]

Why the other options are incorrect:

- **B. Hypocalcemia** — would not cause brown tumors or osteolysis; hypocalcemia presents with neuromuscular excitability (tetany, Chvostek/Trousseau signs), not confusion.

- **C. Osteosarcoma** — presents as a single aggressive bone lesion with periosteal reaction (Codman triangle, sunburst pattern), not diffuse thin bones with brown tumors.
- **D. Multiple myeloma** — can cause lytic lesions and hypercalcemia but produces "punched-out" lesions without the characteristic brown tumors or subperiosteal resorption of distal phalanges seen here.[6][7]

Would you like to explore the current surgical indications and guidelines for parathyroidectomy in symptomatic primary hyperparathyroidism?

Relevant images

(CONTENT OMITTED)

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Question 839

A 48-year-old woman comes to the physician because of a 4-month history of lightheadedness, intermittent headaches, and easy bruising. Five months ago, she was treated for an episode of thrombophlebitis. Physical examination shows multiple bruises on her limbs. Laboratory studies show a platelet count of 900,000/mm3 and elevated levels of serum lactate dehydrogenase and uric acid. Treatment with a medication is begun that is also used in the treatment of sickle cell disease. Which of the following mechanisms is most likely responsible for the beneficial effect of this drug in sickle cell disease?

Answer Choices:

(A) Inhibition of thrombocyte aggregation
(B) Increase in circulating fetal hemoglobin
(C) Inhibition of stem cell differentiation
(D) Restoration of the body's iron stores

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/1896fd23-27db-49d8-9414-8806d32cb031

OpenEvidence Explanation

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The correct answer is **B. Increase in circulating fetal hemoglobin**.

The clinical vignette describes a patient with features of **essential thrombocythemia** — markedly elevated platelet count (900,000/mm^3), thrombophlebitis, easy bruising, lightheadedness, and headaches, with elevated LDH and uric acid suggesting high cell turnover. **Hydroxyurea** is the preferred first-line cytoreductive agent for essential thrombocythemia and is also the cornerstone disease-modifying therapy for [1][2]sickle cell disease.[3]

In sickle cell disease, hydroxyurea is a ribonucleotide reductase inhibitor that **induces fetal hemoglobin (HbF) production**. HbF inhibits HbS polymerization — the fundamental pathologic event in SCD — thereby reducing red cell rigidity, sickling, and hemolysis.[3][4] This is the primary mechanism responsible for its clinical benefit, including decreased vaso-occlusive crises, acute chest syndrome, hospitalizations, and transfusion requirements.[3][4]

Why the other options are incorrect:

- **A (Inhibition of thrombocyte aggregation):** While hydroxyurea does reduce platelet counts (its role in ET), antiplatelet activity is not the mechanism of benefit in SCD.
- **C (Inhibition of stem cell differentiation):** Hydroxyurea inhibits ribonucleotide reductase and causes cytoreduction, but its therapeutic benefit in SCD is specifically through HbF induction, not through broadly inhibiting stem cell differentiation.
- **D (Restoration of iron stores):** Hydroxyurea has no role in restoring iron stores; iron overload (not deficiency) is actually a concern in SCD patients receiving chronic transfusions.

Would you like to explore the specific dosing and monitoring protocols for hydroxyurea in essential thrombocythemia versus sickle cell disease?

Relevant images

(CONTENT OMITTED)

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Question 840

Candida is injected into the skin of a 38-year-old female patient. Forty-eight hours later, there is a 14 mm raised, slightly hardened area at the injection site. What type of hypersensitivity reaction has occurred and what cell type plays a role?

Answer Choices:

(A) Type I hypersensitivty; eosinophils
(B) Type IV hypersensitivity; mast cells
(C) Type III hypersensitivity; CD4+ T cells
(D) Type IV hypersensitivity; CD4+ T cells

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/5a5a7854-dea0-4152-8f5b-8c98bffa9948

OpenEvidence Explanation

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The answer is **D. Type IV hypersensitivity; CD4+ T cells**.

The clinical scenario describes a classic **delayed-type hypersensitivity (DTH) reaction**, which is a **Type IV hypersensitivity** response. Several features confirm this:

- **Timing (48 hours):** Type IV reactions characteristically develop 24–72 hours after antigen exposure, distinguishing them from immediate (Type I, minutes), cytotoxic (Type II, hours), and immune complex–mediated (Type III, hours) reactions.
- **Induration (raised, hardened area):** The hallmark of a positive DTH skin test is induration, not just erythema, reflecting cellular infiltration at the site.
- **Candida antigen skin testing** is a well-established method to assess intact cell-mediated immunity. Most immunocompetent adults have been previously sensitized to Candida, so a positive response confirms functional T-cell–mediated immunity.

Mechanism: Upon re-exposure to the Candida antigen, previously sensitized **CD4+ T helper cells (Th1 subtype)** recognize the antigen presented by antigen-presenting cells (macrophages, dendritic cells) via MHC class II. These CD4+ T cells release cytokines (IFN-γ, TNF-α, IL-2) that recruit and activate macrophages, leading to the characteristic induration.

Why not the other options?

- **A (Type I; eosinophils):** Type I reactions are IgE-mediated, occur within minutes, and involve mast cell degranulation — inconsistent with the 48-hour timeline.
- **B (Type IV; mast cells):** While correctly identifying Type IV, mast cells are effectors of Type I hypersensitivity, not DTH.
- **C (Type III; CD4+ T cells):** Type III reactions involve immune complex deposition and are complement/neutrophil-mediated, not T-cell–mediated.

Would you like to explore how Candida skin testing is used clinically to evaluate anergy in immunocompromised patients?

Question 841

On routine screening, a 62-year-old man is found to have positive fecal occult blood tests. He is asymptomatic, but his father died of large intestinal cancer. Abdominal and rectal exams are normal. A colonoscopy subsequently reveals a polyp in the descending colon but no other abnormalities. Excisional biopsy of the polyp shows 75% tubular architecture. Which of the following is the most likely diagnosis?

Answer Choices:

(A) Inflammatory polyp
(B) Adenomatous polyp
(C) Hamartomatous polyp
(D) Colorectal cancer

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/52cefc35-2587-4992-bdc4-de002275b2cb

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OpenEvidence Explanation

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The most likely diagnosis is **B. Adenomatous polyp** (specifically, a tubular adenoma).

Colorectal polyps are classified histologically into several categories: adenomatous (neoplastic), hyperplastic, inflammatory, and hamartomatous. Adenomatous polyps are further subclassified based on the proportion of villous architecture:[1]

- **Tubular adenoma**: <25% villous features (≥75% tubular architecture)
- **Tubulovillous adenoma**: 25–75% villous features
- **Villous adenoma**: >75% villous features

In this case, the polyp demonstrates **75% tubular architecture** (i.e., 25% or less villous component), which is consistent with a **tubular adenoma** — the most common type of adenomatous polyp.[2][3] Tubular adenomas account for approximately 66% of all colorectal adenomas.[4][5]

The other options are less likely:

- **Inflammatory polyps** arise in the setting of chronic inflammatory bowel disease and are non-neoplastic — there is no history of IBD here.
- **Hamartomatous polyps** are characterized by disorganized overgrowth of tissues native to the area and are associated with syndromes such as Peutz-Jeghers or juvenile polyposis. They do not exhibit tubular adenomatous architecture.[6]
- **Colorectal cancer** would require invasion through the muscularis mucosae. The biopsy describes a polyp with tubular architecture, not invasive carcinoma.[2]

The clinical context — a 62-year-old man with positive fecal occult blood, family history of colorectal cancer, and a solitary colonic polyp — is classic for an adenomatous polyp, which is the recognized precursor lesion in the adenoma-carcinoma sequence.[3][7]

Would you like to explore the recommended surveillance intervals after polypectomy based on adenoma characteristics?

Relevant images

(CONTENT OMITTED)

References

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Question 842

A 20-year-old male college student presents to the emergency room at 4 AM in the morning with complaints of abdominal cramps, nausea, vomiting, and diarrhea for the past 2 hours. He was studying for his exams last night when he became hungry and ate some food from the afternoon after heating it for a while. He says that his symptoms began an hour after he ate the food. His temperature is 37°C (98.6°F), respiratory rate is 15/min, pulse is 106/min, and blood pressure is 90/78 mm Hg. A physical examination is within normal limits except for signs of dehydration. What is the most likely diagnosis?

Answer Choices:

(A) Cryptosporidiosis
(B) C. difficile colitis
(C) Bacillus cereus infection
(D) Norovirus infection

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/d175e351-9c3a-4346-ae05-c7a9e0a5daef

OpenEvidence Explanation

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The most likely diagnosis is **C. Bacillus cereus infection**. The clinical scenario is classic for *B. cereus* emetic-type food poisoning: a young man reheats leftover food, develops **nausea, vomiting, abdominal cramps, and diarrhea within 1 hour** of ingestion, is afebrile, and shows signs of dehydration from fluid losses.

***Key distinguishing features pointing to* B. cereus:**

- **Very short incubation period (~1 hour):** Preformed toxin-mediated food poisoning from *B. cereus* (emetic type, cereulide toxin) or *Staphylococcus aureus* characteristically presents within 1–6 hours of ingestion, far shorter than infectious causes. The emetic syndrome of *B. cereus* can present as early as 30 minutes to 6 hours after exposure.[1][2][3][4]
- **Reheated leftover food:** *B. cereus* spores survive cooking and germinate when food is left at room temperature. **Rice dishes are the food most commonly implicated** in *B. cereus* outbreaks (50% of cases), and reheated leftovers are the classic vehicle. The scenario of a college student reheating afternoon leftovers is a textbook presentation.[5]
- **Afebrile with no systemic signs of infection:** The absence of fever (37°C) is consistent with a toxin-mediated intoxication rather than an invasive infection.[2]

Why the other options are less likely:

- **A. Cryptosporidiosis** — Caused by the parasite *Cryptosporidium*; incubation period is typically 7–10 days, and it presents with prolonged watery diarrhea, particularly in immunocompromised patients. The acute 1-hour onset rules this out.
- *B. C. difficile colitis* — Occurs in the setting of recent antibiotic use, hospitalization, or healthcare exposure. There are no such risk factors here, and the onset is far too rapid.[6]
- **D. Norovirus infection** — Incubation period is typically 24–48 hours (median ~32 hours), much longer than the 1-hour onset described here. Norovirus is also typically associated with person-to-person spread or contaminated water/shellfish, not reheated leftovers.[1]

The diagnosis of *B. cereus* food poisoning is made clinically based on the characteristic history; laboratory confirmation requires demonstration of toxin

in the implicated food, which is rarely pursued.[2][7] Management is supportive, focusing on **aggressive IV fluid resuscitation** given the tachycardia (106/min) and hypotension (90/78 mmHg) indicating significant dehydration. Most cases resolve within 1–2 days.[2]

Is there any additional information about the specific type of food consumed (e.g., rice) or whether other individuals who ate the same food are also symptomatic?

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Question 843

A 79-year-old woman presents to her physician complaining of a persistent non-productive cough and dyspnea after contracting a cold in the past month. She describes herself as being “generally healthy” before the cold started. Medical history includes hypertension and hyperlipidemia. The patient takes hydrochlorothiazide, lisinopril, and atorvastatin. Her parents are both deceased. She does not smoke and only drinks alcohol occasionally. During a review of symptoms, she described a month-long trip to St. Louis, Missouri, to visit family. At the physician’s office, her temperature is 37.0°C (98.6°F), pulse is 82/min, respirations are 20/min, and blood pressure is 130/82 mm Hg. A focused chest exam reveals mild crepitus on the right side. A chest X-ray shows a cavitary lesion in the right lung which is confirmed on chest computed tomography (CT). A lung biopsy is performed to rule out cancer and reveals necrotic granulomatous inflammation with oval yeast in macrophages. Which of the following is the most likely diagnosis?

Answer Choices:

(A) Blastomycosis
(B) Sporotrichosis
(C) Histoplasmosis
(D) Onychomycosis

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/860d696c-c801-4057-b5ca-d6635476023b

OpenEvidence Explanation

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The most likely diagnosis is **C. Histoplasmosis**.

The combination of clinical and histopathological findings in this case is classic for pulmonary histoplasmosis:

- **Geographic exposure**: St. Louis, Missouri, is located in the Ohio and Mississippi River valleys, which is the primary endemic region for *Histoplasma capsulatum*.[1][2]
- **Histopathology**: The biopsy finding of **small oval yeast within macrophages** (intracellular) with necrotic granulomatous inflammation is pathognomonic for histoplasmosis. *Histoplasma* characteristically appears as 2–4 μm oval yeasts found inside phagocytic cells, with strong staining on GMS or PAS.[1][3][4]
- **Clinical presentation**: Persistent non-productive cough and dyspnea following a respiratory illness, with a cavitary lung lesion on imaging, is consistent with pulmonary histoplasmosis.[1]

The following figure from an NEJM review illustrates the distinctive tissue forms of *Histoplasma* — note Panel D showing small oval yeasts packed within a monocyte, which corresponds to the biopsy findings described in this case.

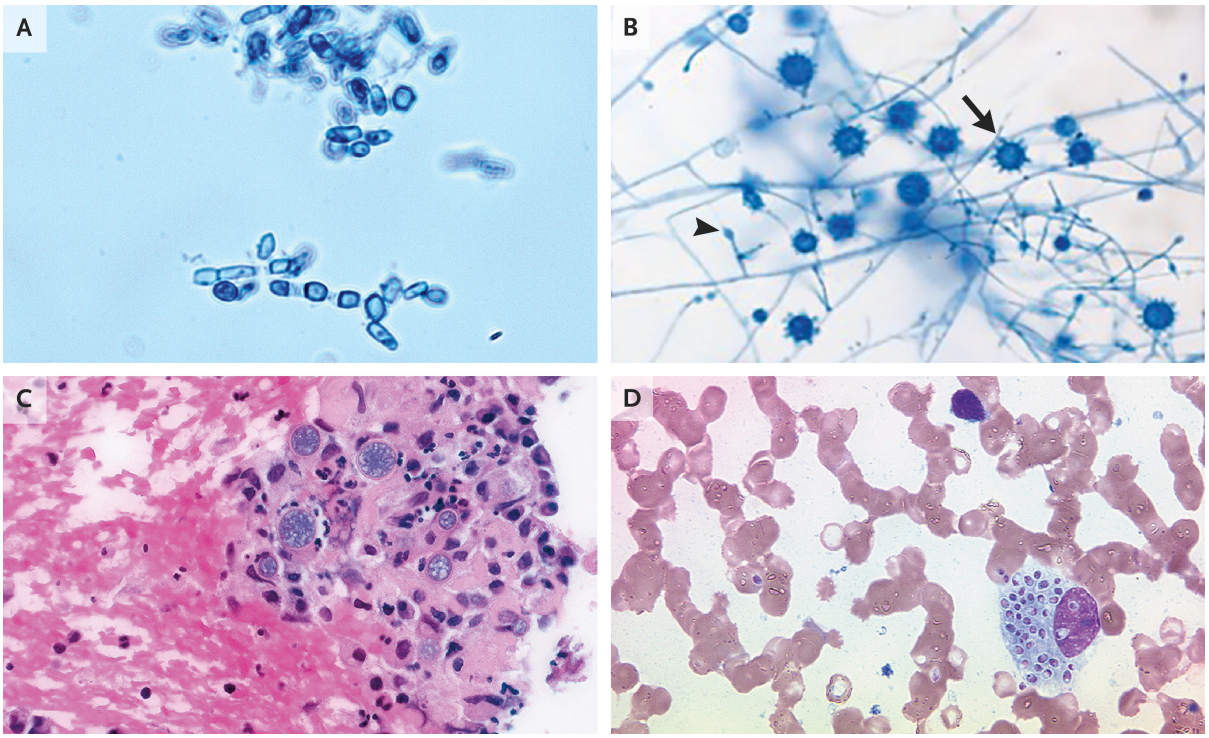


Figure 1. Appearance of Mycelial and Tissue Forms of Histoplasma and Coccidioides.

Used under license from The New England Journal of Medicine.

Why the other options are incorrect:

- **A. Blastomycosis** — *Blastomyces* appears as large (8–15 µm) broad-based budding yeast, not small oval intracellular yeast.[5]
- **B. Sporotrichosis** — *Sporothrix* typically causes lymphocutaneous disease (subcutaneous nodules along lymphatic channels), not primary pulmonary cavitary disease with intracellular oval yeast.[5]
- **D. Onychomycosis** — This is a superficial fungal infection of the nails, not a pulmonary disease.

Would you like to explore the treatment approach for pulmonary histoplasmosis, including when itraconazole versus amphotericin B is indicated based on disease severity?

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Question 844

A 14-year-old girl comes to the physician because she has not yet had her period. She is at the 10th percentile for height and 25th percentile for weight. Examination shows a broad chest with widely spaced nipples, a low posterior hairline, forearms angled 20° away from the body when fully extended, and shortened fourth metacarpals bilaterally. Sexual development is Tanner stage 1. Which of the following statements about this patient's fertility is most accurate?

Answer Choices:

(A) Pregnancy success rate with donor oocytes is similar to patients with primary ovarian failure
(B) Administration of gonadotropins will increase the chances of conceiving
(C) Impaired tubal ciliary function will prevent natural fertilization
(D) The majority of patients become pregnant without medical assistance

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/8cae582c-bb4d-4b33-a96b-affbb0778ed0

OpenEvidence Explanation

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The answer is **A. Pregnancy success rate with donor oocytes is similar to patients with primary ovarian failure**.

This clinical presentation — short stature, broad chest with widely spaced nipples (shield chest), low posterior hairline, increased carrying angle (cubitus valgus), shortened fourth metacarpals, and Tanner stage 1 at age 14 — is classic for **Turner syndrome** (45,X). The key fertility considerations for each answer choice are as follows:

Why A is correct: Turner syndrome causes **gonadal dysgenesis** with accelerated oocyte loss, resulting in streak gonads and primary ovarian insufficiency (POI). Because the uterus is structurally present (it develops from Müllerian ducts, which are not X-chromosome dependent), these patients can carry pregnancies using **donor oocytes** via IVF. Pregnancy rates with oocyte donation in Turner syndrome are reported at **17–40% per embryo transfer**, which is comparable to success rates seen in other causes of primary ovarian failure.[1] The uterus, while often hypoplastic, can be primed with estrogen and progesterone to support implantation.

Why the other options are incorrect:

- **B (Gonadotropins will increase chances of conceiving):** In classic 45,X Turner syndrome, the ovaries are replaced by fibrous streak tissue with essentially no follicles remaining. Gonadotropin administration cannot stimulate follicles that do not exist. Only 2–8% of Turner syndrome patients achieve spontaneous pregnancy, and these are predominantly patients with mosaic karyotypes (especially 45,X/46,XX) who retain some ovarian function.[2][3]
- **C (Impaired tubal ciliary function):** Turner syndrome does not involve ciliary dysfunction. The fallopian tubes are structurally and functionally normal. Ciliary dysfunction causing infertility is characteristic of conditions like primary ciliary dyskinesia (Kartagener syndrome), not Turner syndrome.
- **D (Majority become pregnant without assistance):** This is incorrect. The vast majority of Turner syndrome patients are infertile. Spontaneous pregnancy rates are only 1.3–5.6% overall, and even in the most favorable mosaic karyotype (45,X/46,XX), natural conception occurs in only 15–48%. [3][4][5]

Would you like to explore the cardiovascular screening recommendations and pregnancy-related risks (particularly aortic dissection) that must be addressed before any pregnancy attempt in Turner syndrome patients?

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Question 845

An investigator is studying traumatic knee joint injuries in college athletes. Images and tissue samples are collected from 4 athletes with cartilaginous injury and 4 athletes with bone fractures. After 8 weeks, the athletes with bone fractures show almost complete resolution, while the athletes with cartilaginous injuries show only minimal signs of healing. The investigator hypothesizes that this is due to the absence of progenitor cells for matrix regeneration. Transplant of which of the following tissues would most likely promote healing in the group with cartilaginous injury?

Answer Choices:

(A) Perichondrium
(B) Proteoglycans
(C) Osteoblasts
(D) Mature chondrocytes

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/3aab4dac-cd2a-418e-903d-a9fc2c1e1324

OpenEvidence Explanation

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The answer is **A. Perichondrium**.

The question centers on why cartilage heals poorly compared to bone and what tissue could supply the missing progenitor cells. Cartilage is **avascular** and contains only sparsely distributed mature chondrocytes (~5% of tissue volume) that have very limited proliferative capacity, which accounts for its poor intrinsic healing.[1][2] Bone, by contrast, has a rich blood supply and periosteum containing osteoprogenitor cells, enabling robust repair.

Why perichondrium is the correct answer:

The **perichondrium** is the dense connective tissue that surrounds cartilage and serves as a niche for **chondrogenic progenitor (stem) cells** — the very cells the investigator hypothesizes are absent at the injury site.[3][4] Key evidence includes:

- In a mouse rib cartilage model, cartilage regeneration occurred **only when the perichondrium was intact**; label-retaining progenitor cells within the perichondrium gave rise to new chondrocytes.[5]
- Perichondrium transplanted into full-thickness articular cartilage defects in rats differentiated into **hyaline cartilage** with Col2a1-positive chondrocytes and proteoglycan-rich matrix.[6]
- The inner (cambium) layer of the perichondrium specifically provides cells for new cartilage formation.[7]

Why the other options are incorrect:

- **B. Proteoglycans** — These are extracellular matrix components, not cells. They cannot serve as progenitor cells for matrix regeneration.
- **C. Osteoblasts** — These are bone-forming cells and would produce bone, not cartilage matrix.
- **D. Mature chondrocytes** — These are terminally differentiated cells with very limited proliferative capacity and poor ability to regenerate cartilage tissue. The question specifically asks about progenitor cells, which mature chondrocytes are not.[1][8]

Would you like to explore the specific mechanisms by which perichondrial progenitor cells differentiate into functional chondrocytes and the clinical applications of perichondrial grafting?

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Question 846

A 35-year-old woman comes to the physician for the evaluation of increasing weakness and numbness of the upper extremities for 5 days. During the past 2 days, she has had urinary incontinence not related to sneezing or laughing. Last summer, she had weakness and numbness of her right lower extremity that was worse when she was outside; she regained her strength 3 weeks later. She has no history of serious illness. She has had 10 male sexual partners in her lifetime and uses condoms inconsistently. Vital signs are within normal limits. Examination shows an impaired tandem gait. There is mild spasticity and muscle strength is decreased in both upper extremities. Deep tendon reflexes are 4+ bilaterally. The abdominal reflex is absent. Muscle strength in the right lower extremity is mildly decreased. Sensation to vibration and fine touch is decreased over the upper extremities. Which of the following is the most appropriate next step in diagnosis?

Answer Choices:

(A) Muscle biopsy
(B) Rapid plasma reagin test
(C) MRI of the brain and spine
(D) Lumbar puncture

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/4043aa09-47d0-4c9d-a951-967c0ae7022f

OpenEvidence Explanation

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The correct answer is **C. MRI of the brain and spine**.

This presentation is classic for **multiple sclerosis (MS)**: a young woman with relapsing-remitting neurological deficits disseminated in space (upper extremities, lower extremity, bladder) and time (prior episode last summer, current episode), with upper motor neuron signs (spasticity, hyperreflexia, absent abdominal reflex), posterior column dysfunction (decreased vibration and fine touch), and Uhthoff phenomenon (worsening with heat/being outside). **MRI of the brain and spine is the most appropriate initial diagnostic step** because it is the most sensitive paraclinical tool for detecting demyelinating lesions and is recommended in all patients in whom MS is being considered.[1][2][3]

Why MRI over the other options:

- **MRI of the brain and spine** is abnormal in nearly all patients with established MS and in >80% of patients with clinically isolated syndrome who go on to develop MS. It can demonstrate dissemination in space (lesions in periventricular, juxtacortical, infratentorial, and spinal cord regions) and dissemination in time (simultaneous gadolinium-enhancing and non-enhancing lesions). The ACR Appropriateness Criteria support MRI of the brain and spinal cord as the initial imaging modality for suspected CNS demyelinating disease.[1][2][3][4]

- **Lumbar puncture (D)** can provide supportive evidence (CSF-specific oligoclonal bands), but CSF examination is not usually necessary in patients with typical clinical and MRI findings and is considered more invasive. It plays a supplementary role when MRI findings are insufficient or atypical.[2]

- **RPR test (B)** — while neurosyphilis can mimic MS and should be excluded (especially given this patient's sexual history), syphilis testing is part of the differential diagnosis workup rather than the primary diagnostic step. The clinical presentation here is far more consistent with MS than neurosyphilis.

- **Muscle biopsy (A)** is not indicated, as this presentation reflects an upper motor neuron/central nervous system process, not a primary muscle disorder.

Would you like to explore how the 2024 revisions to the McDonald Criteria have changed the diagnostic approach to MS, including the addition of the optic nerve as a fifth anatomical location and the role of central vein sign?

Relevant images

(CONTENT OMITTED)

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Question 847

A 37-year-old woman presents to your office with heartburn. Following an extensive workup, you diagnose her with a duodenal ulcer secondary to H. pylori infection. You prescribe triple therapy of omeprazole, clarithromycin, and amoxicillin. Which of the following best describes the mechanism of action of omeprazole?

Answer Choices:

(A) Parasympathetic inhibition
(B) Reversible block of H2 receptors
(C) Inhibition of primary active transport
(D) Inhibition of 50S ribosomal subunit

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/fd6a874d-5a85-407c-b8db-e4ede509f05a

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OpenEvidence Explanation

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The correct answer is **C. Inhibition of primary active transport**.

Drug Label

According to the FDA-approved drug label, omeprazole belongs to a class of antisecretory compounds (substituted benzimidazoles) that suppress gastric acid secretion by **specific inhibition of the H^+ /K^+ ATPase enzyme system** at the secretory surface of the gastric parietal cell.[1][2] Because this enzyme system is regarded as the acid (proton) pump within the gastric mucosa, omeprazole is characterized as a gastric acid-pump inhibitor — it blocks the final step of acid production. This effect is dose-related and leads to inhibition of both basal and stimulated acid secretion irrespective of the stimulus.[1][2]

The H^+ /K^+ ATPase is a **primary active transporter** — it uses energy from ATP hydrolysis to pump H^+ ions into the gastric lumen in exchange for K^+ ions, generating the acidic environment of the stomach. Omeprazole irreversibly inhibits this pump by forming covalent disulfide bonds with cysteine residues on the enzyme after being activated in the acidic environment of the secretory canaliculus.[3][4] This is why the correct answer is **inhibition of primary active transport** (option C).

The following figure from Maton (1991) in the NEJM illustrates how omeprazole is selectively activated in the acidic secretory canaliculus and irreversibly binds to the H^+ /K^+ ATPase:

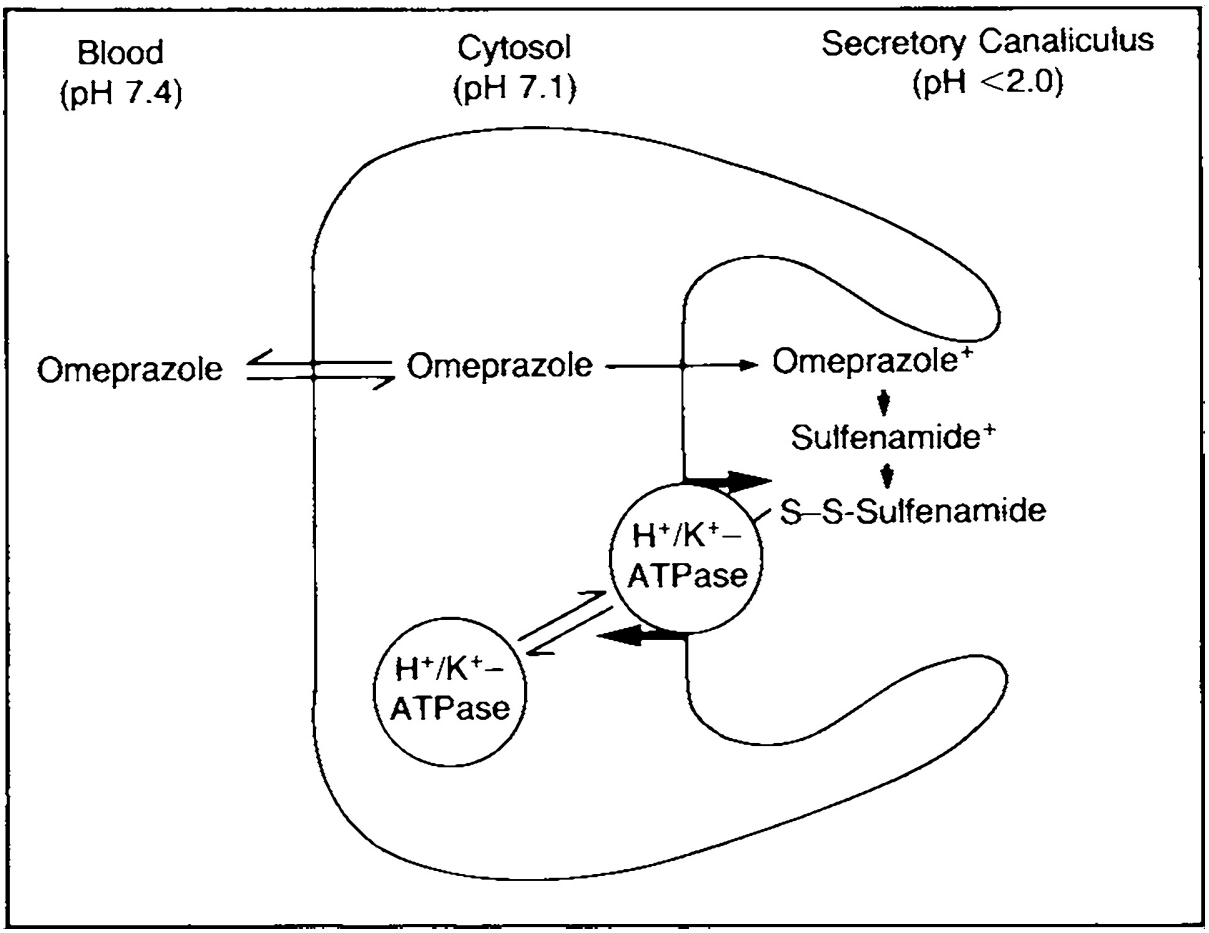


Figure 1. Schematic Diagram of the Action of Omeprazole on a Gastric Parietal Cell.

Used under license from The New England Journal of Medicine.

Why the other options are incorrect:

- **A. Parasympathetic inhibition** — This describes the mechanism of anticholinergic agents (e.g., pirenzepine), which block muscarinic M3 receptors on parietal cells.
- **B. Reversible block of H2 receptors** — This describes H2-receptor antagonists (e.g., ranitidine, famotidine), which block histamine-mediated acid secretion at the basolateral membrane.[6]
- **D. Inhibition of 50S ribosomal subunit** — This describes the mechanism of **clarithromycin**, the macrolide antibiotic included in the same triple therapy regimen, not omeprazole.

Would you like to explore the comparative efficacy of different H. pylori eradication regimens, including bismuth quadruple therapy versus standard triple therapy?

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Question 848

A 47-year-old woman comes to the emergency department because of worsening pain, discoloration, and swelling of her right hand. Two days ago, she was camping outdoors in Texas with her two young children. She was awoken in the middle of the night by “something crawling on my hand.” The following morning, she saw a wound on her hand that was initially painless, but over the next several hours she noticed reddening and blistering. Yesterday, the lesion turned blue with a blackish discoloration at the center. Her temperature is 38°C (100.4°F), pulse is 83/min, and blood pressure is 128/84 mm Hg. Physical examination shows a bluish plaque with a central area of necrosis surrounded by a rim of erythema at the dorsum of the right hand. Which of the following animals is most likely responsible for the patient's symptoms?

Answer Choices:

(A) Diamondback rattlesnake
(B) Brown recluse spider
(C) Striped bark scorpion
(D) Deer tick

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/a47c1b7c-fd07-47d3-a12b-7519078b82b8

OpenEvidence Explanation

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The answer is **B. Brown recluse spider**.

The clinical presentation is classic for **loxoscelism** (brown recluse spider envenomation). Several features point to this diagnosis:

- **Initially painless bite occurring at night** — brown recluse spiders are nocturnal, and bites are often unwitnessed, with patients frequently unaware of the bite at the time it occurs.[1][2]
- **Progression from painless to erythema, blistering, then blue discoloration with central necrosis** — this describes the pathognomonic **"red, white, and blue" sign**, representing concentric zones of erythema, ischemia, and necrosis that typically evolves over 2–3 days. Necrosis usually becomes evident after approximately 72 hours.[1][3]
- **Geographic and environmental context** — *Loxosceles reclusa* is endemic to the **Southern Midwest and Southwestern United States**, including Texas. Camping outdoors increases exposure risk.[2]
- **Low-grade fever** — mild systemic symptoms including fever can accompany cutaneous loxoscelism.[4]

The following figure from the NEJM illustrates the characteristic temporal progression of a brown recluse spider bite, including the evolution through erythema, necrosis, and eventual healing.



Figure 1.

Used under license from The New England Journal of Medicine.

Why not the other options:

- **Diamondback rattlesnake** — snake envenomation causes immediate, severe pain with rapid swelling and ecchymosis; the bite would not be initially painless, and fang marks would be visible.
- **Striped bark scorpion** — causes intense localized pain and muscle cramping at the sting site, not a painless bite progressing to necrosis.[6]
- **Deer tick** — tick bites produce erythema migrans (an expanding erythematous patch, often with central clearing), not necrotic ulceration with blue discoloration.[7][8]

Would you like to explore the current evidence-based management of brown recluse spider bites, including the role of dapsone and wound care strategies?

References

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Question 853

A 22-year-old man is brought to the emergency department by police after he was found undressing himself outside in 110°F weather. The patient refuses to answer any questions as he suspects that his care team is spying on him. The patient recently started college and has presented to the emergency department once before for polysubstance intoxication. The patient attempts to assault a nurse, is restrained, and given diphenhydramine and haloperidol. When the patient is able to be examined, he is somnolent and non-responsive. His temperature is 104°F (40°C), blood pressure is 147/98 mmHg, pulse is 120/min, respirations are 17/min, and oxygen saturation is 98% on room air. He does not comply with any commands, and it is not possible to freely manipulate his extremities due to rigidity. His mucous membranes are dry. Which of the following is the most likely diagnosis?

Answer Choices:

(A) Catatonic schizophrenia
(B) Heat stroke
(C) Neuroleptic malignant syndrome
(D) Oversedation

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/e50dd54a-1857-4ee6-84b1-41702278a797

OpenEvidence Explanation

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The most likely diagnosis is **C. Neuroleptic malignant syndrome (NMS)**.

This patient demonstrates the classic tetrad of NMS following administration of **haloperidol**, a first-generation antipsychotic and potent dopamine receptor blocker:

1. **Exposure to a dopamine-blocking agent** — haloperidol was administered in the ED
2. **Hyperthermia** — temperature of 104°F (40°C)
3. **Severe muscular rigidity** — extremities cannot be freely manipulated ("lead-pipe" rigidity)
4. **Altered mental status** — somnolent and non-responsive, consistent with the catatonic stupor described in NMS[1][2]

Additionally, the patient exhibits **autonomic instability** with hypertension (147/98 mmHg) and tachycardia (120/min), both well-described features of NMS. [1]

Why not the other options?

- **A. Catatonic schizophrenia** — While the patient's paranoia and behavioral disturbance suggest an underlying psychotic disorder, catatonia alone does not explain the acute onset of hyperthermia and autonomic instability temporally linked to haloperidol administration.
- **B. Heat stroke** — Although the 110°F environmental exposure is a risk factor, heat stroke typically presents with **hot, dry skin** rather than rigidity, and the temporal relationship to haloperidol administration makes NMS more likely. Notably, both haloperidol and diphenhydramine impair thermoregulation, which may have contributed to the hyperthermia, but the **lead-pipe rigidity** is the distinguishing feature pointing toward NMS rather than heat stroke.[1][3][4][5]

- **D. Oversedation** — Sedation from diphenhydramine and haloperidol could explain somnolence, but oversedation does not cause high fever, severe rigidity, or autonomic instability.

  "The typical presentation of neuroleptic malignant syndrome is dysautonomia, particularly tachycardia and rapidly fluctuating hypertensive or hypotensive blood pressure; temperature elevation to 40°C or higher; delirium that in the severe form is catatonia; and increased muscle tone."

  —Eelco F.M. Wijdicks, M.D., Ph.D. et al., Mayo Clinic Hospital. Neuroleptic Malignant Syndrome. N Engl J Med. September 26, 2024.

  Used under license from The New England Journal of Medicine.

The key distinguishing feature in this vignette is the **rigidity** — this finding, in the context of recent dopamine-blocking drug exposure, is the cardinal feature that clinches the NMS diagnosis over heat stroke or simple oversedation.[1][2] Immediate management includes discontinuing the offending agent, aggressive supportive care, and consideration of dantrolene or bromocriptine in severe cases.[1][6]

Is there anything about the management approach or workup priorities for this patient that would be helpful to discuss further?

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Question 857

A 71-year-old woman comes to the physician for evaluation of a pigmented lesion on her left foot. She has had decreased appetite and a 6-kg (13-lb) weight loss in the past 2 months. Physical examination shows that on the left medial ankle there is a 2-cm reddish-black nodule with a verrucous surface. A full-thickness excisional biopsy of the lesion shows S100-protein-positive epithelioid cells. A subsequent CT scan of the chest, abdomen, and pelvis shows metastases to the liver; a diagnosis of metastatic melanoma is made. Chemotherapy with aldesleukin is initiated. Which of the following is the mechanism of action for this drug?

Answer Choices:

(A) Stimulating release of acute-phase reactants
(B) Stimulating antigen-processing cells
(C) Activating natural killer cells and cytotoxic T cells
(D) Supporting growth of bone marrow stem cells

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/86435975-917e-4ac8-8184-82dc7b0ad237

OpenEvidence Explanation

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The correct answer is **C. Activating natural killer cells and cytotoxic T cells**.

Aldesleukin (Proleukin) is a recombinant form of **interleukin-2 (IL-2)**, classified as a lymphocyte growth factor. Per the FDA label, its mechanism of action involves enhancement of lymphocyte mitogenesis and cytotoxicity, **induction of killer cell activity (lymphokine-activated killer [LAK] and natural killer [NK] cells)**, and stimulation of interferon-gamma production.[1] It acts by stimulating and enhancing **T-cell and NK cell proliferation and cytotoxic activity**, thereby triggering release of cytokines such as IFN-γ and TNF from activated lymphocytes.[2]

IL-2 mediates its effects through binding to IL-2 receptors: the intermediate-affinity receptor (IL-2Rβγ) found on activated effector T cells and NK cells, and the high-affinity receptor (IL-2Rαβγ) expressed primarily by regulatory T cells.[3] Upon receptor engagement, downstream signaling through JAK-STAT, PI3K-AKT-mTOR, and MAPK pathways promotes immune cell activation and proliferation.[4]

The following figure illustrates the IL-2 receptor types and their downstream signaling pathways:

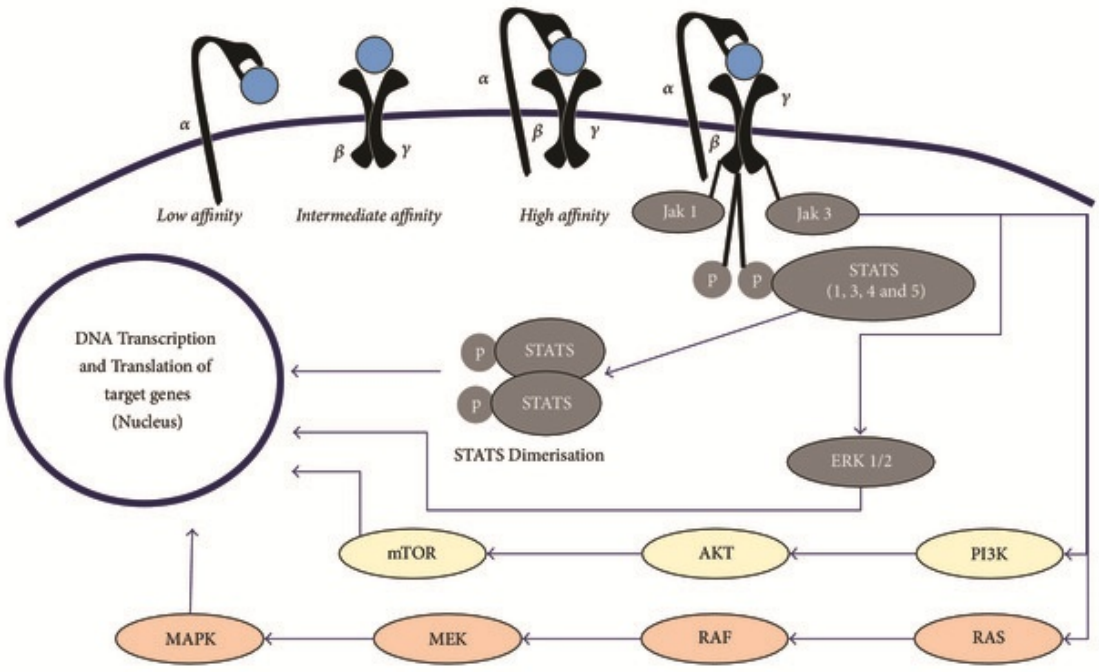


Figure 1. Showing three different types of IL-2 receptors.

Regarding the other answer choices:

- **A (Stimulating release of acute-phase reactants)** — This describes the action of IL-6, not IL-2.
- **B (Stimulating antigen-processing cells)** — While IL-2 can indirectly enhance antigen presentation via IFN-γ production, this is not its primary mechanism; this description better fits IFN-γ or GM-CSF.[5]
- **D (Supporting growth of bone marrow stem cells)** — This describes colony-stimulating factors (e.g., G-CSF, GM-CSF) or IL-3, not IL-2.

Would you like to explore how current immunotherapy approaches (checkpoint inhibitors, TIL therapy) have largely supplanted high-dose IL-2 in the treatment of metastatic melanoma?

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Question 859

A 58-year-old male presents with an acutely elevated blood pressure of 220/140 mmHg. The patient complains of a headache and chest pain, and he has been vomiting for the last several hours. Physical exam demonstrates papilledema and a depressed level of consciousness. To treat this patient's hypertensive emergency, he is started on an IV medication commonly used in this situation. The agent exerts its effect by releasing nitric oxide as a metabolite, which subsequently activates guanylate cyclase and increases production of cGMP in vascular smooth muscle. Which of the following clinical effects would be expected from administration of this medication?

Answer Choices:

(A) Decreased cardiac contractility
(B) Increased left ventricular end-diastolic pressure
(C) Decreased stroke volume
(D) Decreased pulmonary capillary wedge pressure

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/3bfb0252-016f-4e7d-b5ce-09222f7cf43e

OpenEvidence Explanation

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The correct answer is **D. Decreased pulmonary capillary wedge pressure**.

The medication described is **sodium nitroprusside**, which releases nitric oxide (NO), activates guanylate cyclase, and increases cGMP in vascular smooth muscle — leading to both arterial and venous vasodilation.[1]

Why D is correct: Sodium nitroprusside is more active on veins than arteries (though less selectively so than nitroglycerin). Venodilation promotes peripheral pooling of blood and **decreases venous return** to the heart, thereby **reducing left ventricular end-diastolic pressure and pulmonary capillary wedge pressure** (preload).[1][2] This is explicitly stated in the FDA label and confirmed in hemodynamic studies.[3]

Why the other options are incorrect:

- **A (Decreased cardiac contractility):** Nitroprusside does not have a direct negative inotropic effect. Studies comparing it with nifedipine showed that peak dP/dt was unchanged with nitroprusside, confirming no reduction in contractility.[3]
- **B (Increased left ventricular end-diastolic pressure):** The opposite occurs — LVEDP decreases due to venodilation and reduced preload.[1][2]
- **C (Decreased stroke volume):** In patients with elevated afterload (as in hypertensive emergency), afterload reduction with nitroprusside typically increases or maintains stroke volume by facilitating ventricular ejection. In heart failure patients, stroke volume index increased with nitroprusside.[2][3]

In summary, nitroprusside acts as a balanced vasodilator that reduces both preload and afterload, with the net hemodynamic effect of decreased filling pressures (PCWP and LVEDP), decreased systemic vascular resistance, and maintained or improved cardiac output.[4]

Would you like to explore the comparative hemodynamic profiles of different IV antihypertensives used in hypertensive emergencies (e.g., nitroprusside vs. nicardipine vs. clevidipine)?

References

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Question 864

A 26-year-old man with no significant past medical history presents to the ED following a motor vehicle accident. Vital signs on presentation are T 99.0 F, BP 100/60 mmHg, HR 125 bpm, RR 16/min, SpO2 98% on room air. He complains of extreme abdominal pain worse in the left upper quadrant which has worsened over the past 30 minutes. Exam demonstrates abdominal wall rigidity, involuntary guarding, and tenderness on light percussion. Bedside sonography shows evidence for hemoperitoneum. Despite administering more intravenous fluids, repeat vitals are T 98.9 F, BP 82/50 mm hg, HR 180 bpm, RR 20/min, SpO2 97% on room air. Which of the following is the best next step?

Answer Choices:

(A) Normal saline bolus and re-evaluation of hemodynamics after infusion
(B) CT abdomen and pelvis
(C) Morphine
(D) Exploratory laparotomy

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/6ffc7ef7-9ab2-467d-a57b-9fec13fe1998

OpenEvidence Explanation

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The best next step is **D. Exploratory laparotomy**.

This patient presents with blunt abdominal trauma (motor vehicle accident), a **positive FAST exam showing hemoperitoneum**, peritoneal signs (rigidity, involuntary guarding, percussion tenderness), and **hemodynamic instability that is worsening despite fluid resuscitation** (BP dropping to 82/50, HR escalating to 180). This is a classic indication for emergent surgical exploration.

Why the other options are incorrect:

- **A. Normal saline bolus and re-evaluation** — The patient has already received IV fluids and is a non-responder, with worsening hemodynamics. Continued crystalloid resuscitation without hemorrhage control will not address the underlying problem and delays definitive treatment. Every 3 minutes spent in the ED equates to a 1% increased mortality probability in this setting.[1]
- **B. CT abdomen and pelvis** — A hemodynamically unstable trauma patient with a positive FAST does not belong in the CT suite. CT is the gold standard for hemodynamically *stable* patients. Transporting this decompensating patient for imaging would delay life-saving intervention.[2][3][4]
- **C. Morphine** — While pain management is important, analgesics alone do not address the surgical emergency. Additionally, opioids can cause vasodilation and further hemodynamic compromise in a patient already in hemorrhagic shock.

Key principles supporting emergent laparotomy:

The Eastern Association for the Surgery of Trauma (EAST) Level 1 recommendation states that patients who are hemodynamically unstable or who have diffuse peritonitis after blunt abdominal trauma should be taken urgently for laparotomy.[5] The WSES guidelines similarly recommend that hemodynamically decompensated patients with a positive FAST should proceed directly to trauma laparotomy.[1] The left upper quadrant pain localizing to the spleen, combined with hemoperitoneum, is highly suggestive of splenic injury — the second most commonly injured organ in blunt abdominal trauma.[6]

Would you like to explore the damage-control surgery and resuscitation strategies used during emergent laparotomy for hemorrhagic shock?

References

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Question 865

A 74-year-old man undergoes an open cholecystectomy. Surgery is performed under general anesthesia for which the patient is intubated with an endotracheal tube. Directly following the procedure, his temperature is 37°C (98.6°F), pulse is 80/min, and blood pressure is 110/80 mm Hg. He is extubated as soon as he showed signs of alertness. Five minutes later, he becomes unresponsive. He has type 2 diabetes mellitus, coronary artery disease, and hypertension. He underwent stenting of the right coronary artery 10 years ago. He smoked one pack of cigarettes daily for 40 years but quit 2 weeks ago for surgery. He drinks one to two beers daily. His current medications include metformin, enalapril, aspirin, atorvastatin, and a multivitamin. His temperature is 37°C (98.6°F), pulse is 102/min, respirations are 20/min, and blood pressure is 130/80 mm Hg. Pulse oximetry shows an oxygen saturation of 73%. He is put on a non-rebreather mask with an FiO2 of 100%. Three minutes later, he is still unresponsive. His arterial blood gas analysis shows:
pH 7.32
PCO2 33 mm Hg
PO2 73 mm Hg
HCO3 22 mEq/L
O2 saturation 73%
Which of the following is the best next step in the management of this patient?

Answer Choices:

(A) Perform tracheostomy
(B) Continue using the non-rebreather mask
(C) Reintubate
(D) Start BiPAP

Correct Answer:

(C)

OpenEvidence Response:

> (C) ✓

OpenEvidence Link: https://openevidence.com/ask/893d99fa-e79b-45a6-82f4-983928718a2c

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OpenEvidence Explanation

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The best next step is **C. Reintubate** the patient.

This patient has developed acute postextubation respiratory failure with **severe hypoxemia (SpO2 73%)**, unresponsiveness, and failure to improve despite 3 minutes on a non-rebreather mask at 100% FiO2. The critical clue is the **discordance between PaO2 (73 mmHg) and SpO2 (73%)** — a PaO2 of 73 mmHg should correspond to an SpO2 of approximately 94%, not 73%. This discordance suggests either a significant left-shift issue (e.g., methemoglobinemia or carboxyhemoglobinemia from his 40-pack-year smoking history) or, more practically for this question, that the patient has refractory hypoxemia unresponsive to supplemental oxygen, indicating a large intrapulmonary shunt (e.g., from atelectasis or aspiration).

Why reintubation is correct:

- The patient is **unresponsive** — this alone is an indication for definitive airway management, as the patient cannot protect the airway.[1][2]
- Predefined criteria for immediate reintubation in clinical trials include respiratory failure with loss of consciousness, SpO2 <90% despite high FiO2, and hemodynamic instability.[2][3]
- The non-rebreather mask at 100% FiO2 has already failed to improve the patient after 3 minutes (option B is incorrect).
- Noninvasive ventilation (BiPAP, option D) used as rescue therapy in postextubation respiratory failure has been associated with **delayed**

intubation and increased mortality, particularly in patients who are not alert enough to cooperate. BiPAP also requires a cooperative, conscious patient to maintain a mask seal and protect the airway.[4]

- Tracheostomy (option A) is not an emergency airway intervention in this setting — it is an elective procedure performed after prolonged intubation or when long-term ventilation is anticipated.[1]

Key pathophysiology: After extubation, loss of positive end-expiratory pressure can lead to alveolar collapse and atelectasis, particularly in patients with risk factors such as advanced age, abdominal surgery, obesity, and smoking history. This creates intrapulmonary shunting and refractory hypoxemia.[5] This patient's 40-pack-year smoking history, recent abdominal surgery, and coronary artery disease place him at high risk for extubation failure.[5]

Would you like to explore the specific criteria and protocols used to identify patients at high risk for extubation failure before planned extubation?

Relevant images

(CONTENT OMITTED)

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Question 866

An 11-month-old male infant is brought to his pediatrician by his mother. She is concerned about his leg and his inability to stand. He was born vaginally to a 33-year-old woman (gravida 3, para 2) from an uncomplicated pregnancy at 39 weeks. He has met all developmental milestones and is up to date on all vaccinations. His mother explains that he can normally stand without help and can walk briefly on his own. However, he hit his right leg against a chair 2 days ago. The area became edematous and bruised overtime and the infant became unable to stand or crawl and cries when he puts weight on it. The mother denies any child abuse from her family or child care. The patient's vital signs are as follows: blood pressure 80/40 mm Hg, heart rate 137/min, respiratory rate 25/min, and temperature 36.7°C (97.0°F). His length and weight are both between the 15th and 25th percentile. On physical examination, blue-grayish discoloration of the sclerae are noted. Respiratory, cardiovascular, and abdominal examinations are within normal limits for his age. There is joint hypermobility and decreased tone in both upper and lower extremities. The patient's right calf appears slightly deformed, edematous, and warm to the tough. The patient begins to cry loudly when the physician palpates his leg. The patient's X-ray shows an incomplete fracture of the right tibial diaphysis. What is the most likely cause of the patient's symptoms?

Answer Choices:

(A) Insufficient production of procollagen type 1
(B) Mutation in the gene encoding fibrillin-1
(C) Defective collagen type 3
(D) Dysfunctional structure of laminins

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/573bc65f-0869-41c1-b6a1-10dfa53fafd7

OpenEvidence Explanation

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The correct answer is **A. Insufficient production of procollagen type 1**.

This clinical presentation — an infant with **blue-gray sclerae**, **joint hypermobility**, **decreased muscle tone**, and a **fracture from minimal trauma** (tibial diaphysis fracture from hitting a chair) — is classic for **osteogenesis imperfecta (OI) type I**, the mildest form of the disease. OI type I is caused by quantitative deficiency of structurally normal type I collagen, typically due to heterozygous mutations in the *COL1A1* gene that lead to haploinsufficiency and an approximately **50% reduction in procollagen type I synthesis**.[1][2]

Why the other options are incorrect:

- **B. Mutation in the gene encoding fibrillin-1** — This describes **Marfan syndrome**, which is characterized by tall stature, arachnodactyly, lens subluxation, and aortic root dilation, not bone fragility with blue sclerae.[3][4]
- **C. Defective collagen type 3** — This describes **vascular Ehlers-Danlos syndrome (EDS type IV)**, which presents with arterial rupture, organ perforation, and thin translucent skin, not fractures with blue sclerae.[4]
- **D. Dysfunctional structure of laminins** — Laminins are basement membrane glycoproteins. Laminin defects are associated with conditions such as congenital muscular dystrophy and certain forms of epidermolysis bullosa, not the constellation of blue sclerae, joint hypermobility, and bone fragility seen here.[5]

Key distinguishing features in this case supporting OI type I include blue-gray sclerae (a hallmark of type I OI), bone fracture from minor trauma, joint

hypermobility, and normal growth parameters — all consistent with the classic nondeforming form of OI.[1][6][7]

Would you like to explore the diagnostic workup and management of osteogenesis imperfecta in pediatric patients, including the role of genetic testing and bisphosphonate therapy?

Relevant images

(CONTENT OMITTED)

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Question 868

An 80-year-old man is brought to the emergency department because of fatigue and lightheadedness. He does not have chest pain, palpitations, or difficulty breathing. He has a history of hyperlipidemia, type 2 diabetes mellitus, hypertension, osteoarthritis, and asthma. Current medications include simvastatin, metformin, lisinopril, albuterol, and ibuprofen. His pulse is 48/min and blood pressure is 89/50 mm Hg. He responds slowly to questions but is oriented to person, place, and time. Examination shows dry mucous membranes. His lungs are clear to auscultation and bowel sounds are positive with no pulsatile masses or bruits. Pedal pulses are nonpalpable, distal extremities are cold, and capillary refill time is 4 seconds. An ECG shows left axis deviation, a Q wave in lead III, a constant PR interval of 0.15 seconds with every third P wave that is nonconducted, and a QRS interval of .09 seconds. Which of the following is the most appropriate next step in management?

Answer Choices:

(A) Dobutamine
(B) Norepinephrine
(C) Cardiac pacing
(D) Epinephrine

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/6c0f7990-6e34-4960-915d-5aef15be29a8

OpenEvidence Explanation

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The correct answer is **C. Cardiac pacing**.

This patient presents with symptomatic high-grade AV block (specifically **Mobitz type II second-degree AV block** with a 3:1 conduction pattern) causing hemodynamic compromise. The ECG findings — constant PR interval of 0.15 seconds with every third P wave nonconducted, narrow QRS (0.09 seconds), and left axis deviation — describe a fixed conduction ratio (3:1 block) with no progressive PR prolongation, consistent with Mobitz type II or high-grade AV block. The patient has significant hemodynamic instability: heart rate 48/min, blood pressure 89/50, altered mentation, cold extremities, and prolonged capillary refill — all signs of cardiogenic shock from bradycardia.

Why cardiac pacing is the best answer:

Per the AHA bradycardia algorithm, the standard initial pharmacologic intervention for symptomatic bradycardia is **atropine** — but atropine is not listed among the answer choices.[1][2] When atropine is ineffective or unavailable, the 2018 ACC/AHA/HRS guidelines recommend **temporary transvenous pacing** (Class IIa) for second-degree or third-degree AV block with hemodynamic compromise refractory to medical therapy.[3][4] Transcutaneous pacing may also be used as a bridge.[4] Given the severity of this patient's presentation (shock physiology with altered mental status), cardiac pacing is the most definitive and appropriate intervention among the options listed.

Why the other options are less appropriate:

- **Dobutamine (A):** While beta-adrenergic agonists may be considered (Class IIb) for AV block with hemodynamic compromise, dobutamine primarily increases contractility and is not the first-line choice for addressing the underlying conduction abnormality.[3][4]
- **Norepinephrine (B):** A vasopressor that raises blood pressure but does not reliably increase heart rate or improve AV conduction; it does not address the primary problem.

- **Epinephrine (D):** Can increase heart rate and is sometimes used as a temporizing measure, but in the setting of high-grade AV block with shock, cardiac pacing provides more reliable and definitive rate control.[1][2]

The ACC/AHA/HRS guidelines also note that high-grade AV block and Mobitz type II block are Class I indications for permanent pacing regardless of symptoms, given the risk of progression to complete heart block.[4][5]

Would you like to explore the distinguishing ECG features between Mobitz type I and type II second-degree AV block and their implications for management?

Relevant images

(CONTENT OMITTED)

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Question 870

A 41-year-old man presents to the clinic with the complaints of abdominal discomfort and cramping for the past 4 months. He also mentions that he has grossly bloody stool and most of the time an urge to defecate. He has a history of bulimia with laxative abuse several years ago. He admits having lost about 5 lb in the past month. His temperature is 37° C (98.6° F), respiratory rate is 15/min, pulse is 77/min, and blood pressure is 105/86 mm Hg. On physical examination, a mild conjunctival pallor is evident, and the rectum is erythematous, indurated, and tender. Colonoscopy demonstrates continuous mucosal lesions throughout the rectum to the hepatic flexure of the colon. What is the most likely diagnosis?

Answer Choices:

(A) Ulcerative colitis
(B) Celiac disease
(C) Irritable bowel syndrome
(D) Crohn's disease

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/0adf5cfc-bbdf-47df-b2ee-2918ef243f81

OpenEvidence Explanation

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The answer is **A. Ulcerative colitis**.

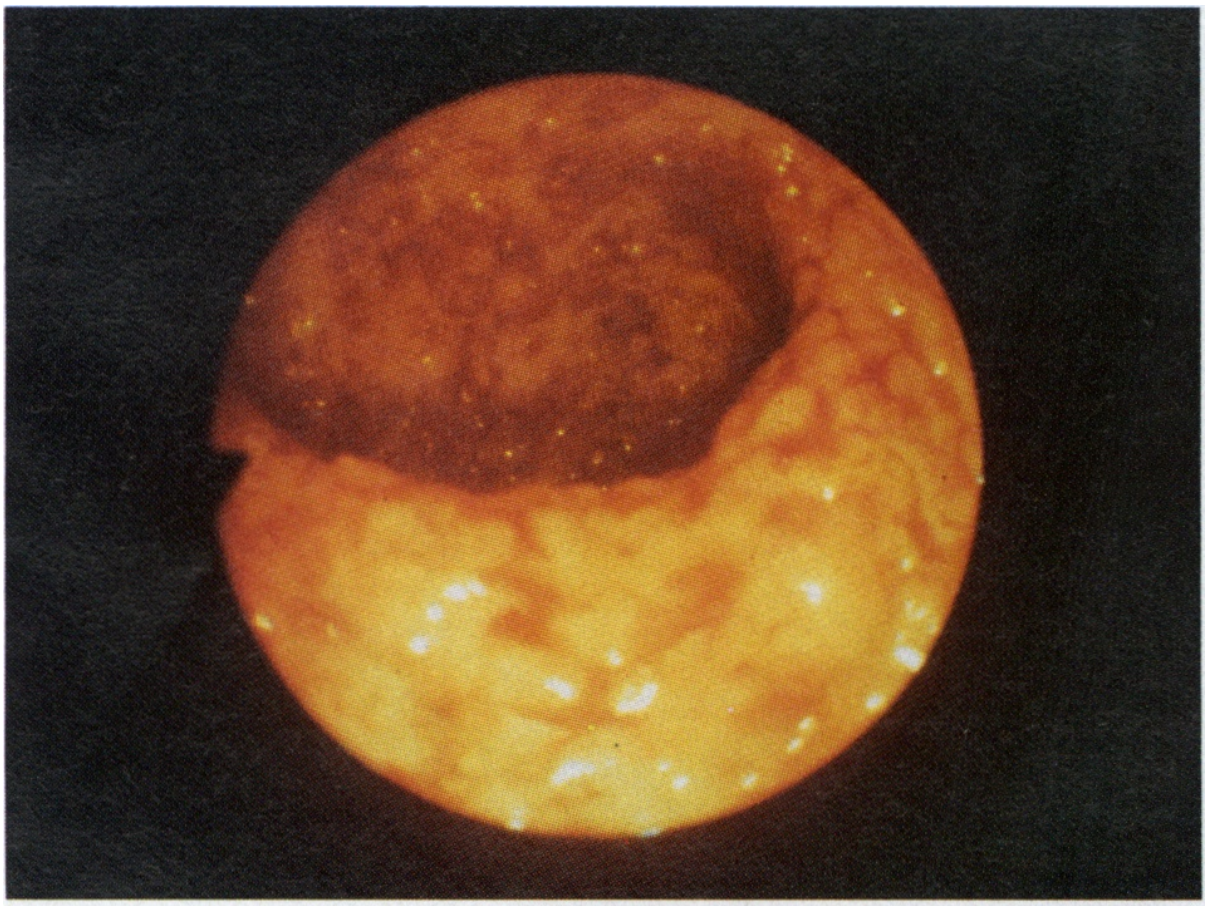
The key features in this presentation are classic for ulcerative colitis (UC):

- **Continuous mucosal lesions from the rectum to the hepatic flexure** — UC characteristically begins at the anorectal junction and extends proximally in a continuous, circumferential pattern without skip areas. This distribution extending proximal to the splenic flexure classifies it as **extensive colitis (E3)** per the Montreal Classification.[1][2][3]
- **Grossly bloody stool and urgency** — hematochezia, increased stool frequency, and bowel urgency are the hallmark presenting symptoms that should raise suspicion for UC.[3]
- **Conjunctival pallor** — consistent with anemia from chronic blood loss, which is a frequent biochemical finding in UC.[2]
- **Erythematous, indurated, tender rectum** — rectal involvement is nearly universal in UC and is a distinguishing feature from Crohn's disease.[4][5]

Why not the other options?

- **Crohn's disease (D):** Crohn's features patchy, discontinuous inflammation with skip lesions, often with rectal sparing, and may involve any part of the GI tract including the terminal ileum. Deep linear/serpiginous ulcers and a cobblestone appearance are characteristic. The continuous pattern described here argues strongly against Crohn's.[4][5]
- **Celiac disease (B):** Celiac disease affects the small intestine (primarily the duodenum and jejunum), not the colon, and presents with malabsorption rather than bloody diarrhea.
- **Irritable bowel syndrome (C):** IBS is a functional disorder without mucosal inflammation or bloody stool. Fecal calprotectin can help distinguish IBS from inflammatory bowel disease.[6]

The following figure illustrates the endoscopic and histologic features characteristic of ulcerative colitis, including diffuse mucosal inflammation, ulceration, and crypt abscesses confined to the mucosa and submucosa.



A

Figure 2. Endoscopic and Histologic Features of Ulcerative Colitis.

Used under license from The New England Journal of Medicine.

Would you like to explore the initial treatment approach for extensive ulcerative colitis, including the role of 5-ASA agents versus early biologic therapy?

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Question 871

A 45-year-old man presents to your office with a 2-year history of moderate-to-severe pelvic pain, irritative voiding urinary symptoms (frequency and dysuria), and occasional frank blood in his semen with painful ejaculation. He has been evaluated by several practitioners, who have all prescribed antimicrobial therapy, including ciprofloxacin, with no improvement and leading to emotional distress and sleep disturbances. The physical examination is unremarkable, except for a mildly tender prostate, without masses or nodules. There are no testicular masses, hernias, or hemorrhoids. Additionally to this health issue, you have also been following him for recurrent abdominal pain, periods of constipation and diarrhea, and fatigability, with all test results within the normal range thus far. A summary of recent tests is shown in the following table:

Urine test		
Sample	White cells	Culture
Mid-stream urine	Negative	Negative
Expressed prostatic secretion	Positive	Negative

What is the most likely diagnosis in this patient?

Answer Choices:

(A) Benign prostatic hyperplasia
(B) Chronic, non-bacterial prostatitis
(C) Chronic prostatitis by resistant Escherichia coli
(D) Interstitial cystitis

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/638eea7d-8566-45ef-9d44-267048b76d5a

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OpenEvidence Explanation

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The most likely diagnosis is **B. Chronic, non-bacterial prostatitis** (also termed chronic prostatitis/chronic pelvic pain syndrome, or CP/CPPS — NIH category III).

Key reasoning:

This patient's presentation is classic for CP/CPPS: **≥2 years of pelvic pain, irritative voiding symptoms, hematospermia, and painful ejaculation, with negative urine cultures and failure to respond to antibiotics**.[1][2] The laboratory findings are particularly instructive:

- **Midstream urine**: WBC negative, culture negative — ruling out cystitis or UTI
- **Expressed prostatic secretions (EPS)**: WBC positive, culture negative — indicating prostatic inflammation without identifiable bacterial infection

This pattern — inflammatory prostatic secretions with sterile cultures — specifically defines **NIH category IIIa (inflammatory CP/CPPS)**.[3] Chronic bacterial prostatitis (NIH category II) requires identification of the same bacterial strain on repeated cultures, which is absent here.[1] The presence of WBCs in EPS with negative cultures directly excludes option C (resistant E. coli prostatitis).

Why the other options are incorrect:

- **A. Benign prostatic hyperplasia (BPH)**: Typically presents in older men with obstructive symptoms (weak stream, hesitancy, nocturia) rather than pelvic pain, hematospermia, and ejaculatory pain. The prostate is not enlarged on exam.

- **C. Chronic prostatitis by resistant E. coli**: Chronic bacterial prostatitis requires positive bacterial cultures from prostatic specimens. All cultures here are negative, and prior antibiotic courses were ineffective — not consistent with a resistant organism that would still grow on culture.[1]

- **D. Interstitial cystitis**: While it can cause pelvic pain and irritative voiding symptoms, it is far more common in women and typically presents with bladder-centric pain that improves with voiding. The prostatic tenderness and EPS findings point toward a prostatic rather than bladder source.[2]

Additional clinical context: The concurrent history of recurrent abdominal pain, alternating bowel habits, and fatigue with normal workup is consistent with **irritable bowel syndrome (IBS)**, which is significantly associated with CP/CPPS (OR ~2.0).[4] These conditions share mechanisms of visceral hypersensitivity and central pain sensitization.[5][6] The emotional distress and sleep disturbances further align with the psychosocial comorbidities commonly seen in CP/CPPS.[1][7]

Would you like to discuss the multimodal treatment approach for CP/CPPS, including alpha-blockers, pelvic floor physical therapy, and management of the overlapping IBS symptoms?

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Question 873

A 2-hour-old, 3.2 kg (7.0 lb) newborn boy born by cesarean delivery is being evaluated by the resident on-call. The child was born to a gravida 2, para 0 mother with known hepatitis B. The mother made it to all of her prenatal appointments and took the recommended dose of folic acid since conception. She gave up smoking when she discovered she was pregnant. The infant's heart rate is 150/min, respiratory rate is 48/min, temperature is 37.5°C (99.5°F), and blood pressure is 80/52 mm Hg. APGAR testing exhibits a score of 7 and 8 at 1 and 5 minutes, respectively. The head is normocephalic. No neural tube defects are present on inspection or palpation of the spine. There is strong flexion in all 4 extremities. Cranial nerves 2–12 are intact. Sensory and deep tendon reflexes are without any abnormalities. Which of the following is the best course of action for the newborn child?
Hepatitis B serology
HBsAg positive
HBeAg positive
IgM HBc negative
Total anti-HBc positive
Anti-HBs negative
Anti-HBc negative
HBV DNA greater than 1 million IU/mL
Alanine transferase normal

Answer Choices:

(A) Administer hepatitis B vaccine
(B) Administer hepatitis B immunoglobulin (HBIG)
(C) Administer hepatitis B vaccine and HBIG
(D) Check hepatitis B serology

Correct Answer:

(C)

OpenEvidence Response:

> (C) ✓

OpenEvidence Link: https://openevidence.com/ask/7e69be6d-3439-4f15-996f-8eaeeffdb62f

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OpenEvidence Explanation

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The answer is **C. Administer hepatitis B vaccine and HBIG**.

Practice Guideline

The American College of Obstetricians and Gynecologists (ACOG) recommends that **neonates of individuals who are HBsAg-positive or whose status is unknown at the time of delivery receive both HBIG and hepatitis B virus vaccine within 12 hours of birth** (Strong Recommendation, Moderate-Quality Evidence).[1] This combined passive-active immunoprophylaxis approach is the standard of care regardless of maternal viral load or whether antiviral therapy was given during pregnancy.[1]

With neonatal postexposure prophylaxis, approximately 1% of neonates exposed to HBV will develop infection.[1] The standard childhood immunization schedule should be followed after the birth dose, and the physician responsible for the newborn's care should be informed of the mother's carrier status so that appropriate prophylaxis can be given as soon as possible.[1]

In this case, the mother is HBsAg-positive with a high viral load (HBV DNA >1 million IU/mL), which further underscores the importance of timely immunoprophylaxis. ACOG also recommends that antivirals be used during pregnancy for patients with HBV DNA >200,000 IU/mL to decrease vertical transmission risk, though this does not change the neonatal management — both vaccine and HBIG remain indicated.[1]

This recommendation is uniformly supported across major guidelines. The ACIP recommends that all infants born to HBsAg-positive women receive HepB vaccine and HBIG within 12 hours of birth, administered at different injection sites.[2] The Society for Maternal-Fetal Medicine similarly recommends combined immunoprophylaxis for all newborns of HBsAg-positive mothers (GRADE 1B), noting that the combination of vaccine and HBIG confers **long-term immunity in 85–95% of cases**.[3] The AASLD 2018 guidance also states that HBIG and HBV vaccine should be administered to newborns of HBsAg-positive mothers immediately after delivery.[4]

Passive-active immunization at birth has an overall efficacy of approximately 95% in preventing mother-to-child transmission.[5] A prospective multicenter study demonstrated that earlier administration (within 1 hour of birth) may provide even better protection, with an overall MTCT rate of only 0.9%.[6]

Why not the other options:

- **Vaccine alone (A)** or **HBIG alone (B)** are insufficient — HBIG alone resulted in 25% of infants becoming infected by 1 year, and vaccine alone does not provide immediate passive immunity.[3]
- **Checking hepatitis B serology on the infant (D)** is not the immediate priority — serologic testing of the infant is recommended at 9–12 months of age after completion of the vaccine series, not at birth.[2]

Would you like to explore the evidence on maternal antiviral therapy with tenofovir during the third trimester for reducing vertical transmission in highly viremic mothers?

Relevant images

(CONTENT OMITTED)

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Question 875

A 64-year-old man with multiple sclerosis comes to the physician because of a 4-month history of urinary incontinence. The urge to urinate occurs suddenly, and he often is unable to make it to the bathroom before leaking urine. He has no incontinence with coughing or laughing. Digital rectal examination shows no abnormalities. Ultrasonography shows a normal post-void residual volume. Which of the following is the most appropriate pharmacotherapy for this patient's incontinence?

Answer Choices:

(A) Midodrine
(B) Rivastigmine
(C) Mirtazapine
(D) Tolterodine

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/eda87e51-b928-4154-b22e-0e97fc6fb8cc

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OpenEvidence Explanation

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The correct answer is **D. Tolterodine**.

This patient presents with **urge urinary incontinence** secondary to neurogenic detrusor overactivity (NDO) from multiple sclerosis. The clinical picture — sudden urge to void with inability to reach the bathroom, absence of stress incontinence (no leakage with coughing/laughing), normal digital rectal exam (excluding prostatic obstruction), and normal post-void residual (excluding overflow incontinence) — is classic for overactive bladder due to uninhibited detrusor contractions.

Antimuscarinic agents such as tolterodine are first-line pharmacotherapy for neurogenic detrusor overactivity in MS.[1][2][3] Tolterodine is a competitive muscarinic receptor antagonist that reduces uninhibited bladder contractions, increases bladder capacity, and decreases urgency and incontinence episodes.[4][5] The AUA/SUFU guidelines recommend antimuscarinics (or beta-3 agonists, or a combination) to improve bladder storage parameters in NLUTD patients, and multiple MS-specific reviews list tolterodine among the standard first-line options for overactive bladder in this population.[1][3][6]

The other options are incorrect:

- **Midodrine** (A) is an alpha-1 agonist used for orthostatic hypotension, not urinary incontinence.
- **Rivastigmine** (B) is a cholinesterase inhibitor used for dementia; it would worsen detrusor overactivity by increasing cholinergic tone.
- **Mirtazapine** (C) is an antidepressant with no established role in treating urge incontinence.

Would you like to explore the comparative efficacy and cognitive safety profile of different antimuscarinics versus beta-3 agonists in MS patients with neurogenic detrusor overactivity?

Relevant images

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Question 876

A 42-year-old woman with a history of depression and headaches presents to the emergency room with severe, pulsating pain around the crown of her head beginning 12 hours ago. She last took ibuprofen 2 hours ago but did not feel any improvement in the pain. She has been nauseous and unable to get out of bed and is currently laying in the dark with the lights off. Her depression has improved, and she has stopped taking her sertraline 2 months ago. Other than ibuprofen as needed, she is not currently taking any additional medications. Which of the following would be the best treatment for her acute symptoms?

Answer Choices:

(A) No treatment necessary
(B) 100% oxygen
(C) Propranolol
(D) Sumatriptan

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/327e5973-0bcc-4232-9255-b9d52d240904

OpenEvidence Explanation

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The answer is **D. Sumatriptan**.

This patient presents with classic features of a **migraine** — severe, pulsating headache, nausea, photophobia (lying in the dark), and functional impairment (unable to get out of bed) — that has not responded to ibuprofen (an NSAID). **Sumatriptan**, a 5-HT_1B/D receptor agonist (triptan), is the first-line migraine-specific treatment for moderate-to-severe attacks or attacks that fail to respond to NSAIDs.[1][2]

Why the other options are incorrect:

- **A. No treatment necessary** — This patient has a debilitating headache with nausea and photophobia requiring treatment escalation beyond the failed NSAID.
- **B. 100% oxygen** — High-flow oxygen is the established acute treatment for **cluster headache**, not migraine. While some limited evidence suggests possible benefit in migraine, it is not a standard or recommended therapy.[3][4]
- **C. Propranolol** — This is a **preventive** (prophylactic) medication for migraine, not an acute treatment. It would not address her current symptoms.[2]

Regarding serotonin syndrome risk: Although the patient has a history of sertraline use, she discontinued it **2 months ago** (well beyond its elimination half-life of ~26 hours). She is not currently taking any serotonergic medications, so sumatriptan can be safely administered. Notably, even when triptans and SSRIs are co-prescribed, the actual risk of serotonin syndrome appears to be very low, and the American Headache Society has questioned the basis for the FDA advisory on this interaction.[2][5]

Would you like to explore the stepwise approach to acute migraine management when initial triptan therapy is also insufficient?

Relevant images

(CONTENT OMITTED)

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Question 877

A pulmonologist is analyzing the vital signs of patients with chronic obstructive pulmonary disease (COPD) who presented to an emergency room with respiratory distress and subsequently required intubation. The respiratory rates of 7 patients with COPD during their initial visit to the emergency room are shown:
Patient 1 22 breaths per minute
Patient 2 32 breaths per minute
Patient 3 23 breaths per minute
Patient 4 30 breaths per minute
Patient 5 32 breaths per minute
Patient 6 32 breaths per minute
Patient 7 23 breaths per minute
Which of the following is the mode of these respiratory rates?

Answer Choices:

(A) 30 breaths per minute
(B) 32 breaths per minute
(C) 10 breaths per minute
(D) 27.7 breaths per minute

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/7e266a86-aff4-42a2-88ea-8a604b58eb89

OpenEvidence Explanation

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The answer is **B. 32 breaths per minute**.

The **mode** is the value that appears most frequently in a dataset. Reviewing the respiratory rates:

- 22 bpm → appears **1** time
- 23 bpm → appears **2** times
- 30 bpm → appears **1** time
- 32 bpm → appears **3** times

Since **32 breaths per minute** occurs most frequently (3 out of 7 patients), it is the mode.

The other options represent different measures or values:

- **27.7 bpm** (option D) is the **mean** ($194 \div 7 \approx 27.7$)
- **30 bpm** (option A) is the **median** (the middle value when arranged in order)
- **10 bpm** (option C) is the **range** ($32 - 22 = 10$)

Would you like to explore how measures of central tendency (mean, median, mode) are applied in clinical research design and biostatistics?

Question 878

A 17-year-old high school student was in shop class when he accidentally sawed off his pointer finger while making a bird house. He fainted when he realized his finger had been cut off. The teacher immediately transported the patient to the emergency department and he arrived within 20 minutes. He has a past medical history of asthma, and his only medication is an albuterol inhaler. The patient's current blood pressure is 122/78 mmHg. Analgesics are administered. The teacher states that he left the amputated finger in the classroom, but that the principal would be transporting it to the hospital. Which of the following is the correct method of transporting the amputated finger?

Answer Choices:

(A) Submerge the finger in ice water
(B) Wrap the finger in moist gauze
(C) Wrap finger in moist gauze, put in a plastic bag, and place on ice
(D) Wrap the finger in moist gauze and submerge in ice water

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/f6984232-926a-49d4-8c65-781f3c73d385

OpenEvidence Explanation

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The correct answer is **C. Wrap finger in moist gauze, put in a plastic bag, and place on ice**.

The established protocol for transporting an amputated digit involves three steps: (1) wrapping the part in **moistened gauze**, (2) placing it in a **sealed plastic bag**, and (3) placing that bag **on ice**.[1][2] This method achieves cold ischemia — which significantly improves replantation success — while critically avoiding **direct contact between the tissue and ice or water**.[3][4]

Key principles behind this approach:

- **Cold preservation extends viability.** Digits tolerate approximately 12 hours of warm ischemia versus up to 24 hours of cold ischemia. A meta-analysis found that digits preserved in cold ischemia for over 12 hours had significantly higher odds of replantation success than those replanted within 0–12 hours of warm ischemia ($P \leq 0.05$).[1][3]
- **Direct submersion in ice water (options A and D) causes tissue damage.** Submerging the amputated part directly in water or placing it in direct contact with ice leads to maceration, frostbite injury, and cellular damage that can render the part non-viable for replantation.
- **Moist gauze alone (option B) is insufficient** because it does not provide the cold environment needed to slow ischemic tissue degradation.

A study examining preservation practices found that only **34.1%** of patients presenting with traumatic amputations had properly preserved parts, and proper preservation was directly correlated with attempted replantation (58.1% vs. 23.3%, $P = .001$).[4] This underscores the clinical importance of correct transport technique.

This patient — a 17-year-old with a clean-cut mechanism — is an excellent candidate for replantation, as pediatric/adolescent finger amputations and sharp-cut injuries are both favorable prognostic factors.[1][5]

Would you like to explore the indications and contraindications for digit replantation, including how mechanism of injury and patient factors influence the decision to replant?

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Question 879

A 15-year-old girl comes to the physician because she has not had menstrual bleeding for the past 3 months. Menses had previously occurred at irregular 15–45 day intervals with moderate to heavy flow. Menarche was at the age of 14 years. She started having sexual intercourse with her boyfriend about 3 months ago. Six months ago she had a manic episode, which was treated with risperidone. Her mother has PCOS and her father has diabetes mellitus. She is very conscious of her weight and appearance. She is 171 cm (5 ft 6 in) tall and weighs 79 kg (174 lb); BMI is 27.02 kg/m2. Her temperature is 37°C (98.6°F), pulse is 60/min, and blood pressure is 116/70 mm Hg. The abdomen is soft and nontender. Pelvic examination shows a normal vagina and cervix. Serum hormone studies show:
Prolactin 16 ng/mL
Thyroid-stimulating hormone 3.8 µU/mL
Follicle-stimulating hormone 6 mIU/mL
Luteinizing hormone 5.1 mIU/mL
Progesterone 0.8 ng/mL (follicular N <3; luteal N >3–5)
Testosterone 2.2 nmol/L (N <3.5)
A urine pregnancy test is negative. Which of the following is the most likely cause of her symptoms?

Answer Choices:

(A) Uterine fibroids
(B) Congenital defect of the Mullerian ducts
(C) Purging behavior
(D) Anovulation

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/2740e652-8009-4fa6-b7a1-4233c01cecc5

OpenEvidence Explanation

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The correct answer is **D. Anovulation**.

This 15-year-old presents with secondary amenorrhea (3 months without menses) against a backdrop of **irregular menses since menarche** (15–45 day intervals), a negative pregnancy test, normal prolactin, normal TSH, and normal testosterone. The key to this question is recognizing that her prior menstrual pattern — irregular cycles with 15–45 day intervals — is itself characteristic of anovulatory cycles, which are common in the first 1–2 years after menarche due to immaturity of the hypothalamic-pituitary-ovarian (HPO) axis.[1][2]

The lab findings strongly support anovulation:

- **Low progesterone (0.8 ng/mL)** in the follicular range confirms the absence of a corpus luteum and therefore no recent ovulation.[1]
- **Normal FSH and LH** without an LH surge pattern are consistent with anovulatory cycling rather than primary ovarian insufficiency or hypogonadotropic hypogonadism.
- **Normal prolactin and TSH** exclude hyperprolactinemia and thyroid disease as causes.
- **Normal testosterone** makes PCOS less likely, though her family history (mother with PCOS, father with diabetes) and BMI of 27 are risk factors worth monitoring.

Why not the other options?

- **A. Uterine fibroids** — These cause abnormal uterine bleeding (menorrhagia), not amenorrhea, and are exceedingly rare in a 15-year-old.

- **B. Congenital defect of the Müllerian ducts** — Müllerian anomalies cause primary amenorrhea, not secondary amenorrhea. This patient already achieved menarche and had prior menses, ruling out structural outflow tract abnormalities.

- **C. Purging behavior** — While the stem mentions she is "very conscious of her weight and appearance," purging would cause amenorrhea through functional hypothalamic amenorrhea (FHA), which typically presents with **low or low-normal gonadotropins** and hypogonadotropic hypogonadism. Her BMI of 27 (overweight) and normal gonadotropin levels argue against significant energy deficit or purging behavior as the primary cause. Anovulation due to HPO axis immaturity is a far more likely explanation in this clinical context.[2][3]

Adolescent anovulation is the most common cause of irregular menses and secondary amenorrhea in the first few years after menarche, and this presentation — with confirmatory low progesterone and otherwise normal hormonal workup — is classic.[1][4]

Would you like to explore the evaluation and management approach for persistent anovulatory cycles in adolescents, including when to initiate further workup for PCOS?

Relevant images

(CONTENT OMITTED)

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Question 883

An immunology expert is delivering a talk on innate immunity. While talking about inflammasomes, he describes the process via an example: products of cellular stress are detected by NLRP3, which includes NOD-, LRR-, and pyrin domain-containing 3; the latter interacts with apoptosis-associated speck-like protein containing CARD (ASC) via the pyrin domain, which leads to the formation of a protein speck that consists of multimers of ASC dimers. Which of the following enzymes will be activated as the next step in the process?

Answer Choices:

(A) Adenosine deaminase
(B) Caspase 1
(C) Protein phosphatase
(D) Tyrosine kinase

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/84706678-4ac6-4ec4-af84-7f1dc2defc96

OpenEvidence Explanation

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The answer is **B. Caspase 1**.

After ASC oligomerizes into a speck structure, the CARD (caspase recruitment domain) of ASC recruits **procaspase-1** via homotypic CARD-CARD interactions. This proximity-induced oligomerization leads to autoproteolytic cleavage of procaspase-1 into **active caspase-1**, which is the next enzymatic step in the NLRP3 inflammasome signaling cascade.[1][2][3]

The sequence described in the question follows the canonical inflammasome pathway:

1. NLRP3 senses danger signals (DAMPs/PAMPs)
2. NLRP3 recruits ASC via PYD-PYD interactions
3. ASC self-oligomerizes into a macromolecular "speck" composed of ASC dimers
4. The CARD domain of ASC then recruits procaspase-1 via CARD-CARD interactions, leading to **caspase-1 activation**

Once activated, caspase-1 cleaves pro-IL-1β and pro-IL-18 into their mature bioactive forms and also cleaves gasdermin D (GSDMD) to trigger pyroptosis.[4][5]

The following figure illustrates this canonical inflammasome assembly and downstream signaling:

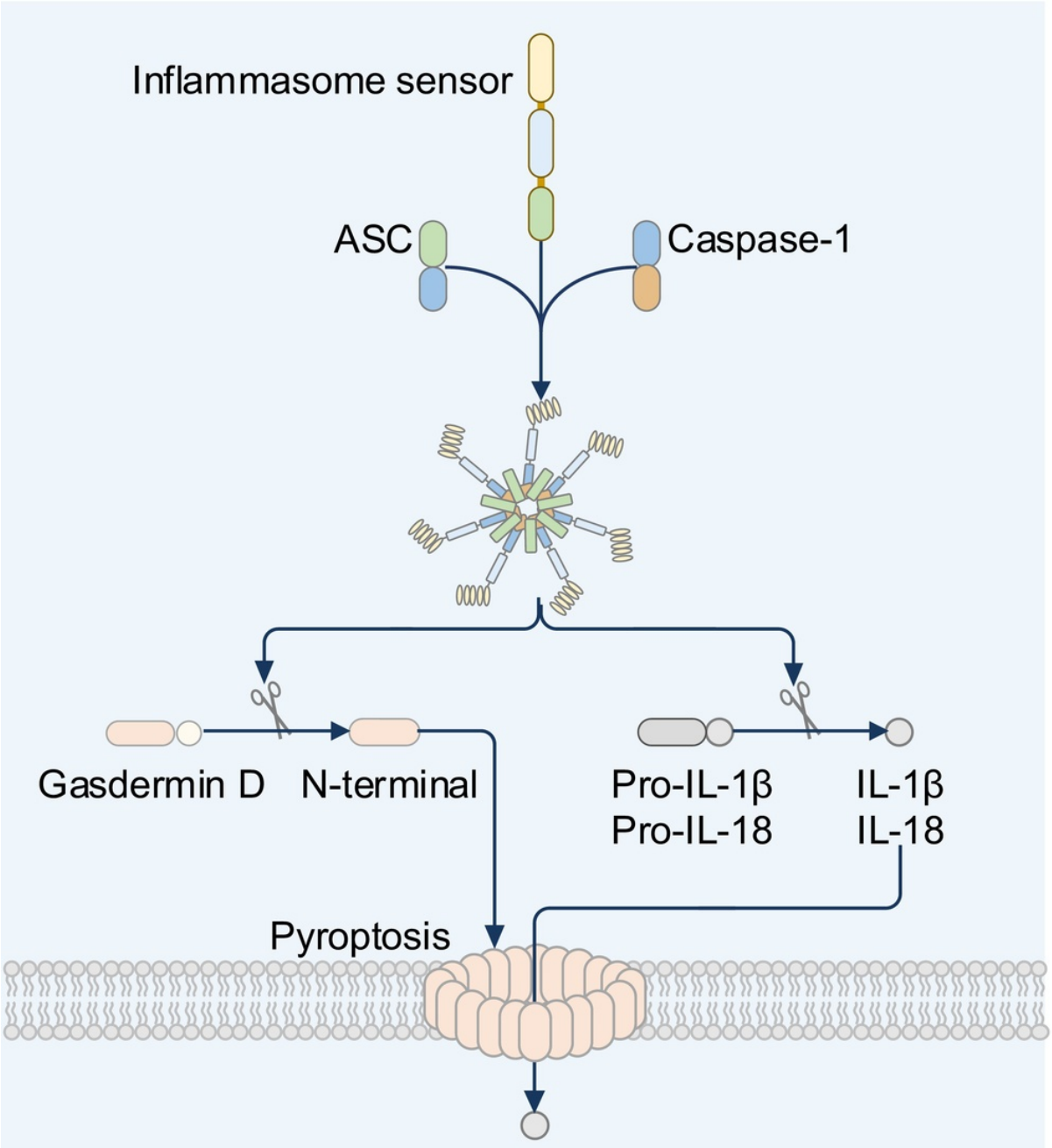


Figure 3. A high-level overview of inflammasome assembly and activation in mammalian cells. Inflammasome sensors can interact directly with their target ligand or respond to a variety of physiological changes. Following activation, most inflammasome sensors recruit an adaptor protein called apoptosis-associated speck-like protein containing a caspase-recruitment domain (also known as ASC or PYCARD) and the cysteine protease caspase-1. Activated caspase-1 cleaves gasdermin D to release the N-terminal domain which induces pyroptosis. Caspase-1 also cleaves pro-interleukin (IL)-1β and pro-IL-18 into their biologically active forms which are released through gasdermin D pores.

The other answer choices — adenosine deaminase, protein phosphatase, and tyrosine kinase — are not direct downstream effectors of ASC speck formation in the inflammasome pathway.

Would you like to explore the downstream effects of caspase-1 activation, including the mechanisms of gasdermin D pore formation and pyroptotic cell death?

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Question 884

The ribosome is an essential organelle that plays an important role in the synthesis of new proteins. The location of the ribosome within the cell can vary and provides a clue to the function of the particular cell. What ribosome location is essential for protein-secreting cells?

Answer Choices:

(A) Rough endoplasmic reticulum
(B) Smooth endoplasmic reticulum
(C) Cytosol
(D) Nucleus

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/62992475-f56a-479f-bd57-338cf09552d7

OpenEvidence Explanation

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The answer is **A. Rough endoplasmic reticulum**.

The **rough endoplasmic reticulum (RER)** is defined by the presence of ribosomes studded along its cytoplasmic surface, giving it its characteristic "rough" appearance. This location is essential for **protein-secreting cells** because ribosomes bound to the RER translate mRNAs encoding secretory, membrane-

bound, and lysosomal proteins. As translation proceeds, the nascent polypeptide is co-translationally translocated into the RER lumen, where it undergoes folding, post-translational modifications (e.g., N-linked glycosylation, disulfide bond formation), and is then trafficked through the Golgi apparatus for secretion via exocytosis.

Key distinctions among the other options:

- **Smooth endoplasmic reticulum (B)** lacks ribosomes and is involved in lipid synthesis, steroid hormone production, and detoxification — not protein synthesis.
- **Cytosolic (free) ribosomes (C)** synthesize proteins destined to remain in the cytoplasm, nucleus, mitochondria, or peroxisomes — not secreted proteins.
- **The nucleus (D)** is the site of ribosomal subunit assembly (in the nucleolus) and transcription, but translation does not occur there in eukaryotic cells.

Cells with high secretory activity — such as plasma cells (antibody secretion), pancreatic acinar cells (digestive enzymes), and goblet cells (mucus) — characteristically have abundant rough endoplasmic reticulum.

Would you like to explore how signal peptide sequences direct ribosomes to the RER membrane via the signal recognition particle (SRP) pathway?

Question 886

A 24-year-old woman comes to the physician for a routine gynecological examination and to refill her birth control pills. Her last pap smear at age 22 showed no intraepithelial lesions nor malignancy of the cervical cells. Menses occur at regular 28-day intervals and last 4 days. Her last menstrual period was 2 weeks ago. She is sexually active with one male partner. Her father died of colon cancer at the age of 75 years and her mother was diagnosed with breast cancer at the age of 40 years. She mentions that she is planning a backpacking trip through Europe in 2 months. Her routine immunizations are all up-to-date. Her temperature is 36.9°C (98.5°F) and her blood pressure is 94/58 mm Hg. Pelvic and speculum examination show no abnormalities. Which of the following is the best recommendation for the patient at this time?

Answer Choices:

(A) Neisseria gonorrhoeae and Chlamydia trachomatis screening
(B) Beta-hCG urine test
(C) Repeat Pap smear
(D) No further testing is necessary

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/9d6a74cd-cc1f-410f-9ac5-db69d763d017

OpenEvidence Explanation

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The best recommendation for this patient is **A. Neisseria gonorrhoeae and Chlamydia trachomatis screening**.

The USPSTF recommends **screening for chlamydia and gonorrhea in all sexually active women aged 24 years and younger**, regardless of symptoms or number of partners.[1][2] This patient is a 24-year-old sexually active woman, making her eligible for routine screening.

The other options are not appropriate:

- **Repeat Pap smear (C):** Per USPSTF and ACOG guidelines, cervical cytology screening in women aged 21–29 years is recommended every **3 years**. Her last normal Pap was at age 22, so the next one is not due until age 25. Repeating it now at age 24 would constitute over-screening.[3][4]
- **Beta-hCG urine test (B):** There is no clinical indication for a pregnancy test. She is on oral contraceptives, her last menstrual period was 2 weeks ago (consistent with a regular 28-day cycle), and there are no symptoms suggestive of pregnancy.
- **No further testing (D):** This would miss the recommended STI screening for a sexually active woman in this age group.

Would you like to explore the recommended pre-travel health interventions for a young woman planning a backpacking trip through Europe, including vaccination updates and travel-specific counseling?

Relevant images

(CONTENT OMITTED)

References

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Question 890

A 51-year-old Caucasian woman presents to the physician for a routine health maintenance examination. She had a Colles' fracture 2 years ago. The rest of her past medical history is unremarkable. She has a sedentary lifestyle. She has been smoking 1 pack of cigarettes daily for 30 years. She drinks alcohol moderately. Her mother had a fracture of the wrist when she was in her late 60s. The physical examination shows no abnormal findings. Dual-energy X-ray absorptiometry (DEXA scan) shows a T-score of -3.2 standard deviations (SDs) in the hip. The patient is educated regarding her risk of falls. Exercise regimen and smoking cessation assistance are provided. Appropriate diet is indicated, as well as supplements with calcium and vitamin D. Which of the following is the most appropriate next step in pharmacotherapy?

Answer Choices:

(A) Alendronate
(B) Calcitonin
(C) Estrogen
(D) Tamoxifen

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/21eb4b9d-2a9d-40d0-8cfd-bee3e67db440

OpenEvidence Explanation

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The answer is **A. Alendronate**.

Bisphosphonates such as alendronate are the first-line pharmacotherapy for postmenopausal osteoporosis in patients at high fracture risk. This patient has established osteoporosis with a hip T-score of −3.2 SD and a history of a fragility fracture (Colles' fracture), along with additional risk factors (smoking, sedentary lifestyle, family history of fracture). Multiple major guidelines support this recommendation:

- The **ACP** (2023) recommends bisphosphonates as first-line treatment for postmenopausal women with osteoporosis (T-score ≤ −2.5), with strong recommendation and high-quality evidence.[1]
- **ACOG** (2022) recommends bisphosphonates as initial therapy for most postmenopausal patients at increased fracture risk.[2]
- The **AACE/ACE** and **Endocrine Society** guidelines similarly list alendronate among first-line agents for high-risk patients.[3]

Why not the other options:

- **Calcitonin (B)** has low antifracture efficacy and is generally reserved for patients who cannot tolerate other therapies. It is not recommended as first-line treatment.[2][4]
- **Estrogen (C)** reduces fracture risk but carries significant risks (stroke, venous thromboembolism, coronary heart disease, breast cancer with combined estrogen-progestin), and is generally reserved for patients who cannot tolerate other osteoporosis therapies.[2][3]
- **Tamoxifen (D)** is a SERM used primarily for breast cancer treatment/prevention and is not FDA-approved for osteoporosis. Raloxifene is the SERM approved for osteoporosis, but even raloxifene is not first-line as it only reduces vertebral fractures without demonstrated hip or nonvertebral fracture reduction.[4]

Notably, given this patient's very low T-score (< −3.0) and prior fracture, current guidelines would also support consideration of an anabolic agent (e.g.,

teriparatide, abaloparatide, or romosozumab) as initial therapy, but among the answer choices provided, alendronate is the most appropriate.[2][5]

Would you like to explore whether this patient's very high fracture risk (T-score < −3.0 with prior fracture) would warrant initial anabolic therapy over bisphosphonates under current guideline recommendations?

Relevant images

(CONTENT OMITTED)

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Question 892

A 55-year-old man presents with complaints of exertional dyspnea and dry cough. He reports using extra pillows at night to sleep and two nighttime awakenings to catch his breath in the last month. The patient lives in a homeless shelter and has not seen a doctor in the last 20 years. He has been drinking 5-8 drinks of alcohol per day for the last 20 years. Family history is non-significant, and the patient does not take any medications. His temperature is 37.1°C (98.9°F), blood pressure is 135/115 mm Hg, pulse is 85/min, and respiratory rate is 24/min. Physical examination reveals 2+ bilateral pitting edema. Chest auscultation reveals bibasilar crackles. Which of the following is associated with this patient's condition?

Answer Choices:

(A) Decreased glomerular filtration rate (GFR)
(B) Decreased extracellular fluid (ECF) volume
(C) Increased renal blood flow
(D) Increased renal tubular sodium reabsorption

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/c4f6b363-d692-4441-a741-3dd06aeee2d1

OpenEvidence Explanation

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The correct answer is **D. Increased renal tubular sodium reabsorption**.

This patient presents with classic findings of **congestive heart failure (CHF)**: exertional dyspnea, orthopnea (extra pillows), paroxysmal nocturnal dyspnea (nighttime awakenings), bibasilar crackles (pulmonary edema), bilateral pitting edema, and elevated diastolic blood pressure — likely due to alcoholic cardiomyopathy given his 20-year history of heavy alcohol use.

Why D is correct:

In heart failure, reduced cardiac output leads to decreased effective circulating volume, which activates the **renin-angiotensin-aldosterone system (RAAS)**, the sympathetic nervous system, and arginine vasopressin secretion. This neurohumoral activation results in **increased proximal tubular sodium and water reabsorption** to maintain effective plasma volumes, ultimately leading to worsening congestion and volume overload.[1][2] Excessive sodium avidity and extracellular volume overload are hallmark features of decompensated heart failure.[2] All three major neurohormonal systems activated in heart failure — RAAS, sympathetic nerves, and vasopressin — reduce renal blood flow and increase tubular sodium reabsorption.[3]

Why the other options are incorrect:

- **A. Decreased GFR** — While GFR can eventually decline in severe decompensated heart failure, early in the disease the GFR is relatively preserved despite reduced renal blood flow, because efferent arteriolar constriction (from elevated renin) increases filtration fraction to compensate. GFR decline is not the primary or earliest renal change in heart failure.[1]

- **B. Decreased ECF volume** — The opposite occurs. Heart failure causes sodium and water retention, leading to **increased** ECF volume, manifested by this patient's edema and pulmonary congestion.[2]

- **C. Increased renal blood flow** — Renal blood flow is **decreased** in heart failure due to reduced cardiac output, increased renal venous pressure, and neurohumoral-mediated renal vasoconstriction.[1][3]

Would you like to explore the specific mechanisms by which chronic alcohol use leads to dilated cardiomyopathy and the recommended workup for newly diagnosed alcoholic cardiomyopathy?

Relevant images

(CONTENT OMITTED)

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Question 894

A 3-year-old refugee with increasing pitting edema and abdominal swelling over the past 2 months is brought to the physician. Her family has been displaced several times over the last few years. Nutrition and housing were frequently inadequate. At the physician's clinic, the boy appears irritated and drowsy. He is difficult to arouse. Physical examination shows pitting edema over the ankles and feet and around his eyes. Abdominal examination is positive for ascites and hepatomegaly. Oral examination shows several missing teeth. Which of the following best explains these findings?

Answer Choices:

(A) Kwashiorkor
(B) Marasmus
(C) Beriberi
(D) Rickets

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/cff5c43d-e66f-4695-ab32-48295da58e0f

OpenEvidence Explanation

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The answer is **A. Kwashiorkor**.

This presentation — a displaced refugee child with **pitting edema** (ankles, feet, periorbital), **ascites**, **hepatomegaly**, **irritability/drowsiness**, and a history of inadequate nutrition — is the classic clinical picture of **kwashiorkor**, a form of severe acute protein-energy malnutrition characterized primarily by protein deficiency.

Key features that point to kwashiorkor and distinguish it from the other options:

- **Edema** is the hallmark of kwashiorkor and is the defining feature that separates it from marasmus. Kwashiorkor produces generalized pitting edema due to hypoalbuminemia from insufficient protein intake.[1][2][3]
- **Hepatomegaly** results from fatty infiltration of the liver, a well-recognized finding in kwashiorkor caused by impaired hepatic lipoprotein synthesis.[4][5][6]
- **Ascites** is attributable to reduced oncotic pressure from hypoalbuminemia.
- **Irritability and altered mental status** (drowsiness, difficulty arousing) are characteristic neuropsychiatric manifestations of kwashiorkor.[3][7]
- **Missing teeth** reflects the broader nutritional deficiency and impaired development seen in severe malnutrition.

Why not the other options:

- **Marasmus (B)** presents with severe wasting and emaciation but characteristically lacks edema — the child appears "skin and bones".[2][8]
- **Beriberi (C)** (thiamine deficiency) can cause edema in its "wet" form but presents with cardiac failure (tachycardia, cardiomegaly) rather than hepatomegaly with fatty infiltration, ascites, and irritability in this pattern.
- **Rickets (D)** (vitamin D deficiency) causes skeletal abnormalities (bowing of legs, craniotabes, rachitic rosary) rather than edema, ascites, or hepatomegaly.

Would you like to explore the evidence-based management protocols for severe acute malnutrition with kwashiorkor, including refeeding strategies and monitoring for refeeding syndrome?

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Question 895

A 2-year-old boy is brought to his pediatrician by his parents for a routine visit. Since his 18-month visit, the parents have become concerned that his speech does not seem to be developing appropriately. The parents report that the patient's vocabulary is still limited to fewer than 10 words, and he is still only using single words to describe things. The parents say that his motor milestones do not seem to be affected, as the patient is very physically active and can run and kick a ball. At times the patient seems hyperactive and can be difficult to redirect. On exam, his temperature is 98.4°F (36.9°C), blood pressure is 110/70 mmHg, pulse is 80/min, and respirations are 14/min. The rest of the exam is unremarkable, except that the patient's face appears to be abnormally long and narrow. The patient is further referred to a geneticist, as he is believed to have a trinucleotide repeat disorder. Which of the following is the most likely inheritance pattern of this disorder?

Answer Choices:

(A) Autosomal dominant
(B) Autosomal recessive
(C) Noninherited somatic mutation
(D) X-linked dominant

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/4f99013b-4085-4aa5-b3e8-1d6e095ee574

OpenEvidence Explanation

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The correct answer is **D. X-linked dominant**.

The clinical presentation — a 2-year-old boy with **speech delay** (fewer than 10 words, single-word use only), **hyperactivity** with difficulty redirecting, intact motor milestones, and a **long, narrow face** — is classic for **Fragile X syndrome (FXS)**. This is the most common inherited cause of intellectual disability and the leading single-gene cause of autism, caused by a CGG trinucleotide repeat expansion (>200 repeats) in the *FMR1* gene on the X chromosome.[1]

Fragile X syndrome is inherited in an **X-linked dominant** pattern.[2][3] Key features of this inheritance:

- The *FMR1* gene is located at Xq27.3 on the X chromosome. A single copy of the full mutation is sufficient to cause disease, making it dominant rather than recessive.[1]
- **Males** (hemizygous, with only one X) are more severely affected, with the vast majority having significant intellectual disability.[1][2]
- **Females** (heterozygous) are variably affected due to X-inactivation — approximately one-third have intellectual disability, one-third borderline IQ, and one-third normal IQ.[1]
- The penetrance is reduced (~80% in males, 30–50% in females), which is characteristic of X-linked dominant conditions with variable expressivity.[3][4]

The clinical features in this vignette align precisely with prepubertal Fragile X syndrome: delayed speech milestones are typically the presenting concern around age 2–3, hyperactivity and behavioral difficulties are prominent, and the elongated face with prominent ears are hallmark connective tissue findings.[1][5][6] Motor milestones may be relatively preserved compared to language, consistent with the described scenario.

The following pedigree illustrates the inheritance pattern and clinical spectrum of FMR1-related disorders across generations:

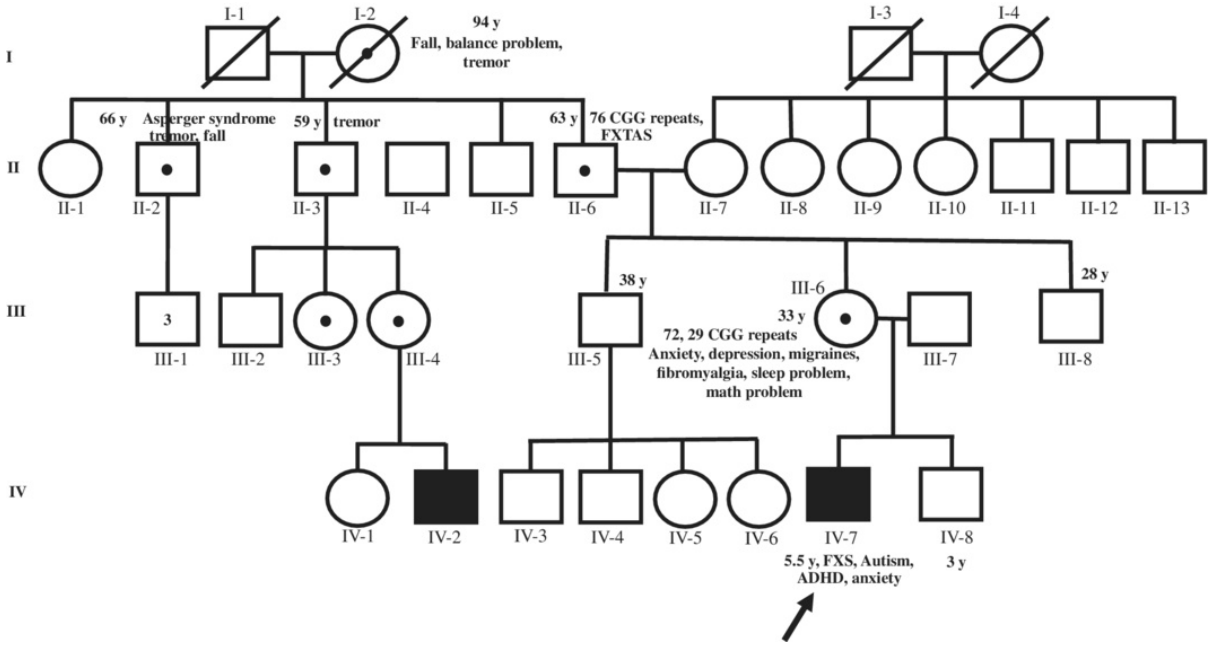


Figure 1. An example family pedigree of a family in which the proband was a boy with fragile X syndrome, autism, attention-deficit/hyperactivity disorder, and anxiety (IV-7) (see arrow pointing to the proband). His mother was a fragile X premutation carrier with significant physical and mental health conditions (III-6). His maternal grandfather had the premutation and developed fragile X-associated tremor/ataxia syndrome at a later age (II-6) and carriers were identified in his family (I-2, II-2, II-3) and his brother's family (III-3, III-4) in addition another boy with FXS (IV-2). The black box represents a full mutation, and the dot means a premutation. ADHD, attention-deficit/hyperactivity disorder; CGG, cytosine-guanine-guanine; FXS, fragile X syndrome; FXTAS, fragile X-associated tremor/ataxia syndrome

Would you like to explore the recommended genetic testing approach and early intervention strategies for children with suspected Fragile X syndrome?

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Question 896

A 23-year-old man is brought to the emergency department by his mother because of a change in his personality. The mother reports that over the past 7 months her son has become increasingly withdrawn; he has not answered any phone calls or visited his family and friends. He had always been a quiet boy, who needed some time on his own, but he used to meet with friends at least once a week. The patient says that he cannot leave the house because aliens are watching him and “stealing his thoughts”. He does not drink alcohol. He used to smoke marijuana occasionally but quit 1 year ago. His vital signs are within normal limits. Physical examination shows no abnormalities. On mental status examination, it is impossible to follow the patient's sequence of thoughts. He is anxious and has a flat affect. Which of the following is the most likely diagnosis?

Answer Choices:

(A) Delusional disorder
(B) Mood disorder with psychotic features
(C) Schizoid personality disorder
(D) Schizophrenia

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/ab61e1cd-2810-49dd-a280-dd75c6593a97

OpenEvidence Explanation

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The most likely diagnosis is **D. Schizophrenia**. This patient meets DSM-5 diagnostic criteria based on the following features:

Criterion A – At least two symptoms present, with at least one being a core positive symptom:

- **Delusions** (bizarre): believing aliens are watching him and "stealing his thoughts" (thought withdrawal is a classic first-rank symptom)[1][2]
- **Disorganized speech**: the examiner cannot follow his sequence of thoughts[3][4]
- **Negative symptoms**: flat affect and social withdrawal[2][3]

Criterion B – Functional decline: He has become increasingly withdrawn, no longer answering phone calls or visiting family and friends, representing a clear decline from his prior baseline.[1][5]

Criterion C – Duration ≥6 months: Symptoms have been present for 7 months, exceeding the required 6-month threshold.[1]

Why the other options are incorrect:

- **Delusional disorder** – Characterized by nonbizarre, systematized delusions with preserved personality and functioning outside the delusional theme. This patient has bizarre delusions (thought stealing by aliens), disorganized thinking, flat affect, and significant functional impairment — features that are inconsistent with delusional disorder.[4][6]
- **Mood disorder with psychotic features** – Psychotic symptoms occur exclusively during mood episodes (depressive or manic). There is no evidence of a primary mood disturbance here; the presentation is dominated by psychotic and negative symptoms.[4][5]
- **Schizoid personality disorder** – Characterized by a lifelong pattern of social detachment and restricted emotional range, but without psychotic symptoms such as delusions or disorganized thinking. This patient has active psychosis, ruling out a personality disorder as the primary diagnosis.[5]

Would you like to explore the recommended first-line pharmacologic and psychosocial treatment approach for a first episode of schizophrenia in a young adult?

Relevant images

(CONTENT OMITTED)

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Question 897

A 37-year-old woman presents to the clinic with pain and swelling of her legs. She states that she first noticed the swelling 6 weeks ago. Initially, the swelling was minimal, but now she is finding it difficult to walk and she can't fit into any of her shoes. Her medical history is significant for systemic lupus erythematosus. She takes ibuprofen and hydroxychloroquine. Her temperature is 99°F (37.2°C), blood pressure is 153/86 mmHg, and pulse is 88 beats/min. Pitting edema to bilateral knees is noted on physical examination. Urinalysis reveals proteinuria. The patient is started on an immunosuppressant. Two days later the patient returns to clinic complaining of blood in her urine. A urinalysis reveals moderate erythrocytes but is negative for leukocyte esterase, nitrites, or crystals. Diffuse oozing of the bladder mucosa with neovascularization is seen on cystoscopy. Which of the following could have prevented the patient's condition?

Answer Choices:

(A) Ifosfamide
(B) Mesna
(C) Methotrexate
(D) Nitrofurantoin

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/95372407-8304-4691-b73d-635bd86e2e54

OpenEvidence Explanation

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The answer is **B. Mesna**.

This patient with SLE and lupus nephritis (evidenced by leg edema, hypertension, and proteinuria) was started on **cyclophosphamide**, a standard immunosuppressant for lupus nephritis.[1][2] She subsequently developed **hemorrhagic cystitis**, as demonstrated by hematuria with diffuse oozing of the bladder mucosa and neovascularization on cystoscopy — classic findings of acrolein-mediated bladder injury.[3][4]

Mesna (2-mercaptoethane sodium sulfonate) is a uroprotective agent that binds and neutralizes **acrolein**, the toxic cyclophosphamide metabolite responsible for hemorrhagic cystitis.[5][6] Mesna is converted to its inactive disulfide form in the bloodstream, then reactivated in the kidney and excreted into the urine, where it directly detoxifies acrolein and other urotoxic metabolites before they can damage the bladder epithelium.[6] Co-administration of mesna with cyclophosphamide is the established prophylactic strategy to prevent this complication.[7][8][9]

Why the other options are incorrect:

- **A. Ifosfamide** — Another oxazaphosphorine alkylating agent that itself causes hemorrhagic cystitis through the same acrolein-mediated mechanism; it would worsen, not prevent, the condition.[7][10]
- **C. Methotrexate** — An antimetabolite immunosuppressant with no uroprotective properties and no role in preventing hemorrhagic cystitis.
- **D. Nitrofurantoin** — An antibiotic used for urinary tract infections. The urinalysis was negative for leukocyte esterase and nitrites, ruling out infection as the cause of hematuria.

Would you like to explore the comparative efficacy of different lupus nephritis induction regimens and their respective side effect profiles?

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Question 898

A 38-year-old woman presents to the office for a routine examination. She has no complaints and offers very little information voluntarily. She answers each question with soft, short sentences and avoids eye contact. She appears timid, anxious and admits that this is one of the very few times she has left the house in the last several years. Medical history is significant for essential hypertension. She takes hydrochlorothiazide and a daily vitamin. She has worked from home as a web graphic designer for 20 years. Questions about her social life reveal that she is very shy with few friends, and she often makes excuses to avoid parties and social gatherings. Despite this, she expresses a strong desire to be in a relationship. Today, her blood pressure is 125/85 mm Hg, heart rate is 95/min, respiratory rate is 18/min, and temperature is 37.0°C (98.6°F). On physical examination, her heart has a regular rhythm and her lungs are clear to auscultation bilaterally. Which of the following is most consistent with her behavior?

Answer Choices:

(A) Schizoid personality disorder
(B) Avoidant personality disorder
(C) Antisocial personality disorder
(D) Agoraphobia

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/d530c948-1c39-4f31-9860-b12cfdccb005

OpenEvidence Explanation

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The answer is **B. Avoidant personality disorder**.

This presentation is most consistent with **avoidant personality disorder (AvPD)**, characterized by a pervasive pattern of **social inhibition, feelings of inadequacy, and hypersensitivity to negative evaluation** beginning in early adulthood.[1] Several key features in this vignette point to AvPD:

- **Desire for relationships despite avoidance**: She expresses a strong wish to be in a relationship but avoids social contact — this is the hallmark distinction from schizoid personality disorder. Individuals with schizoid personality disorder have **limited desire for social intimacy**, whereas those with AvPD avoid relationships due to fear of embarrassment, rejection, or being found inadequate.[1][2]
- **Longstanding pattern**: She has been working from home for 20 years and rarely leaves the house, indicating a pervasive, enduring pattern traceable to early adulthood — consistent with a personality disorder rather than an episodic anxiety disorder.[1][2]
- **Timidity, shyness, and social inhibition**: Her soft speech, avoidance of eye contact, and making excuses to avoid gatherings reflect the core anxiousness and withdrawal traits of AvPD.[1]

Why not the other options:

- **Schizoid personality disorder (A)**: Defined by detachment from social relationships and a restricted range of emotional expression, with **no desire** for close relationships. This patient explicitly desires a relationship, ruling out schizoid PD.[1][2]
- **Antisocial personality disorder (C)**: Characterized by disregard for and violation of the rights of others — entirely inconsistent with this presentation.[2]
- **Agoraphobia (D)**: While she rarely leaves home, agoraphobia involves fear of situations where escape might be difficult or help unavailable (e.g., public

transportation, crowds, open spaces), typically driven by fear of panic-like symptoms. Her avoidance is motivated by social inadequacy and fear of negative evaluation, not panic. The DSM-5 notes that AvPD and agoraphobia can be distinguished by the **motivation for avoidance** — fear of social rejection in AvPD versus fear of panic or physical harm in agoraphobia.[1]

Would you like to explore the overlap and distinction between avoidant personality disorder and social anxiety disorder, which are often considered related conditions?

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Question 900

A 38-year-old man presents with progressive tiredness and shortness of breath on exertion. Past medical history is significant for peptic ulcer disease diagnosed 2 years ago for which he is not compliant with his medications. He reports a 10-pack-year smoking history and occasionally alcohol use. His vital signs include: temperature 37.1°C (98.7°F), blood pressure 142/91 mm Hg, pulse 98/min. Physical examination is unremarkable. Laboratory findings are significant for the following:
Hemoglobin 9.7 g/dL
Hematocrit 29.1%
Red cell count 3.7 million/mm3
Mean corpuscular volume (MCV) 71 µm3
Mean corpuscular hemoglobin (MCH) 21.3 pg/cell
Mean corpuscular hemoglobin concentration (MCHC) 28.4 Hb/cell
Reticulocyte count 0.2 %
Red cell distribution width (RDW) 17.8 (ref: 11.5–14.5%)
White blood cell count 8100/mm3
Platelet count 420,000/mm3
Iron studies show:
Total iron binding capacity (TIBC) 620 µg/dL
Transferrin saturation 9%
Which of the following findings would most likely be found on a bone marrow biopsy in this patient?

Answer Choices:

(A) Hypocellularity with fatty infiltration
(B) ↓ hemosiderin stores
(C) Ringed sideroblasts
(D) Myeloblasts with immature precursors

Correct Answer:

(B)

OpenEvidence Response:

> **(B)** ✓

OpenEvidence Link: https://openevidence.com/ask/ca9a81b4-a898-485e-a454-bc88e7db714b

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OpenEvidence Explanation

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The answer is **B. ↓ hemosiderin stores**.

This patient presents with a classic picture of **iron deficiency anemia (IDA)** due to chronic gastrointestinal blood loss from untreated peptic ulcer disease. The laboratory findings are characteristic:

- **Microcytic, hypochromic anemia**: low MCV (71 μm³), low MCH (21.3 pg), low MCHC (28.4 g/dL)
- **Elevated RDW** (17.8%), reflecting anisocytosis — a hallmark of IDA distinguishing it from thalassemia trait (which typically has a normal RDW)
- **Low reticulocyte count** (0.2%), indicating hypoproliferative marrow response
- **Elevated TIBC** (620 μg/dL) and **low transferrin saturation** (9%), the classic iron study pattern of true iron deficiency[1][2]
- **Reactive thrombocytosis** (420,000/mm³), commonly seen with IDA[3]

On bone marrow biopsy, the definitive finding in iron deficiency is **absent or markedly decreased hemosiderin (iron) stores** on Perl's Prussian blue staining. This remains the gold standard for diagnosing iron deficiency — the ferric ions in hemosiderin react with potassium ferrocyanide to form a blue compound, and in IDA, staining is markedly reduced or absent (Grade 0).[4] The bone marrow also typically shows mild erythroid hyperplasia with depletion of iron in reticulum cells.[3]

Why the other options are incorrect:

- **A (Hypocellularity with fatty infiltration)** — characteristic of aplastic anemia, not IDA
- **C (Ringed sideroblasts)** — pathognomonic for sideroblastic anemia, where iron accumulates in mitochondria around the erythroblast nucleus; this represents iron overload/utilization defects, the opposite of iron deficiency
- **D (Myeloblasts with immature precursors)** — suggests acute leukemia or myelodysplastic syndrome, not consistent with this presentation

Would you like to explore the recommended workup and management approach for iron deficiency anemia in the setting of peptic ulcer disease, including the role of H. pylori testing?

Relevant images

(CONTENT OMITTED)

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Question 901

A 27-year-old G3P1010 makes an appointment with her gynecologist for evaluation of profuse bleeding, which began two days ago. She is 13 weeks pregnant based on the date of her last menstrual period. She is dizzy and weak, and is unable to move around the house and perform her daily tasks. Initially, she had only light spotting, but later on in the day the bleeding increased. Thus far, she has used six sanitary pads. The blood pressure is 90/60 mm Hg, the temperature is 37.8°C (100°F), the pulse is 125/min, and the respiratory rate is 14/min. A saline infusion is started, and blood and urine specimens are sent for analysis. On pelvic examination, the vagina contains blood and the cervical os is open. She also complains of cervical motion and adnexal tenderness on examination. An ultrasound shows an intrauterine gestational sac low in the uterine cavity. No fetal movement or cardiac activity are observed. She is advised to rest for a couple of hours, after which the scan is repeated. Slight downward migration of the gestational sac is observed with no change in the fetal status. Which of the following is the next step in management?

Answer Choices:

(A) Antibiotics
(B) Magnesium sulfate
(C) Methotrexate
(D) Dilation and curettage

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/e8cfe325-6373-4812-89ec-9e8151421fa8

OpenEvidence Explanation

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The correct answer is **D. Dilation and curettage**.

This patient presents with an **inevitable abortion** — characterized by profuse vaginal bleeding, an open cervical os, and a nonviable intrauterine pregnancy (no fetal cardiac activity, gestational sac migrating downward). She is hemodynamically unstable (BP 90/60, pulse 125/min), indicating significant hemorrhage that requires urgent intervention. Additionally, the cervical motion tenderness and low-grade fever raise concern for possible septic abortion, but the immediate priority is surgical evacuation.

Why D is correct: In the setting of hemodynamic instability from hemorrhage with an open os and confirmed nonviable pregnancy, **surgical evacuation (dilation and curettage/suction curettage) is the appropriate urgent intervention**. The ACOG Practice Bulletin on Early Pregnancy Loss notes that medical management (e.g., misoprostol) can be considered in women "without infection, hemorrhage, severe anemia, or bleeding disorders," but this patient has active hemorrhage with hemodynamic compromise, making surgical evacuation the indicated approach.[1] A Cochrane network meta-analysis confirmed that surgical methods (D&C and suction aspiration) are the most effective approaches for completing a miscarriage.[2][3]

Why the other options are incorrect:

- **A. Antibiotics** — While the low-grade fever and cervical motion tenderness may suggest infection, antibiotics alone will not address the ongoing hemorrhage or evacuate the nonviable pregnancy. Antibiotics may be given as an adjunct (e.g., preoperative doxycycline), but are not the definitive next step.[1]
- **B. Magnesium sulfate** — Used for seizure prophylaxis in preeclampsia/eclampsia or for fetal neuroprotection in preterm labor; it has no role in managing a first-trimester miscarriage.

- **C. Methotrexate** — Used for ectopic pregnancy management, not for an intrauterine pregnancy loss. This patient has a confirmed intrauterine gestational sac, making methotrexate inappropriate.[4]

Would you like to explore the role of prophylactic antibiotics and Rh(D) immune globulin administration in the perioperative management of surgical evacuation for early pregnancy loss?

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Question 902

An otherwise healthy 25-year-old woman comes to the physician because of a 2-day history of pain and swelling of her right knee joint and left wrist. She went camping with her new boyfriend 3 weeks ago but does not recall any tick bites. Her temperature is 37.8°C (100.0°F). Examination of the right knee shows swelling, warmth, and tenderness on passive movement. There is a tender pustule on the sole of the left foot. Arthrocentesis of the right knee joint yields 8 mL of cloudy fluid with a leukocyte count of 45,000/mm3 (90% segmented neutrophils with intracellular organisms). Which of the following is the strongest risk factor for this patient's condition?

Answer Choices:

(A) Autoantibody production
(B) Intravenous drug use
(C) Sexually transmitted infection
(D) HLA-B 27 positivity

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/da3a8f0d-e056-4774-ab62-30adeae95172

OpenEvidence Explanation

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The answer is **C. Sexually transmitted infection**.

This clinical presentation is classic for **disseminated gonococcal infection (DGI)**, which is a complication of *Neisseria gonorrhoeae*, a sexually transmitted infection. The key features pointing to this diagnosis include:

- Young, sexually active woman with a new sexual partner
- Migratory polyarthritis (right knee and left wrist involvement)
- Pustular skin lesion on the sole of the foot (characteristic acral pustular lesion of DGI)
- Purulent synovial fluid with high neutrophil count and **intracellular gram-negative diplococci**
- Low-grade fever

Sexually transmitted infection is the strongest risk factor because gonococcal arthritis is a direct complication of gonococcal STI. Without the primary gonococcal infection, dissemination cannot occur. The CDC STI Treatment Guidelines note that DGI results from hematogenous spread of N. *gonorrhoeae* from a primary mucosal site (endocervix, urethra, pharynx, or rectum), and urogenital infections are often asymptomatic in DGI patients.[1] Additional risk factors for dissemination once infected include female sex, menstruation, pregnancy, and terminal complement deficiency.[1][2]

Regarding the other options:

- **A. Autoantibody production** — relevant to rheumatoid arthritis or lupus, not septic arthritis with intracellular organisms.
- **B. Intravenous drug use** — a risk factor for *Staphylococcus aureus* septic arthritis and endocarditis, but the clinical picture here (pustular skin lesion, polyarticular involvement, intracellular diplococci) is specific for gonococcal infection.
- **D. HLA-B27 positivity** — associated with reactive arthritis (formerly Reiter syndrome), which is typically a sterile, post-infectious arthritis without intracellular organisms on synovial fluid analysis.

Would you like to explore the recommended treatment regimen for disseminated gonococcal infection, including duration and transition from parenteral to oral therapy?

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Question 907

A 58-year-old woman comes to the physician because of intermittent painful retrosternal dullness for 4 weeks. The pain is recurrent and occurs when she exerts herself or when she is outside during cold weather. She also experiences shortness of breath and palpitations during these episodes. The symptoms resolve spontaneously when she stops or sits down for a while. Over the past few days, the episodes have increased in frequency. She has hypertension, type 2 diabetes mellitus, and osteoarthritis. Her left leg was amputated below the knee after a motorcycle accident 25 years ago. She is currently waiting for a new prosthesis and walks with crutches. Current medications include captopril, glyburide, and ibuprofen. She does not smoke or drink alcohol. Her pulse is 88/min, respirations are 20/min, and blood pressure is 144/90 mm Hg. Cardiac examination shows no abnormalities. An x-ray of the chest shows no abnormalities. An ECG shows a normal sinus rhythm without any signs of ischemia. Serum cardiac markers are within the reference range. Which of the following is the most appropriate next step in diagnosis?

Answer Choices:

(A) Myocardial perfusion scan under pharmacological stress
(B) Upper endoscopy
(C) Coronary angiography
(D) Echocardiography at rest

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/0711f05c-47e3-4827-a174-ac87c8ac7aca

OpenEvidence Explanation

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The correct answer is **A. Myocardial perfusion scan under pharmacological stress**.

This patient presents with classic features of **stable angina** — exertional retrosternal chest pain with associated dyspnea and palpitations that resolve with rest, in the setting of multiple cardiovascular risk factors (hypertension, type 2 diabetes, age >55). The normal resting ECG, normal cardiac markers, and normal chest X-ray are consistent with stable angina rather than acute coronary syndrome. The key clinical detail is her **below-knee amputation** and current reliance on crutches, which renders her **unable to perform adequate exercise stress testing**.

Why pharmacological stress myocardial perfusion imaging?

The 2021 AHA/ACC Chest Pain Guidelines recommend stress imaging (stress echocardiography, PET/SPECT MPI, or CMR) as a Class 1 recommendation for intermediate-high risk patients with stable chest pain and no known CAD.[1][2] Exercise is the preferred stress modality because it provides functional and prognostic information, but when exercise stress testing cannot be performed due to **physical limitations**, pharmacological stress testing with vasodilators (e.g., adenosine, regadenoson) or dobutamine is indicated.[3] The 2012 ACCF/AHA guidelines specifically state that pharmacological stress with nuclear MPI or echocardiography is recommended (Class I) for patients who are "incapable of at least moderate physical functioning or have disabling comorbidity".[4]

Why not the other options?

- **B. Upper endoscopy** — While retrosternal pain can be gastrointestinal, the exertional pattern, cold-weather provocation, and associated dyspnea/palpitations strongly favor a cardiac etiology. Endoscopy would not be the appropriate next step.
- **C. Coronary angiography** — Invasive angiography is not the initial diagnostic test for stable angina; it is reserved for patients with high-risk

findings on noninvasive testing or refractory symptoms despite guideline-directed medical therapy.[1][2]

- **D. Echocardiography at rest** — Resting echocardiography is indicated when there are pathological Q waves, signs of heart failure, complex arrhythmias, or an unexplained murmur. This patient has a normal cardiac exam and normal ECG, so resting echo would not detect ischemia provoked by exertion.[1]

Would you like to explore the specific pharmacological agents used for stress testing and their contraindications in patients with diabetes or peripheral vascular disease?

Relevant images

(CONTENT OMITTED)

References

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Question 912

A 37-year-old woman presents to her primary care physician after returning from her honeymoon in Cancun. A few days ago, she began to notice an eruption of small red bumps that cover her torso, back, and buttocks. The patient first thought she had acne, but became worried when the rash continued to itch. The patient denies other symptoms. Vital signs are within normal limits. Physical exam is notable for red papules and pustules scattered across the trunk, abdomen, back, and buttocks, while sparing the limbs. Closer examination indicates inflammation of the hair follicles. Culture yields motile, gram-negative rods that are non-lactose fermenting and oxidase positive. What other finding is commonly observed in the culture of the most likely organism?

Answer Choices:

(A) Pink colonies
(B) Blue-green pigment
(C) Yellow sulfur granules
(D) Red pigment

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/b7b1b15a-8fb6-4674-809c-a8a50d322cd5

OpenEvidence Explanation

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The answer is **B. Blue-green pigment**.

The clinical scenario describes a classic case of **"hot tub" folliculitis** caused by *Pseudomonas aeruginosa*, which is consistent with the culture findings of motile, gram-negative rods that are **non-lactose fermenting and oxidase positive**.[1] This presentation — papulopustular folliculitis involving the trunk and buttocks while sparing the extremities — is characteristic of *Pseudomonas* folliculitis acquired from contaminated water (pools, hot tubs, or recreational water exposure, as might occur on a tropical vacation).[1][2]

P. aeruginosa characteristically produces **pyocyanin**, a distinctive **blue-green (greenish-blue) pigment** on culture media. It is the only gram-negative bacillus capable of producing this water-soluble phenazine pigment, and approximately **90–95%** of clinical *P. aeruginosa* isolates produce it.[3][4] Pyocyanin production on selective media such as Tech agar or King's A medium is considered a reliable and unique identification test for this organism.[3][5]

Regarding the other options:

- **A. Pink colonies** — associated with lactose-fermenting organisms on MacConkey agar (e.g., *E. coli*, *Klebsiella*), which is inconsistent with the non-lactose fermenting organism described.
- **C. Yellow sulfur granules** — associated with *Actinomyces israelii*, an anaerobic gram-positive organism.
- **D. Red pigment** — while *P. aeruginosa* can produce a minor red pigment called pyorubrin/aeruginosin A, this is not its hallmark culture finding. Red pigment is more classically associated with *Serratia marcescens* (prodigiosin).[6]

Would you like to explore the management and antibiotic treatment options for *Pseudomonas* folliculitis, including when systemic therapy is indicated?

Relevant images

(CONTENT OMITTED)

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Question 915

A 28-year-old G1P0 woman at 12 weeks estimated gestational age presents with malaise, joint pain, fever, and chills for the past 3 days. Physical examination reveals a mild lace-like rash and arthritis. The patient mentions her friend who is a medical student told her that her symptoms are suggestive of a parvovirus B19 infection which may adversely affect her baby. Which of the following statements regarding the effect of parvovirus B19 infection in this pregnant patient is correct?

> **Answer Choices:**
>
> (A) It can lead to hydrops fetalis secondary to fetal anemia.
> (B) It can cause aplastic crisis in the neonate.
> (C) Fetal loss occurs in more than 40% of primary infections.
> (D) The neonate may be born with a typical slapped-cheek rash.

> **Correct Answer:**
>
> **(A)**
>
> **OpenEvidence Response:**
>
> **(A)** ✓

OpenEvidence Link: https://openevidence.com/ask/7428f537-813c-4f0a-85ca-730537b282cc

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OpenEvidence Explanation

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The correct answer is **A. It can lead to hydrops fetalis secondary to fetal anemia.**

Practice Guideline

The American College of Obstetricians and Gynecologists (ACOG) states that parvovirus B19 infection in utero can lead to **nonimmune hydrops fetalis**, most often resulting from **aplastic anemia** because the virus is cytotoxic to erythroid precursors.[1] Hydrops may also be related to myocarditis or chronic fetal hepatitis.[1] Severe effects are seen most frequently when maternal infection occurs before 20 weeks of gestation.[1]

Key points regarding fetal outcomes from the ACOG Practice Bulletin:

- The rate of **fetal loss** among women with serologically proven parvovirus B19 infection ranges from **8–17% before 20 weeks** and **2–6% after 20 weeks** of gestation — well below the 40% threshold stated in option C.[1]
- An estimated 8–10% (potentially up to 18–27%) of all cases of nonimmune hydrops fetalis are associated with parvovirus B19 infection.[1]
- Serial ultrasonography every 1–2 weeks for 8–12 weeks after exposure is recommended, including Doppler assessment of the fetal middle cerebral artery peak systolic velocity to detect fetal anemia.[1]
- If hydrops fetalis or severe fetal anemia is present, fetal blood sampling and intrauterine transfusion should be considered.[1]

Why the other options are incorrect:

- **B. Aplastic crisis in the neonate** — Aplastic crisis is a complication seen in individuals with pre-existing hemolytic anemias (e.g., sickle cell disease, hereditary spherocytosis), not a typical neonatal consequence of congenital parvovirus B19 infection. The fetal/neonatal concern is severe anemia leading to hydrops, not aplastic crisis per se.[2]
- **C. Fetal loss in more than 40% of primary infections** — The fetal loss rate among maternal parvovirus B19 infections is approximately **5–17%** depending on gestational age, far below 40%. A meta-analysis confirmed an overall fetal loss incidence of approximately 7.6% among infected pregnant women. The higher figure of ~38.7% applies only to confirmed fetal infections (not all maternal primary infections).[1][3][4][5]

- **D. Neonate born with slapped-cheek rash** — The classic "slapped-cheek" rash (erythema infectiosum) is a childhood manifestation of parvovirus B19 and is not a feature of congenital parvovirus infection. Notably, adults with parvovirus B19 often do not exhibit this rash and instead present with arthralgias, as seen in this patient. Parvovirus B19 is not associated with congenital anomalies or a characteristic neonatal rash.[2][6][7]

The mechanism underlying option A is well established: parvovirus B19 has tropism for erythroid progenitor cells, and the fetal liver — the primary site of erythropoiesis during early development — is particularly vulnerable. Destruction of erythroid precursors leads to severe fetal anemia, which can progress to high-output cardiac failure and hydrops fetalis.[2][8]

Would you like to explore the recommended surveillance protocol and timing of intrauterine transfusion for pregnancies complicated by confirmed parvovirus B19 infection?

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Question 916

A 52-year-old man with hypertension and hyperlipidemia comes to the emergency department 30 minutes after the sudden onset of substernal chest pain while sitting in a chair at home. He reports drinking 2 glasses of whiskey earlier that day, after a stressful day at work. Current medications include hydrochlorothiazide and atorvastatin. He has smoked one pack of cigarettes daily for the past 20 years. His pulse is 102/min, and blood pressure is 135/88 mm Hg. Cardiopulmonary examination shows normal heart sounds. An ECG obtained on arrival at the emergency department shows ST-segment elevations in the anterior leads. 15 minutes later, the patient's chest pain has resolved and a repeat ECG shows no abnormalities. Which of the following is the most likely underlying mechanism of this patient's chest pain?

Answer Choices:

(A) Coronary artery vasospasm
(B) Coronary artery vasodilation
(C) Atherosclerotic plaque rupture
(D) Pericardial inflammation

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/0e7b9d24-3ad1-40ba-869e-94a9d13fa5e6

OpenEvidence Explanation

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The correct answer is **A. Coronary artery vasospasm**.

This presentation is classic for **Prinzmetal (variant) angina**, which results from transient focal spasm of an epicardial coronary artery. The key features pointing to this diagnosis are:

- **Transient ST-segment elevation** in the anterior leads that **completely resolved** within 15 minutes along with the chest pain — this pattern of spontaneous resolution is the hallmark of vasospastic angina[1][2]
- **Rest angina** — the patient was sitting in a chair, not exerting himself
- **Heavy smoking** (20 pack-years) — smoking is the most prominent coronary risk factor for vasospastic angina[1][3]
- **Emotional stress and alcohol** as potential triggers — stress is a recognized precipitant of coronary vasospasm[1][4]

The underlying mechanism involves **coronary vascular smooth muscle hyperreactivity**, leading to intense focal vasoconstriction (>90% constriction) of an epicardial coronary artery. This causes transmural ischemia, which manifests as ST-segment elevation corresponding to the territory of the affected artery. When the spasm resolves, blood flow is restored and the ECG normalizes.[5][6]

Why not the other options?

- **Atherosclerotic plaque rupture (C)** — This is the most common cause of STEMI (~64% of ACS), but plaque rupture triggers thrombus formation that does not spontaneously and completely resolve within 15 minutes with full ECG normalization. Plaque rupture typically causes persistent occlusion requiring intervention.[7]
- **Coronary artery vasodilation (B)** — Vasodilation would increase coronary blood flow and would not cause ischemia or ST-segment elevation.
- **Pericardial inflammation (D)** — Pericarditis causes diffuse ST-segment elevation (not localized to anterior leads) and would not resolve this rapidly. Pain is typically pleuritic and positional.

Would you like to explore the diagnostic workup and long-term management of vasospastic angina, including the role of provocative testing and calcium channel blocker therapy?

Relevant images

(CONTENT OMITTED)

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Question 917

A 5-year-old boy is brought to the emergency department by his mother because of a sudden loss of consciousness. He has asthma and has been hospitalized multiple times. His mother has type 2 diabetes mellitus. He is somnolent and diaphoretic. Serum studies show a glucose concentration of 22 mg/dL and a potassium concentration of 2.4 mEq/L. A dextrose infusion is administered, after which his glucose concentration normalizes and his symptoms improve. He is admitted to the hospital for further observation. Overnight, he has another episode of decreased consciousness. Serum studies taken during the episode show a glucose concentration of 19 mg/dL, an insulin concentration of 108 mIU/L (N=2.6–24.9), and a C-peptide concentration of 0.3 ng/mL (N = 0.8–3.1). Which of the following is the most likely diagnosis?

Answer Choices:

(A) Malingering
(B) Primary adrenal insufficiency
(C) Conversion disorder
(D) Factitious disorder imposed on another

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/b8ba82bb-fb61-41f9-8463-acf2d789585a

OpenEvidence Explanation

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The most likely diagnosis is **D. Factitious disorder imposed on another** (formerly Munchausen syndrome by proxy).

The key to this case is the dissociation between the **markedly elevated insulin** (108 mIU/L) and the **suppressed C-peptide** (0.3 ng/mL). When insulin is produced endogenously by pancreatic beta cells, insulin and C-peptide are co-secreted in equimolar amounts, so both should be elevated together. A high insulin with low C-peptide is the hallmark biochemical pattern of **exogenous insulin administration**.[1][2] This pattern rules out endogenous causes of hyperinsulinemic hypoglycemia such as insulinoma or congenital hyperinsulinism, in which both insulin and C-peptide would be elevated.[3][4][5]

The clinical context strongly supports factitious disorder imposed on another rather than the other options:

- The mother has **type 2 diabetes mellitus**, providing access to exogenous insulin at home.
- The child has had **multiple hospitalizations** for asthma, a pattern consistent with the recurrent medical encounters seen in this disorder.[6][7]
- The episodes occur while the child is under the mother's care, including overnight in the hospital.

Why the other options are incorrect:

- **Malingering (A):** Malingering involves intentional symptom production for external gain (e.g., financial, avoiding obligations). A 5-year-old cannot malingering — the child is the victim, not the perpetrator. Additionally, malingering would not produce true biochemical abnormalities.
- **Primary adrenal insufficiency (B):** Adrenal insufficiency can cause hypoglycemia, but it would not produce hyperinsulinemia. The expected pattern would be low cortisol with an appropriate ACTH response, and insulin levels would be low or normal.[1]
- **Conversion disorder (C):** Conversion disorder (functional neurological symptom disorder) involves neurological symptoms without organic cause.

It does not produce measurable biochemical derangements such as profoundly low glucose and elevated insulin levels.

Per the Pediatric Endocrine Society guidelines, a high plasma insulin level with low C-peptide level during hypoglycemia suggests exogenous insulin administration, and the possibility of surreptitious drug administration should be considered.[1] The DSM-5-TR diagnostic criteria for factitious disorder imposed on another require falsification or induction of illness in another person, with identified deception, in the absence of obvious external rewards — the diagnosis is given to the perpetrator (the mother), not the victim.[7]

Table 3. Diagnostic Interpretation of the Results of a 72-Hour Fast.*

Diagnosis	Symptoms or Signs	Glucose†	Insulin‡§	C Peptide§¶	Proinsulin§‖	β-Hydroxybutyrate	Change in Glucose**	Sulfonylurea in Plasma
		mg/dl	*μU/ml*	*nmol/liter*	*pmol/liter*	*mmol/liter*	*mg/dl*	
Normal	No	≥40	<6	<0.2	<5	>2.7	<25	No
Insulinoma	Yes	≤45	≥6††	≥0.2	≥5	≤2.7	≥25	No
Factitious hypoglycemia from insulin	Yes	≤45	≥6‡‡	<0.2	<5	≤2.7	≥25	No
Sulfonylurea-induced hypoglycemia	Yes	≤45	≥6	≥0.2	≥5	≤2.7	≥25	Yes§§
Hypoglycemia mediated by insulin-like growth factor	Yes	≤45	≤6	<0.2	<5	≤2.7	≥25	No
Non–insulin-mediated hypoglycemia	Yes	≤45	<6	<0.2	<5	>2.7	<25	No
Inadvertent feeding during the fast	No	≥45	<6	<0.2	<5	≤2.7	≥25	No
Nonhypoglycemic disorder	Yes	≥40	<6	<0.2	<5	>2.7	<25	No

*Measurements are made at the point the decision is made to end the fast.

†Sequential plasma glucose measurements in the hypoglycemic range fluctuate. Plasma glucose levels ≤45 mg per deciliter at the time a decision is made to end the fast may rise to as much as 56 mg per deciliter when the fast is actually ended approximately one hour later. Plasma glucose levels may be as low as 40 mg per deciliter during prolonged fasting in normal women. To convert values to millimoles per liter, multiply by 0.05551.

‡Measured by double-antibody radioimmunoassay (lower limit of detection, 5 μU per milliliter). To convert values to picomoles per liter, multiply by 6.0.

§In normal subjects plasma insulin, C-peptide, and proinsulin levels may be higher if the plasma glucose level is ≥60 mg per deciliter.

¶Measured by the immunochemiluminometric technique (lower limit of detection, 0.033 nmol per liter).

‖Measured by the immunochemiluminometric technique (lower limit of detection, 0.2 pmol per liter).

**In response to intravenous glucagon (peak value minus value at end of fast). To convert values to millimoles per liter, multiply by 0.05551.

††Ratios of insulin to glucose are of no diagnostic value in patients with insulinomas.

‡‡Plasma insulin levels may be very high (>100 μU per milliliter or >1000 μU per milliliter) in factitious hypoglycemia from insulin.

§§Unlike the first generation of sulfonylurea drugs, which were easily measured, second-generation drugs are not.

Table 3. Diagnostic Interpretation of the Results of a 72-Hour Fast.

Used under license from The New England Journal of Medicine.

This classic NEJM table illustrates the diagnostic patterns during a 72-hour fast, clearly showing that factitious hypoglycemia from insulin is characterized by elevated insulin but suppressed C-peptide — exactly matching this child's laboratory profile.

Would you like to discuss the recommended next steps for child protective services involvement or further workup in suspected cases of medical child abuse?

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Question 918

A 66-year-old woman presents with urinary incontinence, difficulty urinating, incomplete voiding, and dull pain in the suprapubic region. She reports that she has not urinated for the past 2 days and that the urine leakage occurs during both day and night and is not associated with physical exertion. The medical history is significant for arterial hypertension and poorly controlled type 2 diabetes mellitus for 8 years, and depression for 3 years. She is prescribed amlodipine, valsartan, atorvastatin, metformin, and amitriptyline. Her weight is 75 kg (165 lb) and her height is 166 cm (5 ft 40 in). Her vital signs are as follows: blood pressure, 120/80 mm Hg; heart rate, 91/min; respiratory rate, 13/min; and temperature, 36.4°C (97.5°F). The physical examination reveals lower abdominal tenderness with a distended urinary bladder that is palpated in the suprapubic region. The neurological examination shows decreased Achilles reflexes bilaterally, and diminished fine touch and vibratory sensation. On gynecologic examination, the cervix was normally positioned, mobile, and without any visible lesions. Bulging of the posterior vaginal wall was noted. The adnexa were not palpable. An ultrasound examination showed an overdistended urinary bladder with no structural abnormalities. Which of the following is the next step in managing this patient?

Answer Choices:

(A) Installing a vaginal pessary
(B) Bladder catheterization
(C) Cystostomy
(D) Prescribing prostaglandin E2

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/62b3eb50-0877-460c-8208-1eae964ff5f5

OpenEvidence Explanation

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The correct answer is **B. Bladder catheterization**.

This patient presents with **acute urinary retention** (inability to void for 2 days, palpable distended bladder, suprapubic pain, and overflow incontinence). The initial and most immediate management step is **prompt bladder decompression via catheterization**.[1]

Why bladder catheterization is correct:

Acute urinary retention is a urological emergency requiring immediate drainage. Guidelines uniformly recommend bladder catheterization as the first intervention when an overdistended bladder is identified.[1][2][3] Catheterization is appropriate for postvoid residual ≥300 mL in symptomatic patients and ≥500 mL even in asymptomatic patients.[4] This patient clearly has a massively overdistended bladder confirmed by both physical exam and ultrasound.

Why the other options are incorrect:

- **A. Vaginal pessary** — While posterior vaginal wall bulging (rectocele) is present, a pessary addresses pelvic organ prolapse symptoms, not acute urinary retention requiring emergent decompression. Prolapse management can be considered after the acute retention is resolved.[5]
- **C. Cystostomy (suprapubic catheter)** — Suprapubic catheterization is reserved for situations where urethral catheterization is not feasible (e.g., urethral trauma, stricture) or when long-term catheterization is anticipated. There is no indication here that urethral catheterization cannot be performed.[6]

- **D. Prostaglandin E2** — Although prostaglandins have been mentioned in the literature for managing urinary retention, they are not standard first-line therapy and do not address the immediate need for bladder decompression.[3]

Contributing factors in this patient: The urinary retention is likely multifactorial — **amitriptyline** (a tricyclic antidepressant with strong anticholinergic properties) impairs detrusor contractility, **diabetic neuropathy** (evidenced by decreased Achilles reflexes and diminished fine touch/vibratory sensation) causes neurogenic bladder dysfunction, and the **posterior vaginal wall prolapse** may contribute to voiding difficulty.[1][7]

Would you like to explore the long-term management strategy for this patient, including medication adjustment (discontinuing amitriptyline) and addressing the underlying diabetic cystopathy?

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Question 919

A 69-year-old man presents to his primary care physician with hip and back pain. The patient states that this weekend he had a barbecue. When he was lifting a heavy object he suddenly felt pain in his lower back. He describes the pain as in his buttocks but states that at times it travels down his leg. The patient states that it feels, electrical. The patient has a past medical history of obesity, diabetes, depression, anxiety, diverticulosis, constipation, and a surgical repair of his anterior cruciate ligament. His current medications include metformin, insulin, lisinopril, fluoxetine, and sodium docusate. Which of the following is most likely to help confirm the diagnosis?

Answer Choices:

(A) Flexion, abduction, and external rotation of the thigh
(B) Straight leg raise
(C) Internal rotation of the extended hip
(D) Radiography

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/9ac3d251-6ea8-431f-8b3f-ffe945001980

OpenEvidence Explanation

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The answer is **B. Straight leg raise**.

This patient's presentation — acute onset of low back and buttock pain radiating down the leg with an "electrical" quality, precipitated by heavy lifting, in the setting of obesity — is classic for **lumbar radiculopathy due to a herniated disc**. The **straight leg raise (Lasègue's test)** is the most appropriate bedside maneuver to help confirm this diagnosis.

The straight leg raise is performed with the patient supine; passive elevation of the extended leg stretches the sciatic nerve and lumbosacral nerve roots over a protruding disc. The test is considered positive when it reproduces the patient's radiating leg pain at an angle between **30° and 70°**.[1][2] A Cochrane meta-analysis found the straight leg raise has a **pooled sensitivity of 0.92** (95% CI, 0.87–0.95) for lumbar disc herniation, making it highly sensitive, though specificity is low (0.28).[1][3] The crossed straight leg raise (raising the contralateral leg) is complementary, with high specificity (~0.90) but low sensitivity.[1][2]

The following figure illustrates the biomechanics of the straight leg raise test and how nerve root tension over a herniated disc reproduces radicular symptoms.

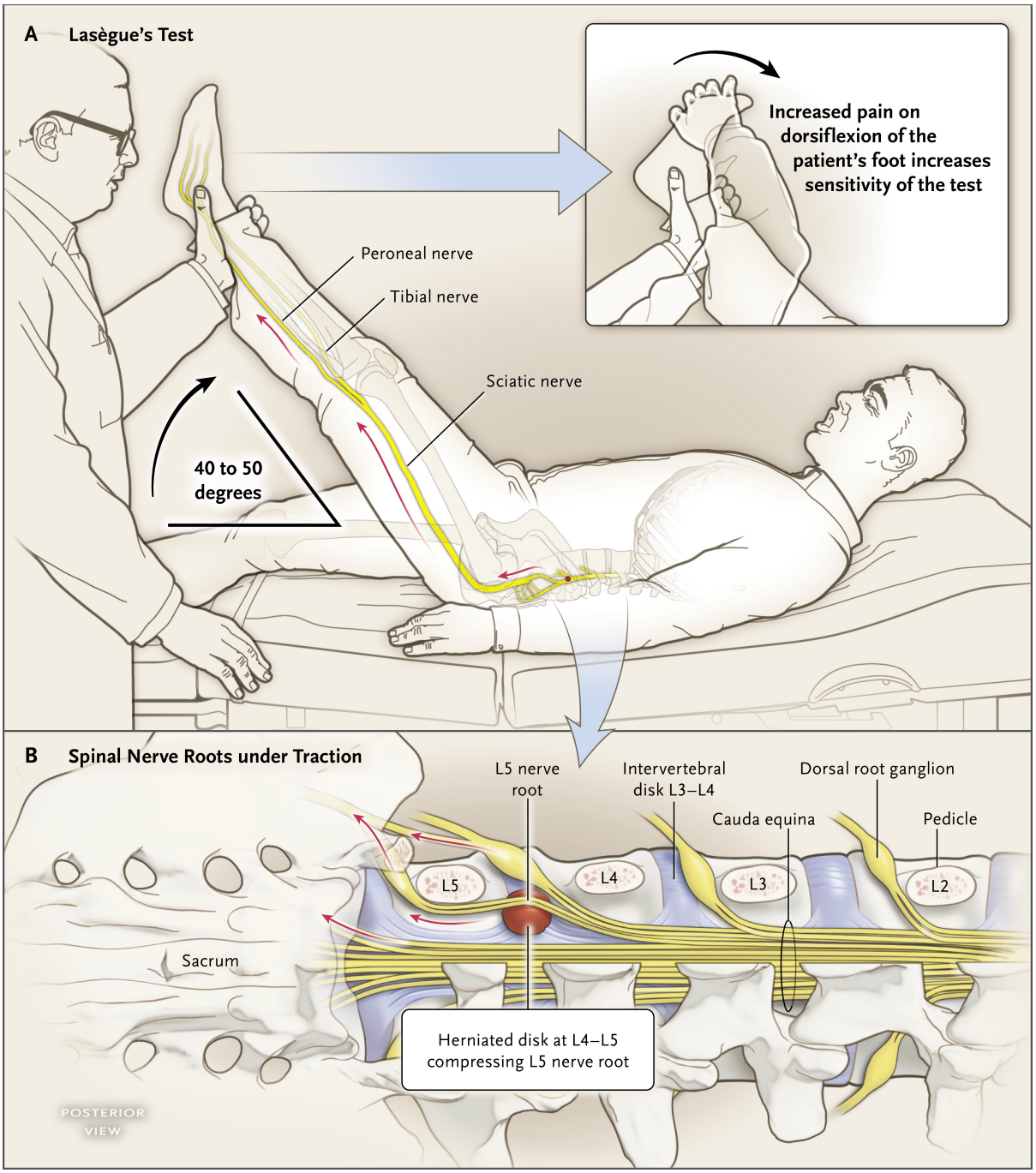


Figure 2. Straight-Leg-Raising Test.

Used under license from The New England Journal of Medicine.

Why not the other options?

- **A. FABER test (flexion, abduction, external rotation)** — This evaluates for hip joint or sacroiliac joint pathology, not radiculopathy.[4]
- **C. Internal rotation of the extended hip** — This tests for hip joint pathology (e.g., osteoarthritis, femoroacetabular impingement), not nerve root compression.

- **D. Radiography** — Plain films are insensitive for disc herniation and are primarily useful for evaluating fractures, spondylolisthesis, or bony abnormalities. MRI is the imaging modality of choice if advanced imaging is needed for radiculopathy, but imaging is not routinely recommended in the acute setting without red flags or progressive neurological deficits.[4][5]

Would you like to explore the indications for advanced imaging (MRI) versus conservative management in acute lumbar radiculopathy?

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Question 921

A 65-year-old female patient comes to the physician's office for her annual check-up. The patient's only complaint is that she feels her vision has been getting more blurry over the past year. The patient has a past medical history of diabetes diagnosed 20 years ago and osteoarthritis. Her medications include metformin, glimepiride, and ibuprofen as needed for pain. Fundoscopic examination of this patient reveals narrowing of retinal arteries and microaneurysms. This patient's symptoms are likely caused by tissue specific differences in expression of which of the following enzymes?

Answer Choices:

(A) Sorbitol dehydrogenase
(B) Galactocerebrosidase
(C) Arylsulfatase A
(D) Sphingomyelinase

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/684ff094-ede4-4001-af53-f6f1ad8ab0d9

OpenEvidence Explanation

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The answer is **A. Sorbitol dehydrogenase**.

This patient presents with classic **diabetic retinopathy** (retinal artery narrowing and microaneurysms) in the setting of longstanding diabetes. The underlying mechanism involves the **polyol pathway**, and the tissue-specific damage is explained by differences in **sorbitol dehydrogenase** expression across tissues.

The Polyol Pathway and Tissue-Specific Damage

In hyperglycemia, excess intracellular glucose is converted to **sorbitol** by aldose reductase (the rate-limiting step), and sorbitol is then converted to **fructose** by sorbitol dehydrogenase.[1][2] The key concept is that tissues such as the **retina, lens, kidneys, and peripheral nerves** have high aldose reductase activity but relatively **low sorbitol dehydrogenase** activity. This imbalance leads to sorbitol accumulation because it is produced faster than it can be metabolized.[3]

Sorbitol cannot easily diffuse across cell membranes, so it accumulates intracellularly, causing **osmotic damage** to retinal endothelial cells and pericytes.[2][4] Additionally, the increased polyol pathway flux depletes NADPH (needed for glutathione regeneration), increases oxidative stress, and promotes formation of advanced glycation end-products (AGEs) — all contributing to microvascular damage seen in diabetic retinopathy.[1][5]

Why the other answers are incorrect:

- **B. Galactocerebrosidase** — deficiency causes Krabbe disease (globoid cell leukodystrophy)
- **C. Arylsulfatase A** — deficiency causes metachromatic leukodystrophy
- **D. Sphingomyelinase** — deficiency causes Niemann-Pick disease

These are all lysosomal storage disorders unrelated to diabetic complications.

Would you like to explore the other major pathways (PKC activation, AGE formation, hexosamine pathway) that contribute to diabetic microvascular complications and how they interact with the polyol pathway?

Relevant images

(CONTENT OMITTED)

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Question 922

A 3-year-old boy is brought to the physician for the evaluation of recurrent skin lesions. The episodes of lesions started at the age of 2 months and multiple treatment options have been attempted without success. He has also had several episodes of respiratory tract infections, enlarged lymph nodes, and recurrent fevers since birth. The boy attends daycare. His older brother has asthma. The patient's immunizations are up-to-date. He is at the 5th percentile for length and 10th percentile for weight. He appears ill. His temperature is 38°C (100.4°F), pulse is 100/min, and blood pressure is 100/60 mm Hg. Examination shows several raised, erythematous lesions of different sizes over the face, neck, groins, and extremities; some secrete pus. Cervical and axillary lymph nodes are enlarged bilaterally. The remainder of the examination shows no abnormalities. Which of the following is the most likely diagnosis?

Answer Choices:

(A) Chronic granulomatous disease
(B) Atopic dermatitis
(C) Wiskott-Aldrich syndrome
(D) Chediak-Higashi syndrome

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/68f66d82-aed0-41b4-8eb7-3a4cab4fed28

OpenEvidence Explanation

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The most likely diagnosis is **A. Chronic granulomatous disease (CGD)**.

This presentation — a young boy with **recurrent purulent skin lesions** beginning in early infancy, **recurrent respiratory tract infections**, **bilateral cervical and axillary lymphadenopathy**, **recurrent fevers**, **failure to thrive** (5th percentile for length, 10th for weight), and **treatment-refractory skin infections** — is classic for CGD. Key distinguishing features include:

- **CGD** is a phagocyte defect caused by impaired NADPH oxidase function, leading to inability to kill catalase-positive organisms (e.g., *S. aureus*, *Aspergillus*, *Serratia*, *Burkholderia*). It typically presents in infancy or early childhood with recurrent skin abscesses, lymphadenitis, pneumonia, and granuloma formation. Skin infections occur in ~40–70% of patients, and lymphadenopathy in ~50–59%. Growth failure is common. The X-linked form (70% of cases) predominantly affects males and is generally more severe.[1][2][3][4][5]

Why the other options are less likely:

- **Atopic dermatitis (B):** While it causes recurrent skin lesions, atopic dermatitis presents with pruritic, eczematous patches — not raised, pus-secreting lesions. It would not explain the recurrent respiratory infections, lymphadenopathy, fevers, or failure to thrive.

- **Wiskott-Aldrich syndrome (C):** This X-linked disorder presents with the triad of **eczema, microthrombocytopenia, and recurrent infections**. The hallmark is thrombocytopenia with small platelets, leading to bleeding manifestations (petechiae, purpura, bloody diarrhea) — none of which are described in this patient. The skin lesions in WAS are typically eczematous, not purulent abscesses.[6][7]

- **Chediak-Higashi syndrome (D):** This autosomal recessive disorder is characterized by **partial oculocutaneous albinism**, recurrent pyogenic infections, and progressive neurologic symptoms. The absence of albinism or neurologic findings makes this diagnosis unlikely.[3]

The combination of a male child with early-onset, treatment-resistant purulent skin infections, suppurative lymphadenitis, recurrent respiratory infections, and growth failure — without thrombocytopenia or albinism — points most strongly to CGD.[1][2][3]

Would you like to explore the recommended diagnostic workup for CGD, including the dihydrorhodamine (DHR) flow cytometry assay and nitroblue tetrazolium (NBT) test?

Relevant images

(CONTENT OMITTED)

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Question 925

A 6-month-old boy presents to a pediatrician for the evaluation of recurrent bacterial infections. He has a history of a variety of bacterial infections since birth. Physical examination reveals light-colored skin with silver-colored hair. The pediatrician suspects an immunodeficiency disorder and decides to order several tests. Study of the boy's neutrophils reveals that they contain large cytoplasmic vacuoles. Genetic studies show a mutation in the LYST gene. Which of the following is the most likely diagnosis in this patient?

> **Answer Choices:**
>
> (A) Acquired immunodeficiency syndrome (AIDS)
> (B) Common variable immunodeficiency
> (C) Chediak-Higashi syndrome
> (D) Leukocyte adhesion deficiency–1

> **Correct Answer:**
>
> (C)
>
> **OpenEvidence Response:**
>
> (C) ✓

OpenEvidence Link: https://openevidence.com/ask/d610040e-fe07-4b19-80ac-fb0132273863

OpenEvidence Explanation

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The correct answer is **C. Chediak-Higashi syndrome**.

Chediak-Higashi syndrome (CHS) is an autosomal recessive disorder caused by mutations in the **LYST gene**, which encodes the lysosomal trafficking regulator protein. This protein is involved in vesicular transport and lysosomal function.[1][2] The clinical presentation in this vignette — recurrent bacterial infections from birth, **partial oculocutaneous albinism** (light-colored skin, silver-colored hair), and **giant cytoplasmic granules** in neutrophils — is pathognomonic for CHS.[1][3]

The key features that distinguish CHS from the other options:

- **Giant granules in neutrophils** result from abnormal fusion of primary (azurophilic) and secondary (specific) granules, impairing chemotaxis, degranulation, and intracellular bacterial killing. The delayed fusion of these giant granules with phagosomes contributes to impaired immunity.[1][3]
- **Partial oculocutaneous albinism** occurs because melanin is trapped within abnormally enlarged melanosomes (lysosome-related organelles) and cannot be properly distributed.[2][4]
- **LYST gene mutation** is confirmatory and is the only gene associated with CHS.[5][6]

The following figure illustrates the characteristic giant perinuclear granules seen in neutrophils of patients with Chediak-Higashi syndrome (Panel B), compared with normal neutrophils (Panel A), as well as the abnormal hair inclusions (Panel F).

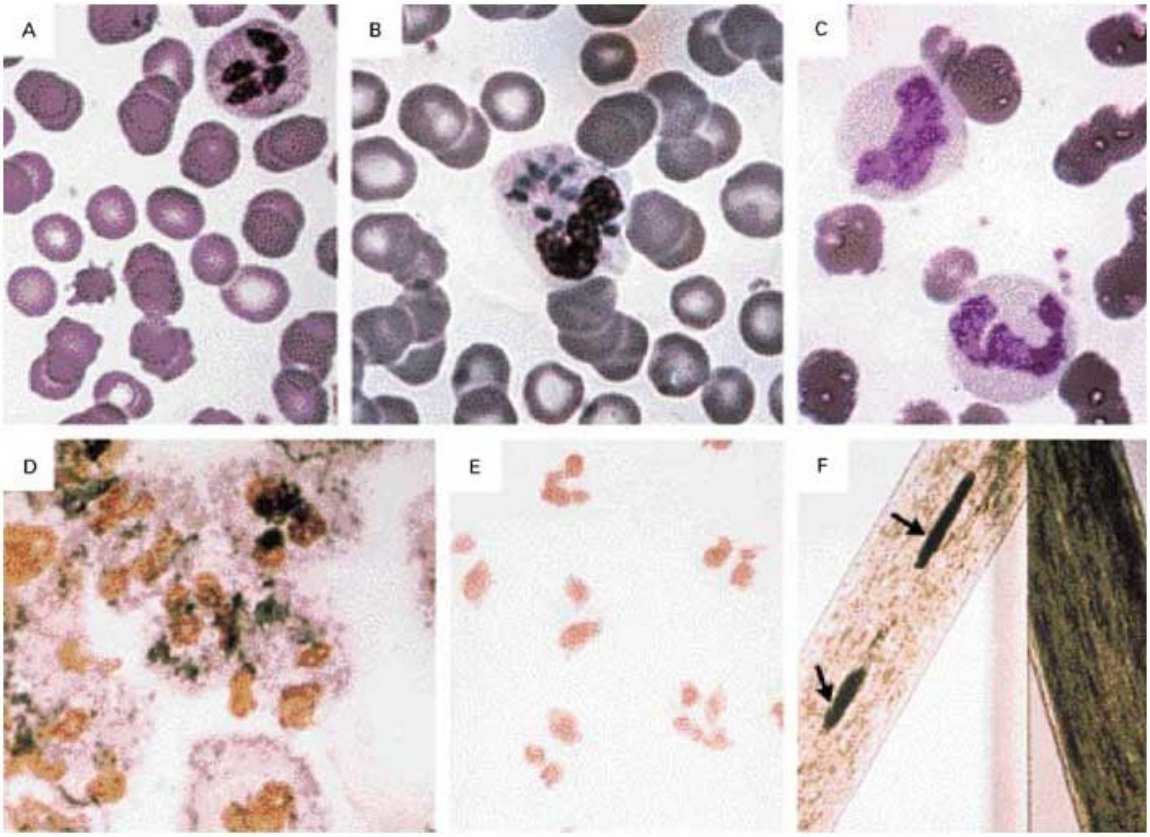


Figure 5. Diagnosis of Phagocytic Defect on the Basis of Light-Microscopical Findings.

Used under license from The New England Journal of Medicine.

Why the other options are incorrect:

- **AIDS (A):** Would not present with albinism or giant granules; caused by HIV infection, not a genetic disorder.
- **Common variable immunodeficiency (B):** A humoral (B-cell) immunodeficiency characterized by hypogammaglobulinemia, not associated with albinism or neutrophil granule abnormalities.[7]
- **Leukocyte adhesion deficiency-1 (D):** Caused by mutations in the CD18 integrin gene (ITGB2), presenting with delayed umbilical cord separation, absent pus formation, and leukocytosis — not associated with albinism or giant granules.[1]

Would you like to explore the management of Chediak-Higashi syndrome, including the role and timing of hematopoietic stem cell transplantation?

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Question 929

A 74-year-old man has been treated for prostate cancer for the past 6 months. He is on an experimental drug (drug X) that is used to reduce the action of testosterone by blocking the androgen receptor. Since the initiation of therapy, the growth of the cancerous tissue has slowed. This medication is known to be excreted by the kidneys at the current dose that he is taking. The patient has no significant complaints, except for excessive sweating at times. On physical examination, a small area of tissue around his nipples is enlarged bilaterally. No other abnormal findings are present. Which of the following drugs most likely belongs to be the same class as drug X?

Answer Choices:

(A) Leuprolide
(B) Finasteride
(C) Flutamide
(D) Anastrozole

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/6f768944-1b0c-47ad-bb07-b7041c965a02

OpenEvidence Explanation

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The correct answer is **C. Flutamide**.

Drug X is described as an **androgen receptor antagonist** — it blocks the androgen receptor to reduce the action of testosterone on prostate cancer cells. **Flutamide** is a nonsteroidal antiandrogen that works by the same mechanism: competitively blocking the binding of testosterone and dihydrotestosterone to the androgen receptor in target tissues.[1][2][3]

The clinical clues in the vignette are consistent with antiandrogen therapy:

- **Gynecomastia** (bilateral periareolar tissue enlargement): Nonsteroidal antiandrogens block the androgen receptor without suppressing testosterone levels. Testosterone continues to be aromatized to estrogen, and with androgen signaling blocked, the relative estrogenic effect causes gynecomastia — a well-known side effect occurring in 49–66% of patients on nonsteroidal antiandrogen monotherapy.[4][5]
- **Excessive sweating (hot flashes)**: A recognized vasomotor side effect of androgen deprivation therapy, reported in up to 61% of patients on flutamide-containing regimens.[3]
- **Renal excretion and slowed tumor growth**: Consistent with the pharmacologic profile of an antiandrogen used in prostate cancer.

The other options act by different mechanisms:

- **Leuprolide (A)** is a GnRH agonist that suppresses testosterone production via pituitary downregulation — it does not block the androgen receptor.[6][7]
- **Finasteride (B)** is a 5-alpha reductase inhibitor that blocks conversion of testosterone to dihydrotestosterone — it does not block the androgen receptor itself.[7][8]
- **Anastrozole (D)** is an aromatase inhibitor used in breast cancer that blocks estrogen synthesis — it has no direct effect on the androgen receptor.

Would you like to explore the differences in side effect profiles and clinical outcomes between first-generation (flutamide, bicalutamide, nilutamide) and second-generation (enzalutamide, apalutamide, darolutamide) antiandrogens?

Relevant images

(CONTENT OMITTED)

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Question 932

A 64-year-old male presents to his primary care physician with a complaint of bilateral knee pain that has been present for the past several years but has worsened recently. He reports pain with climbing stairs and with extended walks of greater than 100 yards. The pain worsens with activity throughout the day and is alleviated by periods of rest. He states that he has minimal morning stiffness, lasting approximately 5-10 minutes after waking up most days. Physical examination reveals tenderness to palpation of the bony structures on the medial aspect of the bilateral knees as well as crepitus and a decreased range of motion, limited at the extremes of flexion and extension. Both knee joints are cool to touch and exhibit bony enlargement upon palpation of the medial joint line. Which of the following studies would be indicated for further work-up of this patient's presenting condition?

Answer Choices:

(A) Complete blood count (CBC)
(B) Erythrocyte sedimentation rate (ESR)
(C) MRI of the knee
(D) No further work-up needed

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/8611b26e-5983-419a-ac22-dad0d51234e6

OpenEvidence Explanation

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The correct answer is **D. No further work-up needed**. This patient's presentation is classic for knee osteoarthritis (OA), which can be diagnosed clinically without additional laboratory tests or imaging.

Why no further work-up is needed: According to the NICE guidelines and multiple international consensus statements, OA can be diagnosed clinically without investigations in patients aged ≥45 years presenting with activity-related joint pain and morning stiffness lasting less than 30 minutes.[1][2] This patient meets all of these criteria: he is 64 years old, has bilateral activity-related knee pain that worsens with use and improves with rest, and has brief morning stiffness (5–10 minutes). Physical examination findings of crepitus, bony enlargement, and restricted range of motion are cardinal signs of knee OA, with bony enlargement being 95% specific for the diagnosis.[3]

Why the other options are incorrect:

- **A (CBC) and B (ESR):** There are no blood or urine tests to diagnose osteoarthritis. Laboratory tests such as CBC and ESR are nonspecific and are only indicated when an inflammatory arthropathy or other diagnosis is suspected — for example, prolonged morning stiffness (>30 minutes), joint warmth/erythema, or resting pain. This patient's cool joints, brief stiffness, and mechanical pain pattern argue against an inflammatory process.[1][4][5]
- **C (MRI of the knee):** MRI is seldom indicated in the assessment of knee OA. It is reserved for rare circumstances such as persistent mechanical symptoms with objective locking (suggesting a displaced meniscal tear), or suspicion of conditions like subchondral insufficiency fracture, tumor, or infection. This patient has no such red-flag features.[3][4]

Would you like to explore the evidence-based first-line management strategies for knee osteoarthritis, including the comparative effectiveness of nonpharmacologic and pharmacologic interventions?

Relevant images

(CONTENT OMITTED)

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Question 934

A 76-year-old man presents to the physician because of dyspepsia and weight loss over the past 6 months. He has no history of any serious illnesses and takes no medications. A diagnostic workup including endoscopy and biopsy shows gastric adenocarcinoma. Before further workup and staging, the biopsy results are discussed with the patient. He refuses any type of life-prolonging treatment, including chemotherapy, radiation, or surgery, but he requests appropriate palliative care without any significant burden of healthcare costs. Regarding this patient's eligibility for hospice care, what is the most appropriate next step?

Answer Choices:

(A) A trial of life-extending treatment
(B) Determining patient's life-expectancy without treatment
(C) Establishing the presence of metastasis
(D) No further steps are required because the patient already qualifies for hospice care

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/b33486b7-6efb-42c1-8f57-6ba30ba64e55

OpenEvidence Explanation

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The answer is **B. Determining patient's life-expectancy without treatment**.

Under the Medicare Hospice Benefit, the key eligibility criterion is that the patient's primary physician and the hospice medical director must certify that the patient has an **expected life expectancy of 6 months or less** if the disease follows its expected course.[1][2][3] The patient meets the other requirements — he has a terminal diagnosis (gastric adenocarcinoma) and is willing to forgo curative/life-prolonging treatments. However, before he can qualify for hospice, his life expectancy without treatment must be determined.

Why the other options are incorrect:

- **A (Trial of life-extending treatment):** Hospice does not require that a patient first attempt life-prolonging therapy. Patients may elect hospice if they choose to forgo curative treatments, as this patient has done.[1][4]
- **C (Establishing the presence of metastasis):** Metastatic disease is not a prerequisite for hospice eligibility. The criterion is a prognosis of ≤6 months, regardless of whether the cancer is localized or metastatic.[5][6]
- **D (No further steps required):** A diagnosis of gastric adenocarcinoma alone does not automatically qualify a patient for hospice. Without staging and prognostic assessment, it is not possible to certify that life expectancy is ≤6 months — some early-stage gastric cancers, even without treatment, may have a life expectancy exceeding 6 months.[2][6]

Since this patient has refused all life-prolonging treatment, the next appropriate step is to complete staging and prognostic workup to estimate his life expectancy without treatment. If the prognosis is ≤6 months, two physicians can certify hospice eligibility, and the patient can be enrolled.[6][7]

Would you like to explore the specific prognostic tools and staging criteria used to estimate life expectancy in untreated gastric adenocarcinoma?

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Question 936

A 23-year-old woman presents to the emergency department with abdominal pain. The patient states she has pain in the right side of her abdomen which started yesterday and has been worsening. She has experienced a few episodes of vomiting and diarrhea during this time. The patient has a past medical history of constipation which is treated with fiber supplements. Her temperature is 99.5°F (37.5°C), blood pressure is 110/68 mmHg, pulse is 110/min, respirations are 17/min, and oxygen saturation is 98% on room air. On physical exam, you note a young woman who appears to be in pain. Cardiopulmonary exam is within normal limits. Abdominal exam is notable for right lower quadrant pain that is reproducible when the left lower quadrant is palpated. The patient is given morphine. Which of the following is the next best step in management?

Answer Choices:

(A) Abdominal radiograph
(B) ß-hCG
(C) CT scan
(D) Stool occult blood

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/245e8a87-de9b-4221-a193-213665ea8d43

OpenEvidence Explanation

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The correct answer is **B. β-hCG**.

In any **woman of reproductive age** presenting with acute abdominal or pelvic pain, obtaining a **β-hCG test to rule out pregnancy (including ectopic pregnancy) is the essential first step** before proceeding with imaging or other workup.[1][2][3]

Why this matters clinically:

The presentation — right lower quadrant (RLQ) pain, vomiting, low-grade fever, tachycardia, and a positive **Rovsing sign** (RLQ pain reproduced by palpation of the left lower quadrant) — is classic for **acute appendicitis**. However, in young women of reproductive age, the most common misdiagnoses for appendicitis include ectopic pregnancy, pelvic inflammatory disease, ruptured ovarian cyst, and urinary tract infection.[4] Ectopic pregnancy is responsible for approximately **6% of maternal deaths** in early pregnancy and is misdiagnosed at the initial visit in up to 40% of cases.[2][5]

Why β-hCG must come before CT:

- A positive β-hCG would shift the differential toward ectopic pregnancy or other pregnancy-related complications and would make **transvaginal ultrasound** the preferred next imaging modality rather than CT.[1][2]
- Knowledge of pregnancy status is critical before ordering CT due to **fetal radiation exposure** concerns.[1]
- A negative β-hCG essentially excludes intrauterine and ectopic pregnancy, allowing the clinician to proceed confidently with CT for suspected appendicitis.[1]

The other options — abdominal radiograph (A), CT scan (C), and stool occult blood (D) — may have roles later in the workup but are not the appropriate **next** step before pregnancy status is established.

Would you like to explore the diagnostic accuracy and optimal imaging strategy for suspected appendicitis in young women after pregnancy has been excluded?

Relevant images

(CONTENT OMITTED)

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Question 938

A 44-year-old obese African-American male presents to clinic with complaints of 3 days of fatigue and dark urine. He has had several similar episodes since birth, all of which resolved spontaneously. He has a 5-year history of poorly controlled type II diabetes mellitus and was started on glipizide one week ago. Prior to the episode, he felt well without any upper respiratory or gastrointestinal symptoms. He predominantly eats fast food, although he tried a new Lebanese restaurant about one month ago. Which of the following is the most likely cause of this patient's symptoms?

Answer Choices:

(A) Bacterial Infection
(B) Food
(C) Medication
(D) Idiopathic

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/ed65f44f-4464-4c12-94c8-aff75c1bf5f1

OpenEvidence Explanation

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The most likely cause of this patient's symptoms is **C. Medication** — specifically, **glipizide** (a sulfonylurea) triggering an acute hemolytic episode in the setting of likely **glucose-6-phosphate dehydrogenase (G6PD) deficiency**.

Key reasoning:

The clinical picture — an **African-American male** with **recurrent episodes of fatigue and dark urine since birth** that resolve spontaneously — is classic for **G6PD deficiency**, an X-linked enzymopathy that is one of the most common genetic disorders worldwide, with high prevalence in populations of African descent.[1][2] Most G6PD-deficient individuals are asymptomatic at baseline but develop acute hemolytic anemia when exposed to oxidative stressors, presenting with fatigue, jaundice, and hemoglobinuria (dark urine).[2][3]

The temporal relationship is critical: the patient was **started on glipizide one week ago**, and symptoms began 3 days ago. Sulfonylureas, including glibenclamide (glyburide) and glipizide, have historically been listed as potentially hemolysis-inducing in G6PD-deficient patients.[4][5] While a large real-world study found that sulfonylureas were prescribed safely to many G6PD-deficient patients without major hemolysis requiring hospitalization, the traditional teaching and the temporal association in this vignette point to the medication as the trigger.[6]

Why not the other options?

- **A. Bacterial infection** — No preceding infectious symptoms (no URI, no GI illness), making infection an unlikely trigger.[2]
- **B. Food** — Fava beans (found in Lebanese cuisine) are a well-known trigger for G6PD hemolysis (favism), and the Lebanese restaurant visit is a deliberate distractor. However, that meal was **one month ago**, far outside the typical 24–72 hour window for fava bean–induced hemolysis. The temporal association with glipizide initiation is much stronger.[1][7]
- **D. Idiopathic** — While some hemolytic episodes in G6PD deficiency have no identifiable trigger, the clear temporal relationship with a new medication makes an idiopathic designation inappropriate here.

Would you like to discuss the workup for confirming G6PD deficiency or alternative diabetes management strategies for this patient?

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Question 939

A 32-year-old woman comes to the physician because of fatigue and joint pain for the past 4 months. Examination shows erythema with scaling on both cheeks that spares the nasolabial folds and two 1-cm ulcers in the oral cavity. Further evaluation of this patient is most likely to show which of the following findings?

Answer Choices:

(A) Decreased lymphocyte count
(B) Increased platelet count
(C) Increased prothrombin time
(D) Decreased gamma globulin

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/cc45ba69-ed31-4850-8df2-e898c4d53133

OpenEvidence Explanation

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The correct answer is **A. Decreased lymphocyte count**.

This clinical vignette describes a young woman with classic features of **systemic lupus erythematosus (SLE)**: fatigue, joint pain, a malar rash (erythema with scaling on both cheeks sparing the nasolabial folds), and oral ulcers. The acute

cutaneous lupus rash is characteristically described as erythema over the malar eminences that **spares the nasolabial folds**.[1][2]

Why decreased lymphocyte count is correct:

Leukopenia — primarily **lymphopenia** — is one of the most common hematologic abnormalities in SLE, occurring in approximately 22% to 42% of patients.[2] Lymphopenia is included in the EULAR/ACR 2019 classification criteria for SLE as part of the hematologic domain.[1] Autoantibodies directed against lymphocytes and complement-mediated destruction contribute to this finding.[3]

Why the other options are incorrect:

- **B. Increased platelet count** — SLE causes **thrombocytopenia** (decreased platelets), not thrombocytosis, affecting approximately 20% of patients.[2]
- **C. Increased prothrombin time** — While antiphospholipid antibodies in SLE can prolong the aPTT (via lupus anticoagulant), the PT is not characteristically increased. Antiphospholipid antibodies cause a paradoxical thrombotic tendency despite the in vitro prolongation of aPTT.[2]
- **D. Decreased gamma globulin** — SLE is characterized by **hypergammaglobulinemia** due to polyclonal B-cell activation and autoantibody production, not decreased gamma globulin.[2]

Would you like to explore the specific autoantibody profiles in SLE and their associations with particular clinical manifestations?

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Question 940

A 66-year-old male with a history of myocardial infarction presents to your primary care office with complaints of dyspnea on exertion and swollen feet and ankles. On exam, you note an elevated JVP and 2+ pitting edema of bilateral lower extremities. What is the most likely explanation for this patient's lower extremity edema?

> **Answer Choices:**
>
> (A) Increase in capillary pressure
> (B) Decrease in plasma proteins
> (C) Increase in capillary permeability
> (D) Increase in interstitial fluid pressure

> **Correct Answer:**
>
> **(A)**
>
> **OpenEvidence Response:**
>
> **(A)** ✓

OpenEvidence Link: https://openevidence.com/ask/0e3d31c5-b33b-4897-ba6e-96e3a0540ff8

OpenEvidence Explanation

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The correct answer is **A. Increase in capillary pressure**.

This patient's presentation — history of myocardial infarction, dyspnea on exertion, elevated JVP, and bilateral lower extremity pitting edema — is classic for **congestive heart failure** with volume overload. The primary mechanism

driving peripheral edema in this setting is **increased capillary hydrostatic pressure** resulting from elevated central venous pressure (CVP).

Pathophysiology in heart failure: Impaired cardiac output following myocardial infarction leads to neurohormonal activation, renal salt and water retention, and expansion of intravascular volume. This raises venous pressures throughout the circulatory system, which in turn increases capillary hydrostatic pressure.[1] According to the Starling equation, this elevated hydrostatic pressure drives increased fluid filtration from capillaries into the interstitial space, exceeding the capacity of the lymphatic system to drain it, resulting in clinically apparent edema.[2][3]

The elevated JVP in this patient directly reflects the elevated right-sided filling pressures that are transmitted backward to the peripheral venous and capillary beds.[4][5] Jugular venous distension is one of the most sensitive signs of congestion in heart failure and a reliable indicator of high intravascular volume.[4]

Why not the other options?

- **B (Decrease in plasma proteins)** — This mechanism causes edema in conditions like nephrotic syndrome, cirrhosis, or malnutrition, not in heart failure with elevated JVP.[4]
- **C (Increase in capillary permeability)** — This is the primary mechanism in inflammatory states (e.g., sepsis, burns, anaphylaxis). While some increase in vascular permeability occurs in chronic heart failure due to systemic inflammation, it is not the predominant mechanism.[2]
- **D (Increase in interstitial fluid pressure)** — Increased interstitial hydrostatic pressure would actually oppose edema formation, not cause it. Edema forms when interstitial pressure is low relative to capillary hydrostatic pressure.[3]

The following figure illustrates the Starling forces governing fluid exchange across capillary walls, including capillary hydrostatic pressure (Pc), which is the key driver of edema in heart failure.

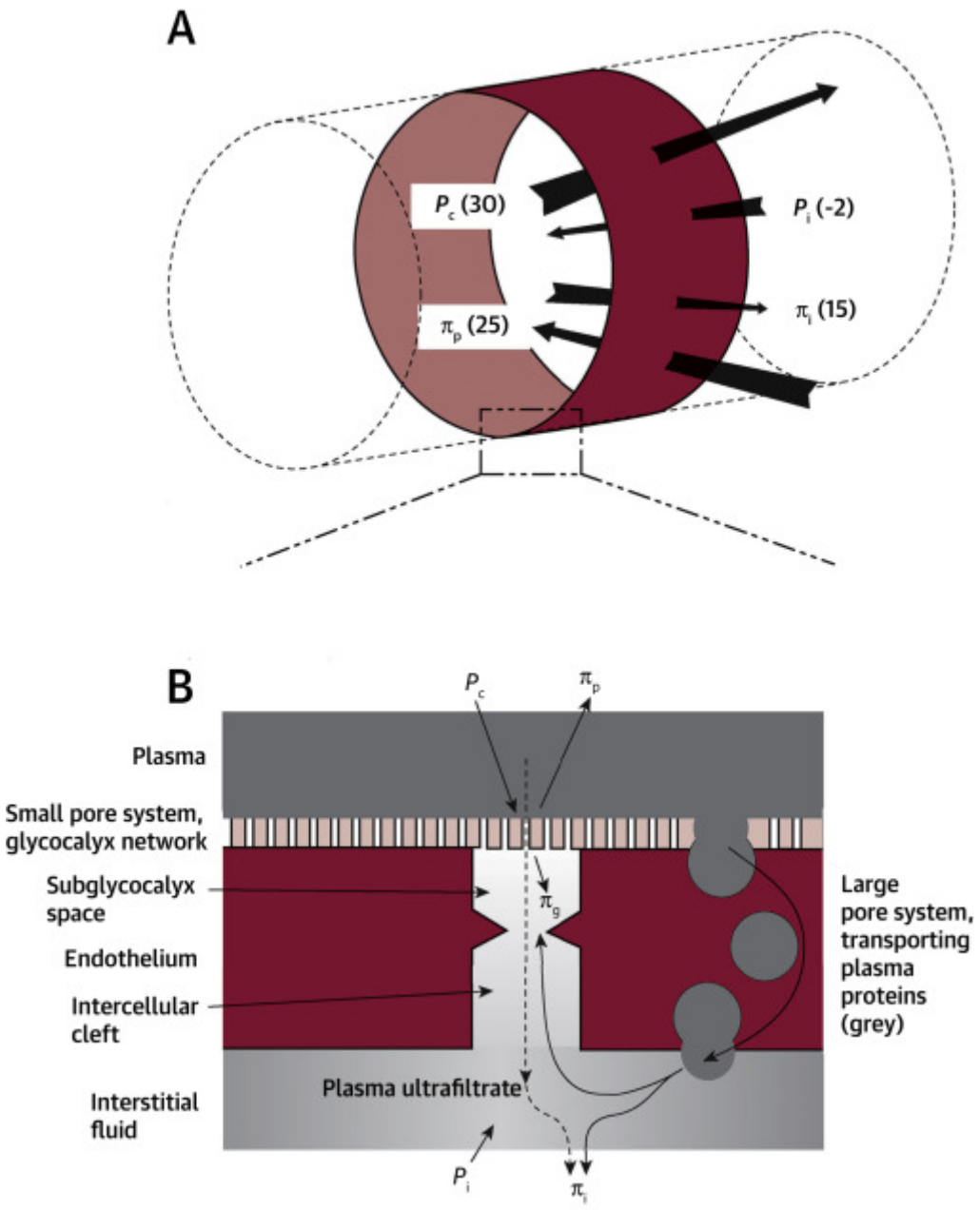


Figure 2. Fluid Efflux Is Determined by Starling Principle

Would you like to explore how the Starling forces differ across organ systems in heart failure, particularly the mechanisms behind pulmonary versus peripheral edema?

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Question 941

A 49-year-old man comes to the physician for a routine health maintenance examination. He feels well and has no history of serious illness. He has smoked one pack of cigarettes daily for the past 25 years and drinks two to three glasses of wine weekly. This patient should be counseled about increased risk for which of the following conditions?

Answer Choices:

(A) Pancreatic adenocarcinoma
(B) Esophageal varices
(C) Porcelain gallbladder
(D) Hepatic steatosis

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/e5692b2b-7ec1-4ef3-b755-bb0b0775a46d

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OpenEvidence Explanation

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The correct answer is **A. Pancreatic adenocarcinoma**. Cigarette smoking is the **leading modifiable risk factor** for pancreatic cancer, with a relative risk of approximately 1.8 (95% CI 1.7–1.9) in current smokers compared with never smokers.[1][2] This patient's 25-pack-year smoking history places him at significantly elevated risk.

A comprehensive meta-analysis of 78 studies demonstrated that pancreatic cancer risk sharply increases even with a low number of cigarettes per day and after only a few years of smoking, with risk rising to an RR of approximately 2.2 for those smoking up to 30 cigarettes/day.[2] Notably, the association may be even stronger in younger individuals (age <60), with one study reporting a hazard ratio of 2.82 for smoking in this age group.[3] Approximately **20–21% of all pancreatic cancer deaths are attributable to smoking**.[1][4]

Regarding the other answer choices:

- **Esophageal varices (B)** result from portal hypertension, most commonly due to cirrhosis. This patient's modest alcohol intake (2–3 glasses of wine weekly) is well below the threshold associated with liver disease and would not warrant specific counseling about varices.
- **Porcelain gallbladder (C)** is a calcification of the gallbladder wall, historically associated with gallbladder carcinoma. It is not a recognized consequence of smoking.
- **Hepatic steatosis (D)** is associated with obesity, metabolic syndrome, diabetes, and heavy alcohol use. This patient's low-level alcohol consumption does not confer meaningful risk for this condition.

Smoking cessation counseling is critical, as the risk of pancreatic cancer decreases after quitting — approaching that of never smokers after approximately 15–20 years of cessation.[5][6]

Would you like to explore the current evidence on smoking cessation interventions and their impact on reducing pancreatic cancer risk over time?

Relevant images

(CONTENT OMITTED)

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Question 942

A 40-year-old woman comes to the physician because of a 6-month history of difficulty sleeping and fatigue. Menses occur at irregular 35- to 50-day intervals and last 3–7 days. Her last menstrual period was 5 weeks ago. She has had an unintentional 10-kg (22-lb) weight gain over this period. She also reports decreased sexual desire and increased hair growth on her face and arms. There is no personal or family history of serious illness. She appears lethargic. Her temperature is 37°C (98.6°F), pulse is 80/min, and blood pressure is 150/90 mm Hg. Physical examination shows central obesity, increased pigmented hair over the chin and upper lip, and purple stretch marks on the abdomen. She has a prominent hump of fat over the base of the dorsum of her neck and decreased proximal muscle tone and strength. Serum studies show:
Na+ 154 mEq/L
K+ 2.8 mEq/L
Cl- 103 mEq/L
HCO3- 30 mEq/L
Creatinine 0.9 mg/dL
Glucose 236 mg/dL
ACTH 2 pg/mL (N = 7–50)
Which of the following is the most appropriate treatment for this patient?

Answer Choices:

(A) Adrenalectomy
(B) Polychemotherapy and radiation therapy
(C) Transsphenoidal hypophysectomy
(D) Partial nephrectomy

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/2329cd2d-82db-444f-b8b2-26d69af9ff37

OpenEvidence Explanation

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The correct answer is **A. Adrenalectomy**.

This patient presents with classic features of **Cushing syndrome** — central obesity, moon facies (implied), dorsal fat pad ("buffalo hump"), purple striae, proximal myopathy, hirsutism, oligomenorrhea, hypertension, hyperglycemia, hypokalemia, and hypernatremia with metabolic alkalosis. The critical lab finding is a **suppressed ACTH level (2 pg/mL)**, which localizes the source to an **ACTH-independent (adrenal) etiology**, most likely a cortisol-producing adrenal adenoma or, less commonly, adrenal carcinoma or bilateral adrenal hyperplasia.

Why adrenalectomy? When ACTH is suppressed, the hypercortisolism is driven by autonomous adrenal cortisol production. Laparoscopic adrenalectomy is the established treatment for unilateral benign cortisol-producing adrenal adenomas and is associated with low morbidity (3%–7%) and mortality (~0.5%).[1] The Endocrine Society guidelines recommend unilateral resection by an experienced adrenal surgeon for all cases of benign unilateral adrenal disease, and bilateral adrenalectomy for bilateral adrenal disorders.[2]

Why not the other options?

- **Transsphenoidal hypophysectomy (C)** is first-line for Cushing *disease* (ACTH-secreting pituitary adenoma), which presents with elevated or inappropriately normal ACTH — not suppressed ACTH.[1][2]
- **Polychemotherapy and radiation therapy (B)** would be considered for adrenocortical carcinoma or ectopic ACTH-secreting malignancies, but this is not the primary surgical treatment for a cortisol-producing adrenal lesion.

- **Partial nephrectomy (D)** is not relevant to the management of Cushing syndrome.

Would you like to explore the diagnostic workup for differentiating adrenal adenoma from adrenocortical carcinoma in ACTH-independent Cushing syndrome?

Relevant images

(CONTENT OMITTED)

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Question 943

A scientist observes a myocyte beating in cell culture. Which step is the most direct necessary component of relaxation for this cell?

Answer Choices:

(A) Influx of sodium ions
(B) Influx of calcium ions from the sacroplasmic reticulum
(C) Influx of calcium ions from outside the myocyte
(D) Efflux of calcium ions

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/f3ac6d98-39da-4d44-96f3-a82b2e306354

OpenEvidence Explanation

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The answer is **D. Efflux of calcium ions**.

Cardiac myocyte relaxation depends on the **removal of calcium ions from the cytoplasm**. During contraction, cytosolic calcium rises and binds troponin C, enabling actin-myosin cross-bridge formation. For relaxation to occur, this

calcium must be actively removed from the cytoplasm through two principal mechanisms:[1][2][3]

1. **SERCA2a** (sarcoplasmic/endoplasmic reticulum Ca^{2+} -ATPase) pumps calcium back into the sarcoplasmic reticulum — this accounts for ~70–92% of calcium removal depending on species.

2. **Na^{+} /Ca^{2+} exchanger (NCX)** on the sarcolemma extrudes calcium out of the cell entirely, accounting for ~7–30% of removal.

Both of these represent **efflux** of calcium from the cytoplasm (either into the SR or out of the cell), which reduces cytosolic calcium concentration, causes calcium to dissociate from troponin C, and allows tropomyosin to re-cover the myosin binding sites on actin — thereby terminating contraction.[4][5]

The other options describe components of contraction initiation rather than relaxation: sodium influx (option A) drives the action potential upstroke, and calcium influx from the SR (option B) and from outside the cell (option C) are the triggers for contraction via calcium-induced calcium release.[6][7]

Would you like to explore how impaired calcium reuptake (e.g., reduced SERCA2a activity or phospholamban dysregulation) contributes to diastolic dysfunction in heart failure?

Relevant images

(CONTENT OMITTED)

References

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Question 947

A 7-year-old girl is brought to the physician by her mother for a well-child examination. The mother reports that she had her first menstrual period 1 week ago. She has no history of serious illness. Immunizations are up-to-date. Physical examination shows Tanner stage 3 breast development and pubic hair. Without treatment, this patient is at greatest risk for which of the following as an adult?

Answer Choices:

(A) Delayed skeletal maturity
(B) Short stature
(C) Genu varum
(D) Coarse facial features

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/08c284f6-ce3b-4372-9643-9ef29b663dc9

OpenEvidence Explanation

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The answer is **B. Short stature**.

This 7-year-old girl with menarche, Tanner stage 3 breast development, and pubic hair has **central precocious puberty** (CPP), defined as onset of secondary

sexual characteristics before age 8 in girls. Without treatment, the greatest long-term risk is **short adult stature** due to premature epiphyseal fusion from early estrogen exposure.

Mechanism: Early activation of the hypothalamic-pituitary-gonadal axis leads to elevated estrogen levels, which accelerate skeletal maturation and cause premature closure of the growth plates. Although these children are initially tall for their age, the early fusion of epiphyses curtails the total duration of linear growth, resulting in reduced final adult height.[1][2] In older series of untreated patients, mean adult heights in girls ranged from **150 to 154 cm**, corresponding to a loss of approximately 12 cm compared with normal adult height.[2] Height loss is inversely correlated with the age at onset of puberty — the earlier the onset, the greater the compromise in adult stature.[2]

> "In older published series of untreated patients, mean heights ranged from 151 to 156 cm in boys and from 150 to 154 cm in girls, corresponding to a loss of about 20 cm in boys and 12 cm in girls as compared with normal adult height."
>
> —Jean-Claude Carel, M.D. et al., INSERM Unité 690 and other institutions. Precocious Puberty. N Engl J Med. May 29, 2008.
>
> Used under license from The New England Journal of Medicine.

Why not the other options:

- **A. Delayed skeletal maturity** — The opposite occurs; precocious puberty causes *advanced* skeletal maturity with accelerated bone age.
- **C. Genu varum** — This is associated with rickets, Blount disease, or physiologic bowing, not precocious puberty.
- **D. Coarse facial features** — This is characteristic of conditions such as mucopolysaccharidoses or acromegaly, not precocious puberty.

GnRHa treatment in CPP has been shown to improve adult height by approximately **+2.7 cm** on average compared to untreated controls, with greater benefit when initiated at younger ages.[3][4]

Would you like to explore the current guidelines on when to initiate GnRH agonist therapy versus observation in girls presenting with early puberty between ages 6 and 8?

Relevant images

(CONTENT OMITTED)

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Question 949

A 61-year-old man comes to the emergency department because of a 2-day history of a productive cough and worsening shortness of breath. He has had frequent episodes of a productive cough over the past 3 years. He had smoked 2 packs of cigarettes daily for 30 years but quit 1 year ago. He appears distressed. Pulse oximetry on room air shows an oxygen saturation of 91%. Chest auscultation reveals diffuse wheezes and coarse crackles. A chest x-ray shows increased lung lucency bilaterally and flattening of the diaphragm. Which of the following is the most appropriate initial pharmacotherapy?

Answer Choices:

(A) Prednisone and albuterol
(B) Albuterol and montelukast
(C) Prednisone and tiotropium
(D) Albuterol and theophylline

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/950a24b0-dfcf-40bc-b3b5-0909aa30dc55

OpenEvidence Explanation

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The correct answer is **A. Prednisone and albuterol**.

This patient presents with a classic **acute exacerbation of COPD** — a 60-pack-year smoking history, chronic productive cough, hypoxemia (SpO_2 91%), diffuse wheezes and crackles, and chest x-ray findings of hyperinflation (increased lucency, diaphragmatic flattening). The cornerstone of initial pharmacotherapy for a COPD exacerbation is a **short-acting beta$_2$-agonist (albuterol)** combined with **systemic corticosteroids (prednisone)**.

The 2026 GOLD guidelines recommend short-acting inhaled beta$_2$-agonists as the initial bronchodilator for acute exacerbations, along with systemic corticosteroids (40 mg prednisone daily for 5 days), which improve lung function, oxygenation, and shorten recovery time and hospitalization duration.[1][2] An NEJM review similarly confirms that therapy includes short-acting inhaled beta$_2$-agonists and systemic glucocorticoids, with 5 days of prednisone 40 mg being as effective as longer courses.[3]

Why the other options are incorrect:

- **B. Albuterol and montelukast** — Montelukast is a leukotriene receptor antagonist used in asthma; it has no established role in COPD exacerbation management.
- **C. Prednisone and tiotropium** — Tiotropium is a long-acting muscarinic antagonist (LAMA) used for maintenance COPD therapy, not acute exacerbation management. Short-acting bronchodilators (SABAs) are the recommended initial bronchodilators in an exacerbation.[1][2]
- **D. Albuterol and theophylline** — Methylxanthines (theophylline) are explicitly **not recommended** for COPD exacerbations due to increased side effect profiles, and this combination omits the critical systemic corticosteroid component.[2]

Would you like to explore the evidence-based criteria for when to add antibiotics during a COPD exacerbation?

Relevant images

(CONTENT OMITTED)

References

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Question 953

A 70-year-old man presents to the Emergency Department after 3 days of shortness of breath, orthopnea, and lower limb edema. His personal history is significant for a myocardial infarction 6 years ago that required revascularization and hypertension. His medication consists of simvastatin and lisinopril. In the ED, he has a blood pressure of 100/80 mm Hg, a pulse of 88/min, a respiratory rate of 28/min, and a temperature of 36.5°C (97.7°F). On physical examination, he has jugular vein distention, displaced point of maximal impulse (PMI), an S4-gallop, a holosystolic murmur, and 2+ pitting edema up to the mid calf. He is started on furosemide, carvedilol, and oxygen therapy. After 6-hours of continued therapy, his blood pressure remains low, and his serum creatinine is found to be 1.9 mg/dL. Which of the following test would be more useful to differentiate between prerenal and intrinsic kidney disease?

Answer Choices:

(A) Sulfosalicylic acid test
(B) Urine sodium content
(C) Fractional excretion of urea (FEUrea)
(D) Nitrates in urine

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/a6fb9b98-b5db-44f8-872a-3d770d6d26f4

OpenEvidence Explanation

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The correct answer is **C. Fractional excretion of urea (FEUrea)**.

The key clinical detail in this scenario is that the patient is **actively receiving furosemide** (a loop diuretic). This is critical because diuretics directly interfere with sodium-based markers used to differentiate prerenal from intrinsic AKI.

Why FEUrea is preferred here:

Urine sodium content (option B) and fractional excretion of sodium (FENa) are traditionally used to distinguish prerenal azotemia (FENa <1%, urine sodium <20 mEq/L) from intrinsic renal disease such as acute tubular necrosis (FENa >1%). However, **diuretics decrease sodium reabsorption and artificially increase urinary sodium excretion and FENa**, rendering these markers unreliable. A meta-analysis found that in patients on diuretics, FENa specificity dropped to just **54%** for differentiating prerenal from intrinsic AKI.[1]

In contrast, urea reabsorption is primarily dependent on passive forces and is **not significantly modified by diuretic use**.[2][3] The landmark study by Carvounis et al. demonstrated that while only 48% of diuretic-treated prerenal patients had a FENa <1%, **89% of the same group had a FEUrea <35%**.[3] FEUrea was essentially identical in prerenal patients regardless of diuretic exposure (27.9% vs. 24.5%), while ATN patients had markedly higher values (58.6%).[3] A 2026 meta-analysis of 12 studies (1,240 patients) confirmed that in the diuretic-only subgroup, FEUrea specificity rose to **0.87**.[4]

Why the other options are incorrect:

- **A. Sulfosalicylic acid test** — detects proteinuria (including non-albumin proteins like Bence Jones); not used to differentiate prerenal from intrinsic AKI.
- **B. Urine sodium content** — unreliable in patients receiving diuretics, as furosemide increases urinary sodium excretion regardless of the underlying etiology.[1][2]

- **D. Nitrates in urine** — used to detect urinary tract infections (bacterial conversion of nitrates to nitrites); irrelevant to AKI differentiation.

Would you like to explore the optimal management approach for cardiorenal syndrome in this patient, including strategies for diuretic resistance and hemodynamic optimization?

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Question 954

A 26-year-old Caucasian woman is admitted to the emergency department after 4 days of fever, malaise, vomiting, and nausea for which she has been taking ibuprofen and diclofenac. She has also noticed a decrease in urination. Her family and past medical history are unremarkable. Her temperature is 38.2°C (100.7°F), blood pressure is 118/76 mm Hg, heart rate is 74/min, and respiratory rate is 15/min. Upon physical examination, her mucous membranes are moist and she has no abdominal tenderness. Four hours after admission, she has a urinary output < 0.3 mL/kg/h and laboratory tests significant for the following:
Differential blood count
White blood cells 8.1 x 109/L
Neutrophils 4.8 x 109/L
Lymphocytes 2.1 x 109/L
Eosinophils 0.9 x 109/L
Monocytes 0.3 x 109/L
Basophils 0.04 x 109/L
Serum creatinine (SCr) 1.9 mg/dL
Blood urea nitrogen (BUN) 25 mg/dL
Na+ 135 mEq/L
K+ 5.4 mEq/L
Cl- 106 mEq/L
Urine dipstick
Urine density 1.010
pH 6.2
Red blood cells per field of high power 2
WBC casts Present
Which of the following skin manifestations would you also expect to find in this patient?

Answer Choices:

(A) Janeway lesions
(B) Diffuse maculopapular rash

(C) Malar rash
(D) Erythema nodosum

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/c8dad6a2-3038-4af4-807f-f757a37219f0

OpenEvidence Explanation

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The answer is **B. Diffuse maculopapular rash**.

This clinical presentation is consistent with **drug-induced acute interstitial nephritis (AIN)**, caused by NSAID use (ibuprofen and diclofenac). The key findings supporting this diagnosis include:

- **Acute kidney injury** (elevated creatinine, oliguria) in the setting of recent NSAID use
- **Peripheral eosinophilia** (eosinophils 0.9 × 10^9/L, elevated)
- **WBC casts** in the urine, characteristic of interstitial nephritis[1][2]
- **Fever, malaise, nausea, and vomiting** — nonspecific systemic symptoms seen in AIN[3][4]

The classical triad of drug-induced AIN includes **fever, skin rash, and eosinophilia**.[3] The skin manifestation associated with this hypersensitivity reaction is a **diffuse maculopapular (morbilliform) rash**, which results from a

type IVb hypersensitivity reaction mediated by eosinophilic inflammation via CD4+ and Th2 pathways.[2] While this full triad is seldom present (particularly with NSAID-induced AIN, which classically has fewer hypersensitivity features than antibiotic-induced AIN), among the answer choices, a diffuse maculopapular rash is the expected dermatologic finding.[5]

Why the other options are incorrect:

- **A. Janeway lesions** — painless erythematous lesions on palms/soles associated with infective endocarditis, not AIN
- **C. Malar rash** — butterfly rash characteristic of systemic lupus erythematosus
- **D. Erythema nodosum** — tender subcutaneous nodules associated with sarcoidosis, inflammatory bowel disease, and infections, not typical of drug-induced AIN

Would you like to explore the management approach for NSAID-induced AIN, including the role and timing of corticosteroid therapy?

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Question 955

A 59-year-old woman presents to the outpatient clinic for worsening symptoms of congestive heart failure. She states that while she used to be able to go for short walks, she is no longer able to do so. Now, even simple tasks like getting ready in the morning have become burdensome for her. When she gets tired, sitting down helps to alleviate her symptoms. Her blood pressure is 136/92 mm Hg and heart rate is 76/min. On physical examination, she has regular heart sounds but does have 1+ pitting edema to her bilateral lower extremities. What is her New York Heart Association Functional Classification for congestive heart failure?

Answer Choices:

(A) New York Heart Association Class IIa
(B) New York Heart Association Class IIb
(C) New York Heart Association Class III
(D) New York Heart Association Class IV

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/9ac62270-5140-4508-a222-0b324f57fd74

OpenEvidence Explanation

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The correct answer is **C. New York Heart Association Class III**.

The NYHA functional classification is an ordinal system (Classes I–IV) — notably, there are no subclasses "IIa" or "IIb," which makes options A and B invalid designations.[1][2][3]

This patient's presentation fits **NYHA Class III**, defined as **marked limitation of physical activity; comfortable at rest, but less than ordinary activity causes symptoms of heart failure**.[2][3] Key clinical features supporting this classification:

- She was previously able to take short walks but can no longer do so, indicating worsening functional capacity.
- Simple activities of daily living (e.g., getting ready in the morning) now produce symptoms — these are "less than ordinary" activities.
- She is **comfortable at rest** — sitting down alleviates her symptoms, which distinguishes Class III from Class IV.

NYHA Class IV, by contrast, describes patients who are **unable to perform any physical activity without symptoms or who have symptoms at rest**.[4][5] This patient clearly improves with rest, ruling out Class IV.

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Computed value for NYHA Functional Class: Class III

Computed value for Description: Marked limitation of physical activity; comfortable at rest; less than ordinary activity causes fatigue, palpitation, or dyspnea.

Computed value for Class Number: 3

Would you like to explore the guideline-directed medical therapy recommendations that differ based on NYHA functional class, particularly for patients with Class III heart failure?

References

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Question 956

A 36-year-old woman comes to the physician for intermittent stabbing face pain. The pain typically occurs in waves of several individual episodes lasting about one second. It is bilateral, but rarely occurs on both sides simultaneously. Touching her face or brushing her teeth can trigger an attack. Four months ago, she had an episode of weakness in her right arm that lasted for about a week. Family history is notable for migrainous headaches in her mother and brother. Vital signs are within normal limits. There is decreased sensation in the V2 and V3 distribution of her face bilaterally. Muscle strength is 3/5 in the left upper extremity and 5/5 in the right upper extremity. There is spasticity of the lower extremities with sustained clonus. Further evaluation is most likely going to reveal which of the following findings?

Answer Choices:

(A) Multiple periventricular sclerotic plaques
(B) Erythematous papules in the V2/V3 nerve distribution
(C) Photophobia and phonophobia
(D) Rhinorrhea, lacrimination, and ptosis

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/be350899-d49a-43d6-882f-6039f321a14a

OpenEvidence Explanation

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The answer is **A. Multiple periventricular sclerotic plaques**.

This presentation is classic for **multiple sclerosis (MS)** with secondary trigeminal neuralgia. Several key features point to this diagnosis:

- **Trigeminal neuralgia in a young patient**: The intermittent stabbing facial pain lasting about one second, triggered by touching the face or brushing teeth, is characteristic of trigeminal neuralgia. In a 36-year-old woman, this raises strong suspicion for secondary trigeminal neuralgia due to MS rather than classical (vascular compression) trigeminal neuralgia, which typically presents in patients over age 50.[1]

- **Bilateral involvement with facial sensory loss**: Patients with MS-related trigeminal neuralgia are more likely to have bilateral pain and sensory loss compared to classical trigeminal neuralgia. The decreased sensation in V2/V3 bilaterally is consistent with demyelinating plaques affecting the trigeminal fascicle in the ventral pons.[1]

- **Dissemination in time and space**: The episode of right arm weakness four months ago represents a prior clinical attack in a different CNS location, and the current left upper extremity weakness (3/5) and lower extremity spasticity with sustained clonus indicate upper motor neuron lesions — fulfilling the MS diagnostic requirement of dissemination in both time and space.[2][3]

- **Upper motor neuron signs**: Spasticity and sustained clonus in the lower extremities indicate corticospinal tract involvement, consistent with demyelinating plaques in the spinal cord or periventricular white matter.[3]

MRI in MS characteristically shows **periventricular white matter plaques** (hyperintense on T2/FLAIR sequences) in over 90% of patients, along with lesions in juxtacortical, infratentorial, and spinal cord regions.[2][4] The risk of trigeminal neuralgia is increased 20-fold in MS patients compared to the general population.[1]

The other options are incorrect: erythematous papules (B) would suggest herpes zoster (shingles); photophobia and phonophobia (C) suggest migraine; rhinorrhea, lacrimation, and ptosis (D) suggest trigeminal autonomic cephalalgias

such as cluster headache — none of which explain the multifocal neurological deficits seen here.

Would you like to explore the current evidence on first-line disease-modifying therapies for relapsing-remitting MS and how trigeminal neuralgia management differs in the MS population?

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Question 958

A 61-year-old man presents to the clinic with complaints of excessive thirst, frequent urination, and partial visual loss in both eyes for 1 day. His family history is significant for type 2 diabetes mellitus in his mother and cousin. His weight is 112 kg (246.9 lb), height 187 cm (6 ft 1 in), blood pressure: 150/90 mm Hg, heart rate: 89/min, respiratory rate: 14/min, and temperature: 36.7°C (98.4°F). The physical examination is significant for dry skin, a pustular rash over the patient's shoulders and back, an accentuated second heart sound (S2) best heard in the second intercostal space at the right sternal border, and distal loss of vibration sensitivity in both feet. A fundoscopic examination shows small red dots in the superficial retinal layers suggestive of microaneurysms. The HbA1c is 9% and the urinalysis shows the following:
Color Pale yellow (light/pale-to-dark/deep amber)
Clarity Cloudy
pH 6.6
Specific gravity 1.010
Glucose 199 mg/dl
Ketones None
Nitrites Negative
Leukocyte esterase Negative
Bilirubin Negative
Urinary bilirubin Traces
Red blood cells 3 RBCs
Protein 120 mg/d
RBCs ≤ 2 RBCs/hpf
WBCs 22 WBCs/hpf
Epithelial cells 27 squamous epithelial cells/hpf
Casts 5 hyaline casts/lpf
Crystals Occasional
Bacteria None
Yeast Present
Which of the following statements best describes the cause of this patient's glucosuria?

Answer Choices:

(A) There is a disruption of primary active transport of glucose in the proximal renal tubules
(B) Secondary active transporters fail to completely reabsorb glucose in the renal tubules
(C) There is a disruption of passive transport of the glucose in the proximal renal tubules
(D) Glucosuria results from increased glomerular filtration rate

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/67a5a902-6746-41b2-b3a9-a84ea4bd1c0b

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OpenEvidence Explanation

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The correct answer is **B. Secondary active transporters fail to completely reabsorb glucose in the renal tubules**.

This patient presents with uncontrolled type 2 diabetes (HbA1c 9%, obesity, family history, diabetic retinopathy with microaneurysms, peripheral neuropathy, and proteinuria). The glucosuria (urine glucose 199 mg/dL) results from hyperglycemia exceeding the kidney's maximum reabsorptive capacity for glucose.

Mechanism of renal glucose reabsorption and glucosuria:

Glucose reabsorption in the proximal tubule is mediated by **sodium-glucose cotransporters (SGLT2 and SGLT1)**, which are **secondary active transporters**. These cotransporters move glucose against its concentration gradient by coupling it to sodium, which moves down its electrochemical gradient. This sodium gradient is maintained by the basolateral Na^+ /K^+ ATPase (the primary active transporter).[1][2] SGLT2 in the S1 segment handles ~90% of glucose reabsorption, while SGLT1 in the S2/S3 segments handles the remaining ~10%.[1][3]

Under normal conditions, all filtered glucose (~180 g/day) is completely reabsorbed. However, when plasma glucose exceeds the renal threshold (~180–200 mg/dL), the filtered glucose load surpasses the maximum tubular reabsorptive capacity (TmG, ~375 mg/min), and the **secondary active transporters become saturated and fail to completely reabsorb glucose**, resulting in glucosuria.[1][2][3]

Why the other options are incorrect:

- **A (primary active transport):** Glucose reabsorption via SGLTs is secondary active transport, not primary. The Na^+ /K^+ ATPase on the basolateral membrane is the primary active transporter, but it transports sodium and potassium — not glucose directly.[1][2]
- **C (passive transport):** Glucose entry from the tubular lumen into epithelial cells via SGLTs is an active process coupled to sodium, not passive. Passive transport (via GLUT2) occurs only on the basolateral side when glucose exits the cell into the blood.[1]
- **D (increased GFR):** While diabetic hyperfiltration can increase the filtered glucose load, glucosuria fundamentally results from the filtered load exceeding tubular reabsorptive capacity — not from increased GFR per se. Moreover, in diabetes, the TmG is actually increased (maladaptive upregulation of SGLT2), which would counteract any GFR-related effect.[3][4]

Would you like to explore how SGLT2 inhibitors therapeutically exploit this mechanism to lower blood glucose in type 2 diabetes?

Relevant images

(CONTENT OMITTED)

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Question 959

A 65-year-old male presents to his primary care physician for stiffness in his arm. He states that he has been having trouble combing his hair and reaching objects that are high on the shelf. The patient has a past medical history of diabetes mellitus type II, obesity, and hypertension. His current medications include metformin, insulin, lisinopril, and hydrochlorothiazide. The patient admits to leading a sedentary life in which he tends to stay home and watch television. He does not engage in any physical or strenuous activity. On physical exam the patient has decreased passive and active range of motion of his shoulder. Strength of the patient's upper extremity is 4/5. Which of the following is the most likely diagnosis?

Answer Choices:

(A) Rotator cuff impingement
(B) Adhesive capsulitis
(C) Glenohumeral osteoarthritis
(D) Subacromial bursitis

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/8cda2646-37ce-4406-8fb7-063b96d920dc

OpenEvidence Explanation

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The most likely diagnosis is **B. Adhesive capsulitis** (frozen shoulder).

This presentation is classic for adhesive capsulitis based on several key features:

Decreased passive and active range of motion is the hallmark finding. Adhesive capsulitis is defined by global restriction of both active and passive glenohumeral joint movements, which distinguishes it from other shoulder pathologies.[1][2][3] The patient's difficulty with overhead activities (combing hair, reaching high shelves) reflects the characteristic loss of motion in multiple planes.

Diabetes mellitus is a strong risk factor. Meta-analyses demonstrate that patients with diabetes have approximately **3.7 times higher odds** of developing adhesive capsulitis compared to non-diabetic individuals.[4][5] Poor long-term glycemic control further increases this risk in a dose-dependent fashion.[6]

Sedentary lifestyle and immobility contribute to capsular contracture, and the patient's age (65 years) falls within the typical demographic (40–65 years).[4]

Why not the other options?

- **Rotator cuff impingement (A):** Typically presents with a painful arc during active abduction (60–120°) but preserved passive range of motion, since the capsule itself is not restricted.[7]
- **Glenohumeral osteoarthritis (C):** Also causes restricted motion, but would be expected to show crepitus on exam and radiographic joint space narrowing. The APTA guidelines note that GHOA diagnosis should include radiographic confirmation.[8]
- **Subacromial bursitis (D):** Presents primarily with pain (especially with overhead activities) rather than true loss of passive range of motion. Passive motion is generally preserved when pain is controlled.[7]

The combination of **global restriction of both active and passive motion**, **diabetes**, and **sedentary lifestyle** in a middle-aged to older adult makes adhesive capsulitis the most likely diagnosis.[1][2][9]

Would you like to explore the evidence-based management approach for adhesive capsulitis in diabetic patients, including the role of corticosteroid injections versus physical therapy?

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Question 960

A 52-year-old man presents to the clinic with a headache and dizziness for the past month. The patient reports that about 4 weeks ago he developed a "nagging" headache. He thought he had a cold, so he tried over the counter ibuprofen that provided only mild and temporary relief. Recently, he also started feeling dizzy and nauseous, which only resolves when he steps outside to shovel the snow. The patient's medical history is significant for hypertension, type II diabetes mellitus, and asthma. His medications include amlodipine, metformin, glimepiride, and a fluticasone/salmeterol inhaler. The patient has been living at his upstate cabin for the past 5 weeks but denies other recent travel. He denies smoking tobacco or illicit drug use. The patient's temperature is 99°F (37.2°C), blood pressure is 130/78 mmHg, pulse is 72/min, and respirations are 16/min with an oxygen saturation of 98% on room air. The patient is currently asymptomatic while sitting in the office, and physical examination is unremarkable. Labs are drawn, as shown below:

Hemoglobin: 20 g/dL
Hematocrit: 60%
Leukocyte count: 10,050 cells/mm^3 with normal differential
Platelet count: 350,000/mm^3

Which of the following underlies the patient's most likely diagnosis?

Answer Choices:

(A) Medication side effect
(B) Myeloproliferative neoplasm
(C) Neuronal hyperexcitability
(D) Toxic exposure

Correct Answer:

(D)

OpenEvidence Response:

> **(D)** ✓

OpenEvidence Link: https://openevidence.com/ask/61323dbe-5e0e-4133-9d4f-5c80146b942b

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OpenEvidence Explanation

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The answer is **D. Toxic exposure**, specifically chronic carbon monoxide (CO) poisoning from a faulty heating system at the patient's upstate cabin.

Several key clinical clues point to this diagnosis:

- **Symptoms resolve outdoors**: The headache, dizziness, and nausea improve when the patient steps outside to shovel snow, which removes him from the CO source and exposes him to fresh air. CO has an elimination half-life of approximately 5 hours in room air but decreases to 85 minutes with high-flow oxygen.[1]
- **Temporal association**: Symptoms began 4 weeks ago, coinciding with his 5-week stay at the cabin during winter, when heating systems are in heavy use. Faulty furnaces and inadequately ventilated heating sources are among the most common causes of CO exposure.[2][3]
- **Nonspecific flu-like symptoms**: The patient initially attributed his headache to a "cold." CO poisoning is frequently misdiagnosed because it presents with nonspecific symptoms such as headache, dizziness, nausea, and fatigue that mimic viral illness.[4]
- **Polycythemia** (hemoglobin 20 g/dL, hematocrit 60%): Chronic CO exposure causes secondary polycythemia. CO binds hemoglobin with >200 times the affinity of oxygen, forming carboxyhemoglobin and shifting the oxyhemoglobin dissociation curve leftward, which impairs oxygen delivery. The resulting chronic tissue hypoxia stimulates erythropoietin production and compensatory erythrocytosis.[2][5][6]

Why not the other options?

- **A (Medication side effect)**: None of his medications (amlodipine, metformin, glimepiride, fluticasone/salmeterol) cause polycythemia or this symptom pattern.
- **B (Myeloproliferative neoplasm)**: Polycythemia vera would present with an elevated platelet count and leukocytosis more typically, and symptoms would not resolve with going outdoors. The normal WBC differential and the clear environmental exposure pattern argue against this.
- **C (Neuronal hyperexcitability)**: This would suggest a seizure disorder or migraine, neither of which explains the polycythemia or the symptom resolution pattern tied to leaving the cabin.

Would you like to explore the diagnostic workup and management of chronic carbon monoxide poisoning, including the role of carboxyhemoglobin levels and hyperbaric oxygen therapy?

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Question 962

A 19-year-old female presents to the emergency room with 6 days of lower abdominal pain. She states that her symptoms have progressed and she now feels feverish as well. She also notes an episode of nonbloody diarrhea 2 days ago and has been increasingly nauseous. While being evaluated in the emergency room, she vomits three times. The patient has no significant past medical history but was recently treated with ciprofloxacin for an uncomplicated urinary tract infection. She also notes irregular periods, with a last menstrual period 6 weeks ago. She is a college student who has had 3 sexual partners in the last year with inconsistent use of barrier protection. Her temperature is 100.5°C (38.1°F), blood pressure is 102/68 mmHg, pulse is 97/min, and respirations are 14/min. On exam, the patient is noticeably uncomfortable. There is marked tenderness to palpation in the suprapubic region and right lower quadrant, with voluntary guarding but no rebound. Pelvic exam shows moderate purulent discharge in the vaginal vault, cervical motion tenderness, and a tender adnexal mass on the right side. Which of the following is the best next step in treating this patient's condition?

Answer Choices:

(A) Intramuscular ceftriaxone and oral doxycycline with outpatient follow-up
(B) Intravenous cefotetan and doxycycline with inpatient admission
(C) Oral vancomycin with outpatient follow-up
(D) Methotrexate with outpatient follow-up

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/6ce70dc8-16b6-4377-a2e5-edabf5feaf9f

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OpenEvidence Explanation

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The best next step is **B. Intravenous cefotetan and doxycycline with inpatient admission**.

This patient presents with pelvic inflammatory disease (PID) complicated by a likely **tubo-ovarian abscess** (TOA), evidenced by fever, purulent cervical discharge, cervical motion tenderness, and a tender adnexal mass. Several features mandate inpatient parenteral therapy rather than outpatient management:

Why inpatient parenteral antibiotics are required:

- The presence of a **tubo-ovarian abscess** is a clear indication for hospitalization per CDC STI Treatment Guidelines. The CDC recommends >24 hours of inpatient observation for women with TOA.[1][2]
- Additional indications for hospitalization in this case include **severe illness with inability to tolerate oral medications** (she is actively vomiting), and the need to exclude competing diagnoses such as appendicitis (right lower quadrant pain, fever).[3][4]
- **IV cefotetan plus doxycycline** is one of the CDC's recommended parenteral regimens for PID, providing broad-spectrum coverage against gram-positive, gram-negative, and anaerobic organisms.[1][3]

Why the other options are incorrect:

- **A (IM ceftriaxone + oral doxycycline, outpatient):** This is the standard outpatient regimen for mild-to-moderate PID without complications. It is inappropriate here given the TOA, vomiting (inability to take oral medications), and severity of illness.[3]

- **C (Oral vancomycin):** This has no role in PID treatment. Oral vancomycin is used for *Clostridioides difficile* colitis, not pelvic infections.
- **D (Methotrexate):** This is used for ectopic pregnancy, not PID/TOA. While the 6-week LMP raises ectopic pregnancy as a consideration, the clinical picture (purulent discharge, cervical motion tenderness, fever) is classic for PID with TOA, and a pregnancy test would need to be obtained before considering ectopic pregnancy management.

Would you like to explore the approach to differentiating tubo-ovarian abscess from ectopic pregnancy in patients with adnexal masses and a missed menstrual period?

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Question 965

A 52-year-old woman presents to the emergency department due to severe pain of her first metatarsophalangeal (MTP) joint. This pain started acutely, and she describes the pain as sharp. Her medical history is significant for obesity, hypertension, inflammatory bowel disease, and extensive alcohol use. She takes a number of medications but does not remember what they are. On physical exam, her right first MTP joint appears warm, swollen, erythematous, and exquisitely painful to the touch. After resolution of this acute episode, the patient is started on a drug to prevent recurrence of the symptoms. One month later on follow-up, she is found to have pancytopenia. Which of the following describes the mechanism of the drug most likely prescribed in this case?

Answer Choices:

(A) Antibody to soluble factor
(B) Inhibitor of microtubule polymerization
(C) Inhibitor of proximal tubule reabsorption
(D) Inhibitor of xanthine oxidase

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/2b7ac515-c4fb-43bd-902d-2912125b49cf

OpenEvidence Explanation

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The answer is **D. Inhibitor of xanthine oxidase**.

However, this question requires careful analysis because there is a nuanced interplay between the clinical scenario and the answer choices. Here is the reasoning:

The presentation — acute, severe pain of the first MTP joint with warmth, swelling, and erythema — is classic for **acute gout** (podagra). After resolution of the acute episode, the patient was started on a drug to **prevent recurrence**, and one month later developed **pancytopenia**.

Key clinical clue: the patient has inflammatory bowel disease (IBD). Several medications used for IBD are CYP3A4 or P-glycoprotein inhibitors, which can dramatically increase colchicine levels and cause life-threatening myelosuppression.[1][2][3] Additionally, IBD medications such as azathioprine/6-mercaptopurine (thiopurines) are themselves metabolized by xanthine oxidase. When **allopurinol** (a xanthine oxidase inhibitor) is co-administered with a thiopurine, it blocks thiopurine metabolism, leading to accumulation of active thiopurine metabolites and resulting in severe **pancytopenia**.[4]

This makes the most likely scenario:

- The patient is on **azathioprine or 6-mercaptopurine** for her IBD (she "does not remember" her medications)
- She was started on **allopurinol** (first-line urate-lowering therapy for gout prophylaxis)[4][5]
- Allopurinol inhibited xanthine oxidase, blocking thiopurine metabolism, causing **pancytopenia**

Allopurinol works by **inhibiting xanthine oxidase**, the enzyme that converts hypoxanthine to xanthine and xanthine to uric acid, thereby reducing serum urate levels.[4]

Why not the other choices?

- **A (Antibody to soluble factor)** — Refers to agents like canakinumab (anti-IL-1β); not first-line for gout prophylaxis[6]

- **B (Inhibitor of microtubule polymerization)** — This is colchicine's mechanism. While colchicine can cause pancytopenia, the question specifies a drug started to "prevent recurrence" (i.e., urate-lowering therapy), and the IBD medication interaction with allopurinol better explains the pancytopenia[2][7]

- **C (Inhibitor of proximal tubule reabsorption)** — Refers to uricosuric agents like probenecid; not typically associated with pancytopenia

Would you like to explore the specific drug interaction between allopurinol and thiopurines, including recommended dose adjustments when co-administration is necessary?

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Question 967

A 16-year-old girl comes to the emergency department because of left wrist pain and swelling for 5 hours. She fell on an outstretched hand while playing basketball. She ignored it initially as she thought it was just a bruise, but the pain and swelling worsened throughout the day. The analgesic spray she used did not provide adequate relief. There is no family history of serious illness. Her only medication is an oral contraceptive pill. Her immunizations are up-to-date. She appears anxious. Her temperature is 37.1°C (99°F), pulse is 88/min, and blood pressure is 118/72 mm Hg. Examination shows a swollen and tender left wrist; range of motion is limited. The anatomical snuffbox is tender to palpation. The grip strength of the left hand is decreased. The thumb can be opposed towards the other fingers. Finkelstein's test is negative. X-rays of the wrist shows no abnormalities. Which of the following is the most appropriate next best step in management?

Answer Choices:

(A) Corticosteroid injections
(B) Thumb spica cast and repeat x-rays in 2 weeks
(C) Rest, ice, and repeat x-rays in 2 weeks
(D) Percutaneous pinning

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/a268509b-2d40-41af-b506-368ac9eab528

OpenEvidence Explanation

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The correct answer is **B. Thumb spica cast and repeat x-rays in 2 weeks**.

This presentation is classic for a **suspected occult scaphoid fracture**: fall on an outstretched hand (FOOSH), anatomical snuffbox tenderness, decreased grip strength, and normal initial radiographs. Up to **16% of scaphoid fractures are missed on initial plain radiographs**.[1] The standard management when clinical suspicion is high but radiographs are negative is **empiric immobilization in a thumb spica cast with repeat imaging at 2 weeks**, at which point bone resorption at the fracture site may make the fracture line visible.[1][2]

Why the other options are incorrect:

- **A. Corticosteroid injections** — These have no role in acute fracture management and could impair bone healing.
- **C. Rest, ice, and repeat x-rays in 2 weeks** — While rest and ice are supportive, they do not provide adequate immobilization. An untreated scaphoid fracture is at risk for **nonunion and avascular necrosis** due to the scaphoid's retrograde blood supply. Immobilization with a thumb spica cast is essential to prevent displacement and promote healing.[1]
- **D. Percutaneous pinning** — Surgical fixation is not indicated when no fracture has been confirmed. Even confirmed nondisplaced scaphoid waist fractures are typically managed with cast immobilization first, with surgery reserved for displaced fractures, proximal pole fractures, or nonunion.[3][4]

It is worth noting that more recent evidence supports early advanced imaging (MRI or CT) as a cost-effective alternative to empiric casting, as it can confirm or exclude fracture immediately and reduce unnecessary immobilization.[5][6] However, among the answer choices provided, thumb spica cast with repeat imaging at 2 weeks remains the most appropriate option.

Would you like to explore the comparative effectiveness of early MRI versus empiric immobilization for suspected occult scaphoid fractures?

References

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Question 968

A 46-year-old man comes to the physician with a 1-week history of yellowish discoloration of his eyes, generalized fatigue, and pruritus. He was diagnosed with ulcerative colitis 7 years ago. At the time of diagnosis, a pANCA test was also positive. Physical examination shows scleral icterus and multiple scratch marks on the trunk and extremities. Abdominal examination is unremarkable. Serum studies show a total bilirubin concentration of 3.2 mg/dL, direct bilirubin concentration of 2.5 mg/dL, and alkaline phosphatase level of 450 U/L. Magnetic resonance cholangiopancreatography shows focal areas of intrahepatic bile duct strictures alternating with areas of dilation. Histologic examination of a liver biopsy specimen is most likely to show which of the following findings?

Answer Choices:

(A) Periductal concentric scarring and fibrosis
(B) Periportal lymphocytic infiltration and piecemeal necrosis
(C) Irregular ductal glands lined by atypical and pleomorphic cells
(D) Ductopenia and fibrotic degeneration of periportal hepatocytes

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/50f19b0d-3d37-4919-b8fd-f16f2267ba42

OpenEvidence Explanation

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The answer is **A. Periductal concentric scarring and fibrosis**.

This clinical presentation — a middle-aged man with **ulcerative colitis**, positive **pANCA**, cholestatic jaundice (elevated direct bilirubin and alkaline phosphatase at 450 U/L), pruritus, and MRCP showing **alternating intrahepatic bile duct strictures and dilation** — is classic for **primary sclerosing cholangitis (PSC)**.

The histological hallmark of PSC is **concentric "onion-skin" periductal fibrosis**, in which layers of connective tissue concentrically surround and obliterate bile ducts.[1][2][3] While this finding is actually seen in fewer than 40% of needle biopsies due to the patchy distribution of disease, it remains the most characteristic and nearly pathognomonic histologic feature.[4][5][6]

The following figure illustrates the progressive histopathologic changes in PSC, including the classic onion-skin periductal fibrosis:

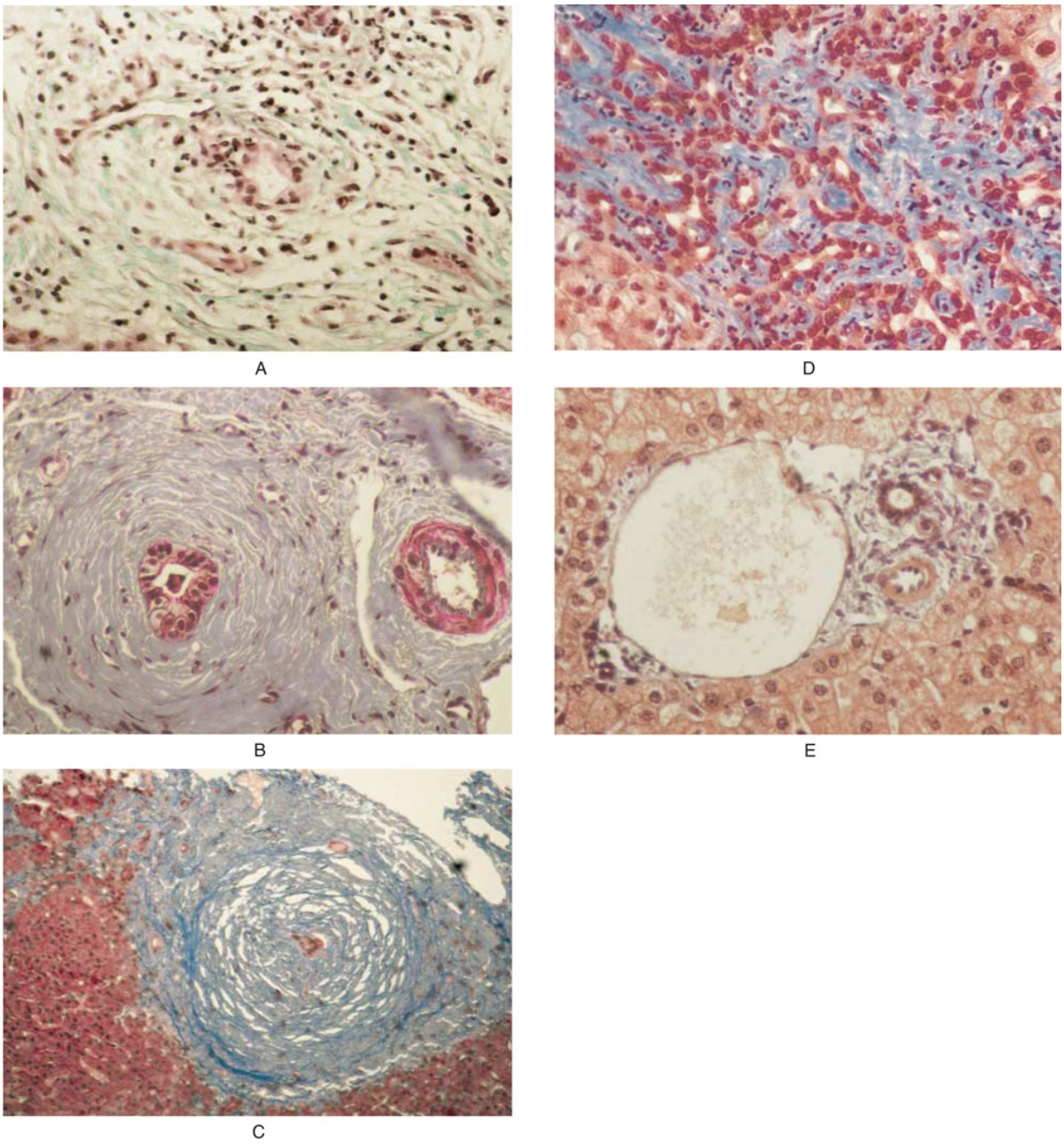


Figure 1. Lesions in Primary Sclerosing Cholangitis.

Used under license from The New England Journal of Medicine.

Why the other options are incorrect:

- **B. Periportal lymphocytic infiltration and piecemeal necrosis** — This describes interface hepatitis, characteristic of **autoimmune hepatitis**, not PSC.
- **C. Irregular ductal glands lined by atypical and pleomorphic cells** — This describes **cholangiocarcinoma**, a feared complication of PSC but not the expected biopsy finding in this presentation.

- **D. Ductopenia and fibrotic degeneration of periportal hepatocytes** — Ductopenia with granulomatous destruction of bile ducts is more characteristic of **primary biliary cholangitis (PBC)**, which predominantly affects women and is associated with anti-mitochondrial antibodies, not pANCA.[8]

Would you like to explore the surveillance strategies for cholangiocarcinoma in patients with PSC, given the significantly elevated cancer risk in this population?

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Question 970

A 67-year-old man presents with feelings of nervousness and anxiety. He mentions that lately, he has been feeling increasingly restless and is unable to control feelings of nervousness pertaining to all his daily tasks. He noticed that these feelings were more prominent in the last 2 months but have been present on and off for the last year. On many occasions, his mind will be racing with thoughts that keep him up at night. During these moments, he finds his heart racing and feels light-headed and dizzy to the point of blacking out. He has also been experiencing back and neck pain with increased muscle tension in these areas. The patient reports no smoking or alcohol use but mentions that he had tried cocaine and heroin in his 20s and 30s. Which of the following would be the best course of treatment for this patient's symptoms?

Answer Choices:

(A) Diazepam
(B) Ramelteon
(C) Buspirone
(D) Alprazolam

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/de2ba423-a93c-4d7a-b362-877f7ed87154

OpenEvidence Explanation

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The best course of treatment is **C. Buspirone**.

This patient presents with classic features of **generalized anxiety disorder (GAD)**: persistent, uncontrollable worry across multiple domains for over 6 months, accompanied by restlessness, racing thoughts, insomnia, muscle tension, and somatic symptoms (back/neck pain). The critical detail guiding medication selection is the **history of cocaine and heroin use**.

Why buspirone is the best choice:

- Buspirone is an azapirone anxiolytic with FDA approval for GAD. It has demonstrated **no potential for abuse or diversion**, causes neither tolerance nor physical/psychological dependence, and is not a controlled substance. In clinical studies, volunteers with a history of recreational drug use could not distinguish buspirone from placebo, whereas they showed a preference for diazepam.[1][2]

- It is effective for GAD specifically, with efficacy demonstrated in network meta-analyses alongside SSRIs/SNRIs, and is recommended as a second-line or adjunctive agent in major treatment guidelines.[3][4]

Why the other options are inferior here:

- **Diazepam (A) and Alprazolam (D)** are benzodiazepines. While efficacious for anxiety, they carry significant risks of **dependence, misuse, and withdrawal** — risks that are amplified in a patient with a prior substance use history. Guidelines recommend benzodiazepines be avoided in patients with current or past substance use disorders. Additionally, benzodiazepines in elderly patients increase fall risk and cognitive impairment.[3][5][6][7]

- **Ramelteon (B)** is a melatonin receptor agonist approved for insomnia, not for the treatment of GAD.

The following table from a JAMA review summarizes pharmacologic options for anxiety disorders, highlighting the distinction between first-line agents and those with abuse potential:

Table 3. Overview of Pharmacologic Therapy for Anxiety Disorders[a]

Class	Example medications	Typical class adverse effects[b]	Select safety and use considerations[b]
First-line therapy			
Selective serotonin reuptake inhibitors (SSRIs)	Citalopram Escitalopram Fluoxetine Fluvoxamine Paroxetine Sertraline	Initial anxiety and jitteriness, nausea, dyspepsia, diarrhea, drowsiness or insomnia, palpitations, headache, sweating, increased or decreased appetite Weight gain and sexual dysfunction SSRI discontinuation symptoms with abrupt withdrawal	Class warning suicidality (<24 y) Caution in epilepsy, cardiac arrhythmia/QTc prolongation (citalopram dose limitations), angle closure glaucoma, bleeding, hepatic impairment, hyponatremia, syndrome of inappropriate antidiuretic hormone secretion, risk hypomania/mania with monotherapy bipolar Varying effects by drug on drug metabolism and interactions including risk serotonin syndrome
Serotonin-norepinephrine reuptake inhibitors (SNRIs)	Duloxetine Venlafaxine extended release	Overlaps SSRI adverse effects, eg, nausea, dizziness, drowsiness, sedation, insomnia, headache, constipation, dry mouth SNRI discontinuation symptom risk	Overlaps SSRI class warnings as above Potential hypertensive effects, hepatic enzyme elevations
Second- or third-line therapy[c]			
Benzodiazepines	Alprazolam Clonazepam Diazepam Lorazepam	Drowsiness, sedation, dizziness, ataxia. Cognitive impairment, falls in elderly individuals Physiological dependence, withdrawal, interdose rebound (benefits longer acting more lipophilic agents)	Risk for misuse and dependence Consider substance use disorder history and age May interfere with cognitive behavioral therapy
Azapirones	Buspirone	Dizziness, drowsiness, nausea, headache	Evidence limited to generalized anxiety disorder as monotherapy Less effective if prior benzodiazepine use Serotonin syndrome interaction
Tricyclics	Clomipramine Doxepin Imipramine	Anticholinergic adverse effects Dry mouth, dizziness, sedation, drowsiness, orthostatic hypotension, headache, tremor, diaphoresis, weight gain, sexual dysfunction	Class warning suicidality (<24 y), risk mania in bipolar disorder Overdose lethality risk Cardiac conduction/QTc prolongation/arrhythmia risk, dose-related central nervous system depression, hyponatremia, falls, serotonin syndrome risk
Anticonvulsants	Gabapentin Pregabalin	Somnolence, dizziness, dry mouth, ataxia, fatigue, peripheral edema, weight gain	Class risk increased suicidal ideation and behavior Some misuse potential (especially if prior substance use disorder) and potential for abrupt discontinuation symptoms including anxiety[53]
Antihistamines	Hydroxyzine	Drowsiness/sedation, dry mouth, headache	Older studies with generalized anxiety disorder
β-blockers	Propranolol	Hypotension, dizziness, bradycardia	Use limited to as-needed use for performance anxiety only but minimal research; assess tolerability prior first event
Treatment refractory and/or comorbid conditions			
Monoamine oxidase inhibitors (MAOIs)	Phenelzine	Sedation or insomnia, orthostatic hypotension, gastrointestinal, headache Weight gain, sexual dysfunction	Class warning suicidality (<24 y) Low tyramine diet to prevent hypertensive crisis (with irreversible MAOIs, ie, phenelzine) High-risk drug interactions (risk hyperadrenergic crisis or serotonin syndrome) Use limited by risk profile
Atypical antipsychotics	Olanzapine Quetiapine Risperidone	Sedation, weight gain, hyperglycemia/diabetes/hyperlipidemia (metabolic syndrome), extrapyramidal (lower than first-generation antipsychotics, eg, 4% quetiapine meta-analysis)[54]	Use limited by adverse effect risk profiles

[a] This table considers data and/or recommendations from literature search (see the Methods section), including guidelines, meta-analyses, systematic reviews, UpToDate, Food and Drug Administration drug labels, and/or Micromedex.

[b] Adverse effect types, frequencies, and risks vary somewhat by drug within classes, across trials and disorders, and are not consistently reported for anxiety disorders in meta-analyses, trials, or drug labels. See specific drug labels/prescribing guidelines for more comprehensive details and special population considerations (eg, pregnancy, geriatric, hepatic or kidney impairment, cardiovascular disease).

[c] Recommendations are inconsistent in formally distinguishing second- and third-line agents across guidelines and meta-analyses.

Table 3. Overview of Pharmacologic Therapy for Anxiety Disordersa

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Would you like to explore the comparative efficacy and safety of buspirone versus SSRIs/SNRIs as treatment options for GAD in older adults?

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Question 971

Two hours after undergoing open cholecystectomy for complicated cholecystitis, a 48-year-old woman develops dizziness, lethargy, abdominal pain, and nausea. She has systemic lupus erythematosus and hypertension. Prior to hospitalization, her medications included nifedipine and prednisolone. Her pulse is 112/min and blood pressure is 90/64 mm Hg. Examination shows central obesity. The abdomen is soft and non-tender, and the laparoscopic incisions have no discharge. Her serum cortisol and serum ACTH are decreased. Which of the following additional findings is most likely in this patient?

Answer Choices:

(A) Normal anion gap metabolic acidosis
(B) Hyperkalemia
(C) Hyperglycemia
(D) Hyponatremia

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/66374111-13a8-4acd-a377-889178db00cb

OpenEvidence Explanation

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The answer is **D. Hyponatremia**.

This patient is presenting with an **adrenal crisis** (secondary/glucocorticoid-induced adrenal insufficiency) triggered by the physiological stress of surgery. The key clinical clues are:

- **Chronic prednisolone use** → hypothalamic-pituitary-adrenal (HPA) axis suppression
- **Central obesity** → cushingoid features from exogenous glucocorticoid use
- **Both cortisol and ACTH are low** → consistent with secondary or glucocorticoid-induced adrenal insufficiency (not primary, where ACTH would be elevated)
- **Postoperative hypotension, tachycardia, lethargy, nausea** → classic adrenal crisis presentation

Why hyponatremia? In secondary adrenal insufficiency, cortisol deficiency leads to impaired free water excretion via increased ADH (vasopressin) secretion, resulting in dilutional **hyponatremia**. This is the most common electrolyte abnormality in both primary and secondary adrenal insufficiency, occurring in up to 88% of cases.[1] Hyponatremia is reported in 4%–10% of patients with secondary adrenal insufficiency even at baseline, and is a hallmark of adrenal crisis across all subtypes.[2][3]

Why not the other options?

- **Hyperkalemia (B)** occurs in **primary** adrenal insufficiency due to aldosterone deficiency. In secondary/glucocorticoid-induced adrenal insufficiency, the renin-angiotensin-aldosterone axis remains intact, so aldosterone secretion is preserved and hyperkalemia does not occur.[3][4]
- **Normal anion gap metabolic acidosis (A)** is also primarily a feature of mineralocorticoid (aldosterone) deficiency in primary adrenal insufficiency, not secondary.
- **Hyperglycemia (C)** is the opposite of what occurs — cortisol deficiency impairs gluconeogenesis, predisposing to **hypoglycemia**, not hyperglycemia.[1][4]

Would you like to explore the perioperative stress-dose steroid protocols recommended for patients on chronic glucocorticoids undergoing surgery?

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Question 973

A 63-year-old female complains of weakness, light-headedness, palpitations, and soreness of the tongue. She has a past medical history of Hashimoto's thyroiditis. Her hematocrit is 29%. On peripheral blood smear, you notice neutrophils with 7 lobes and large oval-shaped red blood cells. On physical exam, you notice the patient has decreased position sense and a loss in vibratory sensation in her lower extremities. Which of the following is most likely present in this patient?

Answer Choices:

(A) Atrophy of G cells
(B) Anti-intrinsic factor antibodies
(C) Decreased methylmalonic acid levels
(D) Antithrombotic state

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/05b9ec8e-d15e-4199-813a-eccba0c49560

OpenEvidence Explanation

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The answer is **B. Anti-intrinsic factor antibodies**.

This clinical presentation is classic for **pernicious anemia**, an autoimmune condition in which anti-intrinsic factor antibodies impair vitamin B12 absorption. The key findings supporting this diagnosis include:

- **Megaloblastic anemia**: hematocrit of 29% with hypersegmented neutrophils (7 lobes) and oval macrocytes on peripheral smear[1][2]
- **Glossitis** (tongue soreness), a well-described mucosal manifestation of B12 deficiency[3]
- **Subacute combined degeneration**: decreased position sense and loss of vibratory sensation reflect demyelination of the dorsal columns of the spinal cord, characteristic of vitamin B12 deficiency[1][4]
- **Hashimoto's thyroiditis**: pernicious anemia and autoimmune thyroid disease frequently coexist as part of polyglandular autoimmune syndrome type IIIb, with approximately 10–40% of Hashimoto's patients having associated gastric autoimmunity[5][6]

Why the other options are incorrect:

- **A. Atrophy of G cells** — Pernicious anemia involves autoimmune destruction of **parietal cells** (not G cells). G cells produce gastrin and are actually stimulated (not atrophied) in pernicious anemia due to loss of acid-mediated negative feedback.[7]
- **C. Decreased methylmalonic acid levels** — Methylmalonic acid is **elevated** (not decreased) in B12 deficiency because B12 is a cofactor for L-methylmalonyl-CoA mutase; without it, methylmalonic acid accumulates.[1]
- **D. Antithrombotic state** — B12 deficiency causes hyperhomocysteinemia, which is associated with a **prothrombotic** (not antithrombotic) state.[1][2]

Anti-intrinsic factor antibodies are highly specific (>95%) for pernicious anemia, though they have limited sensitivity (~60–70%).[3][8] Anti-parietal cell antibodies are more sensitive (~90%) but less specific.[9]

Would you like to explore the diagnostic workup and management of pernicious anemia, including the role of methylmalonic acid and homocysteine levels in confirming B12 deficiency?

Relevant images

(CONTENT OMITTED)

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Question 974

A 45-year-old man presents to the doctor's office with shortness of breath, cough, and fatigue for 3 days. This has been progressively worsening. He has a medical history significant for chronic obstructive pulmonary disease and osteoarthritis. He takes albuterol, ipratropium and aspirin. He smoked 2 and a half packs per day, and had done so for the past 26 years. After ceasing tobacco use for 1 year, he has recently begun smoking again. The blood pressure is 138/88 mm Hg, the respiratory rate is 12/min, the heart rate is 76/min, and the pulse oximetry is 87% on room air. On physical examination, the patient appears disoriented and is only somewhat comprehensible. The pupils are equal, round, and reactive to light with extraocular movements intact. Cranial nerves VII-XII also intact. The auscultation of the heart is absent of murmur, rubs, or gallops. The auscultation of the lungs demonstrate audible rales in the bases bilaterally. Which of the stages of change is the patient currently experiencing based on the clinical vignette?

Answer Choices:

(A) Precontemplation
(B) Contemplation
(C) Maintenance
(D) Relapse

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/c549f983-b785-4f24-932e-b9a09d04eef9

OpenEvidence Explanation

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The correct answer is **D. Relapse**.

In the Transtheoretical Model (Stages of Change), this patient had previously progressed through the stages of change by successfully quitting smoking for **1 year**, which placed him in the **maintenance stage** (defined as sustained abstinence for more than 6 months).[1][2] However, he has now **resumed smoking**, which represents a return to the problematic behavior — this is the **relapse** stage.

The key clinical details supporting this are:

- He had a 26-year, 2.5 pack-per-day smoking history
- He successfully quit for 1 year (achieving maintenance)
- He has recently begun smoking again (relapse)

Why the other options are incorrect:

- **A. Precontemplation** — This stage describes individuals who are not thinking about quitting and are unaware of or discount the severity of their problem. There is no indication this patient was never aware of the need to quit; in fact, he previously quit successfully.[1][3]
- **B. Contemplation** — This stage describes individuals who are thinking about quitting within the next 6 months but have not committed to action. The vignette does not describe him as merely thinking about quitting.[1]
- **C. Maintenance** — This stage describes sustained abstinence for more than 6 months. While the patient was previously in this stage during his year of abstinence, he has now returned to smoking and is no longer maintaining cessation.[1][2]

The Transtheoretical Model recognizes that individuals may cycle through stages multiple times before achieving permanent cessation, and relapse is a common part of this process. Most individuals make an average of 3–4 quit attempts

before succeeding, and when they relapse, they typically move back to the contemplation or preparation stages.[4][5]

Would you like to explore evidence-based relapse prevention strategies and pharmacotherapy options for patients with COPD who resume smoking?

Relevant images

(CONTENT OMITTED)

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Question 975

A 28-year-old man reports to his physician that he is having second thoughts about his long-term compatibility with his wife ever since they relocated to a new city. He admits that he has noticed himself flirting with some of the female co-workers at his new workplace. When he goes on a dinner date with his wife after work one evening, he accuses her of giving their waiter flirtatious looks and asks her whether she has been cheating on him or trying to spend time with other men. The man's actions are most consistent with which of the following psychological defense mechanisms?

> **Answer Choices:**
>
> (A) Displacement
> (B) Dissociation
> (C) Projection
> (D) Repression

> **Correct Answer:**
>
> (C)
>
> **OpenEvidence Response:**
>
> (C) ✓

OpenEvidence Link: https://openevidence.com/ask/c2356d88-2ab8-422d-8e6f-bda2e555cb7d

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OpenEvidence Explanation

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The answer is **C. Projection**.

Projection is a defense mechanism in which an individual attributes their own unacceptable thoughts, feelings, or impulses to another person. In this scenario, the man is the one experiencing doubts about his marriage and flirting with female co-workers, yet he accuses his wife of being flirtatious with the waiter and questions her fidelity. He is unconsciously redirecting his own unacceptable desires onto his wife.

Why the other options are incorrect:

- **Displacement (A):** Involves redirecting emotions from a threatening target to a less threatening one (e.g., a man angry at his boss kicks his dog instead). The man here is not redirecting an emotion to a safer target — he is attributing his own behavior to his wife.
- **Dissociation (B):** Involves a disruption in consciousness, memory, identity, or perception as a way to avoid emotional distress (e.g., feeling detached from oneself during a traumatic event). There is no evidence of this here.
- **Repression (D):** Involves unconsciously blocking unacceptable thoughts or feelings from awareness entirely. While the man may not be fully aware of his motivations, the key feature of this vignette is the attribution of his impulses to his wife, which defines projection rather than simple repression.

Would you like to explore how projection and other defense mechanisms are classified along the spectrum of maturity (immature, neurotic, and mature defenses)?

Question 976

A 25-year-old, G2P2L2 woman presents with a complaint of missed menstrual cycle for 4 weeks. Her previous menstrual cycles were regular, occurring every 28–35 days consistently. The patient does not have any other complaints currently. Her past medical history reveals two uncomplicated and normal vaginal deliveries at term. She has a 2-year-old boy and a 6-month-old girl. The patient and her partner use the withdrawal method for contraception. The urine pregnancy test result is positive. The patient returns to the clinic after 1 week expressing her desire to discontinue with the pregnancy and inquires about the possibility of an elective abortion. Which of the following procedures is the most appropriate for elective termination of pregnancy in this patient?

Answer Choices:

(A) Dilatation and evacuation (D&E)
(B) Oxytocin-induced labor
(C) Manual uterine aspiration
(D) Oral mifepristone + misoprostol

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/49c62f1e-7bb4-4ec9-b604-89f7ece1af46

OpenEvidence Explanation

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The correct answer is **D. Oral mifepristone + misoprostol**.

This patient has an estimated gestational age of approximately **5 weeks** (4 weeks of missed menses plus ~1 week since returning to clinic, with last menstrual period approximately 5 weeks prior). At this very early gestational age, **medication abortion with mifepristone and misoprostol is the most appropriate method** for elective pregnancy termination.

Why mifepristone + misoprostol is correct:

- The FDA-approved regimen of 200 mg oral mifepristone followed by 800 mcg misoprostol (buccal, vaginal, or sublingual) 24–48 hours later is approved for medication abortion through **70 days' gestation** (10 weeks). At ~5 weeks, this patient is well within that window.[1]
- Combined mifepristone–misoprostol regimens achieve **complete abortion rates of 95–97%** at early gestational ages, with major complications occurring in <0.5% of cases.[2][3]
- ACOG and the Society of Family Planning recommend combined mifepristone–misoprostol as the **preferred therapy** for medication abortion (Level A evidence).[1]
- Medication abortion is noninvasive, can be self-administered at home, and avoids the risks of surgical instrumentation.[1][4]

Why the other options are incorrect:

- **A. D&E** is a surgical procedure used for **second-trimester** abortions (typically ≥13–14 weeks), not for early first-trimester pregnancies.
- **B. Oxytocin-induced labor** is used for pregnancy termination at **later gestational ages** (second/third trimester) and is not appropriate at 5 weeks.
- **C. Manual uterine aspiration (MVA)** is a valid surgical option for first-trimester abortion, but at this very early gestational age, the gestational sac may not yet be visible on ultrasound, making confirmation of complete evacuation difficult. Medication abortion is preferred at this stage as it avoids unnecessary instrumentation and is equally effective.[5]

Would you like to explore the evidence on very early medication abortion before ultrasonographic confirmation of intrauterine pregnancy, including the recent NEJM randomized trial on this topic?

References

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Question 978

A 72-year-old man presents to his primary care physician with a 6-month history of shortness of breath. He says that he used to enjoy playing golf with his friends but now he cannot walk for long enough to play. The shortness of breath is now starting to complicate his ability to get around in daily life. His past medical history is significant for diabetes, hypertension, and early stage prostate cancer that was removed 10 years ago without recurrence. He has smoked 1 pack per day for the past 55 years and drinks about 6 drinks per week. On presentation he is found to be breathing with pursed lips. Physical exam reveals decreased breath sounds on auscultation, increased chest diameter, and hyperresonance to percussion. Which of the following findings would most likely be seen in this patient?

Answer Choices:

(A) Decreased residual volume and decreased 1 second forced expiratory volume
(B) Decreased residual volume and increased 1 second forced expiratory volume
(C) Increased residual volume and decreased 1 second forced expiratory volume
(D) Normal residual volume and decreased 1 second forced expiratory volume

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/5b55870b-9946-41b7-a90b-d2f30edf9484

OpenEvidence Explanation

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The answer is **C. Increased residual volume and decreased 1 second forced expiratory volume**.

This patient's presentation — heavy smoking history (55 pack-years), progressive dyspnea on exertion, **pursed-lip breathing**, barrel chest (increased AP diameter), decreased breath sounds, and hyperresonance to percussion — is classic for **chronic obstructive pulmonary disease (COPD)/emphysema**.

Pulmonary function findings in COPD/emphysema:

- **FEV_1 is decreased** due to airflow obstruction from airway inflammation, loss of elastic recoil, and small airway collapse during expiration. The FEV_1/FVC ratio is also reduced (<0.70), which is the hallmark diagnostic criterion for COPD.
- **Residual volume (RV) is increased** because of air trapping. Destruction of alveolar walls and loss of elastic recoil prevent complete exhalation, leaving a larger volume of air trapped in the lungs at end-expiration. Total lung capacity (TLC) is also typically increased due to hyperinflation.

The other options are incorrect because:

- **A and B** (decreased RV) — RV decreases in restrictive lung diseases (e.g., pulmonary fibrosis), not in obstructive diseases where air trapping is the hallmark.
- **D** (normal RV) — Air trapping is a defining feature of emphysema, making a normal RV inconsistent with this presentation.

Pursed-lip breathing is a compensatory mechanism that creates back-pressure to stent open collapsing airways during expiration, reducing air trapping — further supporting the diagnosis of obstructive lung disease with hyperinflation.

Would you like to explore how spirometric severity staging (GOLD classification) guides pharmacologic management in COPD?

Question 979

A 67-year-old male comes into the ED complaining of dyspnea and a heavy feeling in his chest. He reports that over the past month he has become more easily “winded to the point that he now sleeps in his living room because he can’t make it up the stairs. A review of systems is notable for headaches and fatigue. On physical exam you note decreased breath sounds and a dullness to percussion on the right. A chest radiograph is obtained, which shows a right-sided pleural effusion. Thoracocentesis is performed and the fluid is analyzed, with results shown below:

Volume: 30 cc of fluid
Pleural fluid protein: 5.8 g/dL
Serum protein ratio: 7.0 g/dL
Lactate dehydrogenase (LDH): 258 U/L

Which of the following conditions may have led to the findings in this patient’s pleural cavity?

Answer Choices:

(A) Congestive heart failure
(B) Liver cirrhosis
(C) Lymphoma
(D) Nephrotic syndrome

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/360dccee-2e8a-48d9-8274-d04b9c1c1c2d

OpenEvidence Explanation

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The answer is **C. Lymphoma**.

Applying **Light's criteria** to this patient's pleural fluid analysis confirms an **exudative** effusion:[1][2]

- **Pleural fluid protein/serum protein ratio** = 5.8 / 7.0 = **0.83** (>0.5 → exudative)
- **Pleural fluid LDH = 258 U/L** (>200 U/L → exudative)

Since at least one criterion is met, this is classified as an exudative pleural effusion. Among the answer choices, only **lymphoma** is a cause of exudative effusions.[1] The other three options — congestive heart failure, liver cirrhosis, and nephrotic syndrome — are classic causes of **transudative** effusions, which result from imbalances in hydrostatic or oncotic pressures rather than local pleural inflammation or infiltration.[1][2]

Lymphoma is a well-recognized neoplastic cause of exudative pleural effusions, listed alongside lung cancer, breast cancer, and mesothelioma as common malignant etiologies.[1] The clinical presentation in this patient — progressive dyspnea, fatigue, headaches, and a unilateral effusion in a 67-year-old male — is consistent with a malignant process. Malignancy accounts for approximately 26% of all pleural effusions and is the second most common cause overall after heart failure.[3]

Would you like to explore the recommended diagnostic workup for suspected malignant pleural effusions, including the role of cytology, pleural biopsy, and imaging?

Relevant images

(CONTENT OMITTED)

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Question 981

A 22-year-old woman presents to her primary care physician in April for seasonal allergies. She has suffered from seasonal allergies for the past 2 years and takes diphenhydramine as needed when her symptoms worsen. She has not yet seen a physician for her allergies. She reports that diphenhydramine has been helpful in controlling her symptoms, but she does not like feeling drowsy from the medication. Her past medical history is also notable for well-controlled asthma. She uses an albuterol inhaler on an as-needed basis. She smokes marijuana daily. Her temperature is 99.2°F (37.3°C), blood pressure is 120/70 mmHg, pulse is 76/min, and respirations are 16/min. She has a prominent nasal crease. Her nasal turbinates are boggy and bluish-gray. She has copious thin and watery nasal mucus. The physician suggests replacing diphenhydramine with fexofenadine to improve her drowsiness. What characteristic of fexodenadine allows it to be less sedating than diphenhydramine?

Answer Choices:

(A) Alpha-adrenergic antagonism
(B) Beta-adrenergic antagonism
(C) Relative lipophobicity
(D) Serotonergic antagonism

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/712adc55-d334-46cf-831b-ad5b6eed94db

OpenEvidence Explanation

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The correct answer is **C. Relative lipophobicity**.

Fexofenadine is a second-generation antihistamine that is **lipophobic** (poorly lipid-soluble), which prevents it from readily crossing the blood-brain barrier (BBB). In contrast, diphenhydramine is a first-generation antihistamine that is highly **lipophilic**, allowing it to easily penetrate the BBB and bind central H1-receptors, causing sedation.[1][2]

Multiple mechanisms contribute to fexofenadine's non-sedating profile:

- **Lipophobicity** limits passive diffusion across the BBB.[1][2]
- **P-glycoprotein efflux** — fexofenadine is a substrate of P-glycoprotein, an efflux pump expressed at the BBB that actively transports the drug back out of the CNS, further reducing brain penetration.[3]
- **PET imaging studies** confirm that fexofenadine achieves essentially **0% brain H1-receptor occupancy** (−8.0% to −0.1%), compared to 56.4% for diphenhydramine 30 mg.[4][5]

The American Academy of Allergy, Asthma, and Immunology guidelines note that second-generation antihistamines are specifically designed through chemical modifications that limit transfer across the BBB to reduce sedation compared to first-generation agents like diphenhydramine.[6]

The other answer choices are incorrect: alpha-adrenergic antagonism (A), beta-adrenergic antagonism (B), and serotonergic antagonism (D) are not the pharmacologic properties responsible for the difference in sedation between these two antihistamines.

Would you like to explore the comparative efficacy and safety profiles of different second-generation antihistamines for allergic rhinitis management?

Relevant images

(CONTENT OMITTED)

References

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Question 982

A 55-year-old male visited his primary care physician complaining of chest pain and progressive shortness of breath worsened by exertion. His vital signs were within normal limits. He reports that he worked in a naval shipyard for 10 years during his twenties. A CT scan of his chest shows diffuse thickening of the pleura and a diagnosis of mesothelioma is made. Assuming this diagnosis is correct, which of the following is most likely to also be present in this patient?

Answer Choices:

(A) Pneumothorax
(B) Pleural effusion
(C) Systemic inflammatory response syndrome
(D) Bronchioalveolar carcinoma

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/f25f62b6-a6b8-47dd-bb1a-7cb6466b0222

OpenEvidence Explanation

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The answer is **B. Pleural effusion**.

Pleural effusion is the finding most likely to also be present in a patient with mesothelioma. It is the hallmark clinical feature of malignant pleural mesothelioma, occurring in approximately **60% of patients** at presentation.[1] The NCCN Guidelines for Pleural Mesothelioma identify "recurrent pleural effusion and/or pleural thickening" as the typical initial presentation prompting workup.[2]

The clinical vignette is classic for mesothelioma: a middle-aged male with a history of **occupational asbestos exposure** (naval shipyard work), presenting with chest pain and exertional dyspnea, with CT showing diffuse pleural thickening. Mesothelioma has a latency period of **20–50 years** after asbestos exposure, consistent with this patient's timeline (exposed in his twenties, presenting at age 55).[3]

Breathlessness caused by pleural effusion and chest wall pain from direct tumor invasion are the two most common presenting symptoms, each occurring in about 60% of patients.[1][4] The NCCN algorithm begins the diagnostic workup with thoracentesis for cytologic assessment when pleural effusion is present.[2]

Regarding the other options:

- **Pneumothorax** is not a typical feature of mesothelioma.
- **Systemic inflammatory response syndrome (SIRS)** is not a characteristic presentation of mesothelioma, though constitutional symptoms such as fatigue and weight loss may occur later in the disease course.[1]
- **Bronchoalveolar carcinoma** (now reclassified as adenocarcinoma in situ or lepidic-predominant adenocarcinoma) is a separate malignancy. While asbestos exposure is a risk factor for lung cancer, it is not a concurrent finding expected with mesothelioma, and the question asks what is most likely to be present alongside the mesothelioma diagnosis.

Would you like to explore the current first-line treatment options for malignant pleural mesothelioma, including the role of immune checkpoint inhibitors versus chemotherapy?

Relevant images

(CONTENT OMITTED)

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Question 983

A 56-year-old man recently diagnosed with cirrhosis secondary to alcohol use presents to the clinic for a follow up evaluation. He states that he has abstained from alcohol and attends a support group regularly. He has not taken any new medications or encountered any sick contacts. The patient's blood pressure is 110/70 mmHg, pulse is 65/min, and respirations are 15/min. His physical exam is grossly unremarkable. He has brought an gastroduodenoscopy report for review, which reveals that the patient has small esophageal varices with red spots. What is the next best step to prevent bleeding?

Answer Choices:

(A) Endoscopic sclerotherapy
(B) Metoprolol
(C) Nadolol
(D) Repeat endoscopy

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/29dc2b54-4bdd-4c4b-8bbe-6792fdb09fcc

OpenEvidence Explanation

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The correct answer is **C. Nadolol**.

Small esophageal varices with **red spots (red wale marks)** are classified as **high-risk varices**, and guidelines uniformly recommend primary prophylaxis with a **nonselective beta-blocker (NSBB)** such as nadolol or propranolol.[1][2][3] Among the answer choices, nadolol is the only NSBB listed.

The following management algorithm illustrates the approach to primary prophylaxis based on variceal size and risk features:

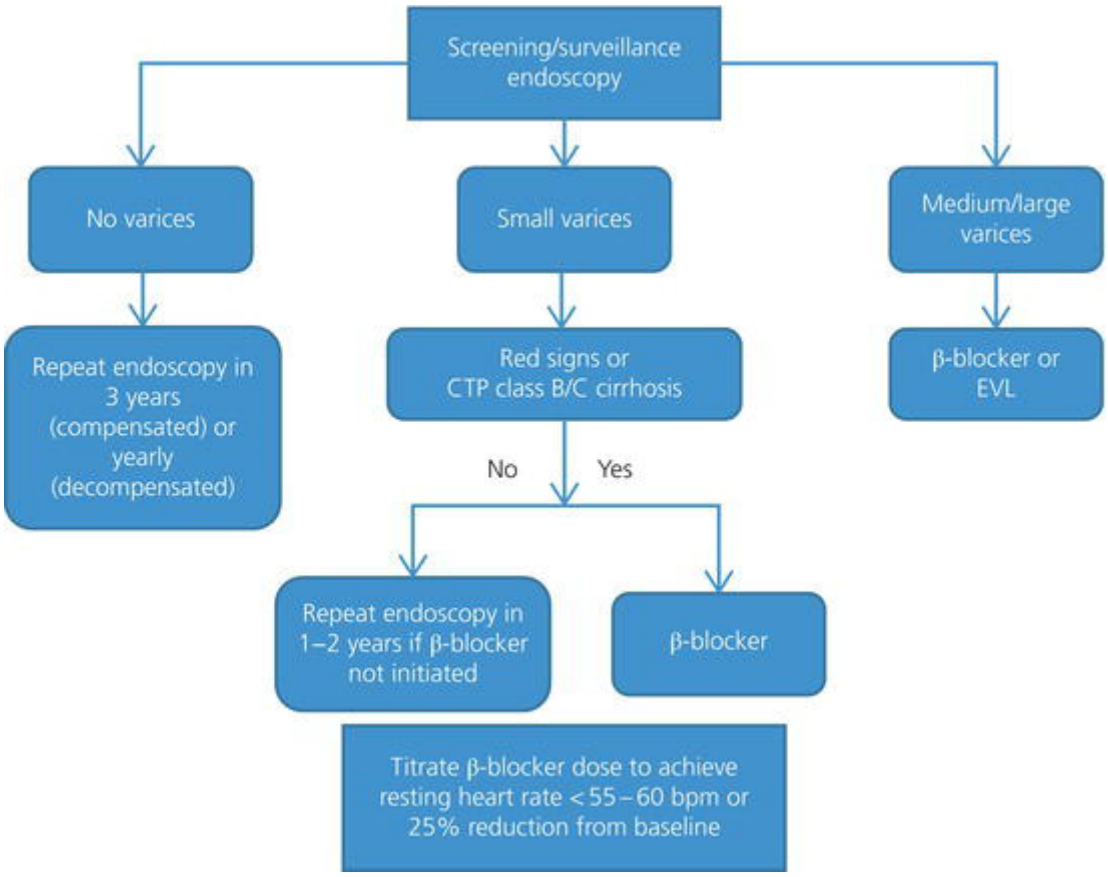


Figure 12. Management algorithm for primary prophylaxis of esophageal variceal bleeding in patients with cirrhosis. bpm, beats per minute; CTP, Child-Turcotte-Pugh; EVL, endoscopic variceal ligation.

Why the other options are incorrect:

- **A. Endoscopic sclerotherapy** – Sclerotherapy has no role in primary prophylaxis of variceal bleeding per AASLD guidelines.[2]
- **B. Metoprolol** – Metoprolol is a cardioselective (β1-selective) beta-blocker and does not reduce portal pressure. Only **nonselective** beta-blockers (which block both β1 and β2 receptors) are effective for portal hypertension by reducing splanchnic blood flow.[5][6]
- **D. Repeat endoscopy** – Surveillance endoscopy alone would be appropriate for small varices **without** high-risk features. The presence of red spots

elevates the bleeding risk and necessitates active prophylaxis rather than observation.[3][7]

The AASLD Practice Guidance specifically notes that for high-risk small varices, NSBB is the only technically feasible prophylactic method, as endoscopic variceal ligation (EVL) is not recommended for small varices.[1][7]

Would you like to explore the comparative efficacy and dosing of different nonselective beta-blockers (nadolol, propranolol, carvedilol) for portal hypertension prophylaxis?

References

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Question 987

An 11-month-old boy is brought to the emergency department by his mother after she observed jerking movements of his arms and legs for about 30 seconds earlier that morning. He has not had fever, cough, or a runny nose. He has been healthy, except for occasional eczema. He was delivered at home in Romania. His mother had no prenatal care. She reports that he has required more time to reach developmental milestones compared to his older brother. The patient's immunization records are not available. He takes no medications. He appears pale with blue eyes and has a musty odor. He has poor eye contact. Which of the following would have most likely prevented the patient's symptoms?

Answer Choices:

(A) Levothyroxine therapy during pregnancy
(B) Dietary restriction of phenylalanine
(C) Daily allopurinol intake
(D) Avoidance of fasting states

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/640b5c53-4015-4452-a523-87ccd191825a

OpenEvidence Explanation

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The answer is **B. Dietary restriction of phenylalanine**.

This presentation is classic for **phenylketonuria (PKU)**. The key clinical features pointing to this diagnosis include:

- **Musty odor** — a hallmark of PKU caused by accumulation of phenylalanine metabolites (phenylacetate)[1][2]
- **Pale skin and blue eyes** — generalized hypopigmentation due to impaired melanin synthesis from reduced tyrosine availability[1][3]
- **Seizures** (the jerking movements) — occur in untreated classic PKU[2][4]
- **Developmental delay** — progressive encephalopathy from toxic phenylalanine accumulation in the brain[1][4]
- **Eczema** — a common dermatologic finding in untreated PKU[1][5]
- **Home delivery in Romania with no prenatal care and no immunization records** — strongly suggests the child did not undergo newborn screening, which would have detected PKU via the Guthrie test

PKU is an autosomal recessive disorder caused by deficiency of phenylalanine hydroxylase (PAH), which converts phenylalanine to tyrosine. When diagnosed by newborn screening and treated immediately with **dietary phenylalanine restriction**, patients show essentially normal development.[4] Dietary treatment initiated within the first 20 days of life is effective in preventing intellectual disability.[6] The diet consists of restricting natural protein intake and supplementing with phenylalanine-free amino acid formulas.[4][7]

Why the other options are incorrect:

- **A (Levothyroxine during pregnancy)** — Maternal levothyroxine would address congenital hypothyroidism, which presents with jaundice, lethargy, macroglossia, and umbilical hernia — not musty odor or hypopigmentation.[8]
- **C (Daily allopurinol)** — This would address Lesch-Nyhan syndrome (HPRT deficiency), which presents with hyperuricemia, self-injurious behavior, and dystonia — not musty odor.[5]

- **D (Avoidance of fasting states)** — This would be relevant for fatty acid oxidation disorders or glycogen storage diseases, which present with hypoketotic hypoglycemia, not the constellation seen here.

Would you like to explore the current guidelines on PKU management, including the role of sapropterin (BH4) therapy and newer treatments like pegvaliase?

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Question 991

A 13-year-old boy is brought to the physician because of progressive left leg pain for 2 months, which has started to interfere with his sleep. His mother has been giving him ibuprofen at night for "growing pains," but his symptoms have not improved. One week before the pain started, the patient was hit in the thigh by a baseball, which caused his leg to become red and swollen for several days. Vital signs are within normal limits. Examination shows marked tenderness along the left mid-femur. His gait is normal. Laboratory studies show a leukocyte count of 21,000/mm3 and an ESR of 68 mm/h. An x-ray of the left lower extremity shows multiple lytic lesions in the middle third of the femur, and the surrounding cortex is covered by several layers of new bone. A biopsy of the left femur shows small round blue cells. Which of the following is the most likely diagnosis?

Answer Choices:

(A) Osteosarcoma
(B) Osteochondroma
(C) Ewing sarcoma
(D) Osteoid osteoma

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/42a56fb6-5861-42f9-ae6d-bf8833dd4371

OpenEvidence Explanation

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The answer is **C. Ewing sarcoma**.

This presentation is classic for **Ewing sarcoma**, with every key feature pointing to this diagnosis:

- **Age and demographics**: A 13-year-old boy, fitting the peak incidence around age 15 with a slight male predominance.[1][2]
- **Location**: Mid-femur (diaphyseal), which is the characteristic location for Ewing sarcoma. Unlike osteosarcoma, which favors the metaphysis, Ewing sarcoma has a predilection for the **diaphysis** of long bones.[3]
- **Clinical features**: Progressive bone pain worsening at night, unresponsive to NSAIDs, with elevated inflammatory markers (leukocyte count 21,000/mm^3, ESR 68 mm/h). Systemic findings including fever and leukocytosis are well-described in Ewing sarcoma.[1]
- **Radiographic findings**: Multiple **lytic lesions** with a "moth-eaten" pattern and **lamellated (onion-skin) periosteal reaction** — the "several layers of new bone" described in the stem — are hallmark imaging features of Ewing sarcoma.[1][4]
- **Histology**: **Small round blue cells** on biopsy are the defining histologic feature of Ewing sarcoma, showing sheets of uniform cells with prominent nuclei and scant cytoplasm.[1][5][6]

The following figure from the NEJM illustrates the characteristic radiologic and histologic features of Ewing sarcoma, including the "moth-eaten" lytic pattern, onion-peel periosteal reaction, and small round blue cell histology.

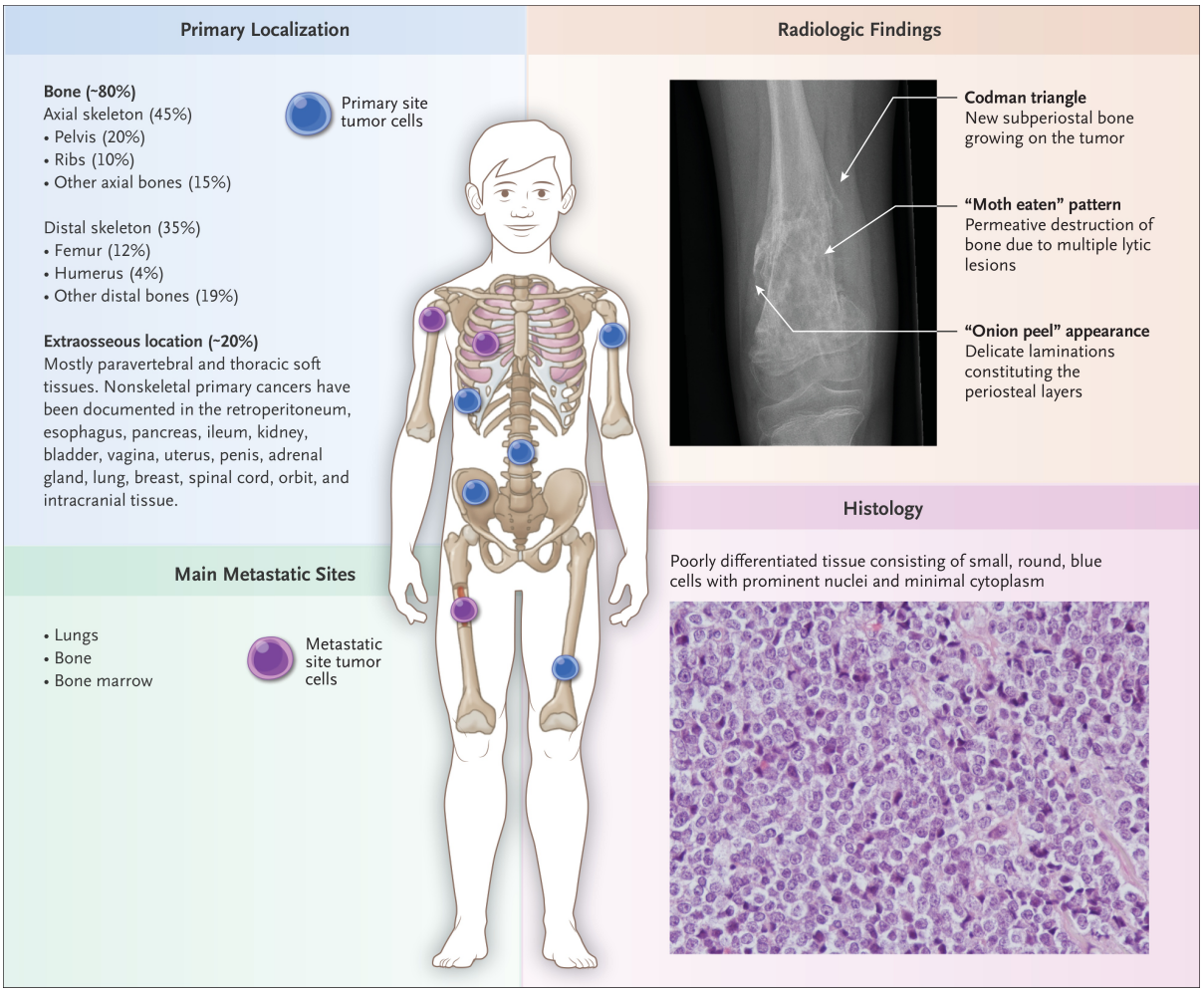


Figure 1. Clinical Features of Ewing's Sarcoma.

Used under license from The New England Journal of Medicine.

Why not the other choices:

- **Osteosarcoma (A)**: Typically occurs in the metaphysis, produces osteoid matrix (osteoblastic lesion with "sunburst" periosteal reaction), and shows malignant spindle cells producing osteoid on biopsy — not small round blue cells.[4][7]
- **Osteochondroma (B)**: A benign cartilage-capped bony exostosis, not a lytic lesion, and would not present with systemic inflammation or small round blue cells.
- **Osteoid osteoma (D)**: A small benign bone tumor (<2 cm) with a characteristic nidus surrounded by reactive sclerosis; it causes nocturnal pain responsive to NSAIDs and does not produce lytic destruction or small round blue cells.

Would you like to explore the current standard-of-care chemotherapy regimens and local control strategies for localized Ewing sarcoma?

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Question 992

A 55-year-old male with a history of stage I colon cancer status-post left hemicolectomy presents to your office for follow-up. You intend to discuss the results from his recent surveillance colonoscopy, which showed no remaining cancer, no polyps, and a well-healed anastmosis. During your meeting, you note that the patient is exhibiting the defense mechanism of suppression. Which of the following statements from the patient is consistent with your impression?

Answer Choices:

(A) Last week I volunteered for the local Cancer Society. Helping other cancer patients just makes me feel better.
(B) Oh, doctor, I'm just so grateful to be seeing you. I just know you've cured my cancer. I probably don't even need to check anymore.
(C) I'm sorry I was late today. I also didn't get any of the labs you asked for.
(D) I really haven't thought about the colonoscopy until today. Worrying before getting the results wasn't going to help anything.

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/7b430be2-d338-4123-a21e-e4e8ddc76cf1

OpenEvidence Explanation

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The correct answer is **D: "I really haven't thought about the colonoscopy until today. Worrying before getting the results wasn't going to help anything."**

Suppression is a **mature (high-adaptive) defense mechanism** defined as the **conscious, intentional decision** to avoid thinking about disturbing problems, wishes, feelings, or experiences.[1] The key distinguishing feature of suppression is that the individual remains fully aware of the stressor but deliberately chooses to postpone or set aside distressing thoughts when dwelling on them would not be productive. As Vaillant describes, suppression is "analogous to a well-trimmed sail; every restriction is precisely calculated to exploit, not to hide, the winds of passion".[1]

In option D, the patient acknowledges awareness of the colonoscopy (a potential source of anxiety) but consciously chose not to worry about it beforehand, recognizing that worrying would not change the outcome. This reflects the hallmark of suppression: a **deliberate, conscious postponement** of distressing thoughts while the underlying conflict remains accessible to awareness.[1]

The other options represent different defense mechanisms:

- **A (Altruism):** Channeling anxiety about one's own cancer into helping other cancer patients — deriving gratification from giving to others what one would like to receive.[1]
- **B (Idealization):** Exaggerating the physician's abilities and minimizing the seriousness of the situation, attributing unrealistic positive qualities to the doctor — a narcissistic-level defense.[1]
- **C (Passive-aggression):** Being late and not completing requested labs represents indirect expression of resistance or hostility — an action-level (immature) defense.[1]

Suppression sits at the highest level (Level 7) of the defense mechanism hierarchy alongside altruism, anticipation, humor, sublimation, self-assertion, self-observation, and affiliation.[1] Unlike **repression**, which is an unconscious process where threatening ideas are kept out of awareness entirely, suppression involves a fully conscious choice to set aside distressing thoughts.[2][3]

Would you like to explore how the various mature defense mechanisms (suppression, sublimation, altruism, humor) differ in their clinical presentation and therapeutic implications?

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Question 997

A 47-year-old woman is brought to the emergency department by paramedics. She was found unconscious on a park bench by a bystander. Her history is unobtainable. Vitals include a pulse of 64/min, a respiratory rate of 7/min, and a blood pressure of 110/70 mm Hg. On examination, the patient is unresponsive to voice and touch but shows a flexor response to pain. Her breathing is shallow. The pupils are constricted, and a response to light cannot be determined. An arterial blood gas sample reveals:
pH 7.26
Pco2 70 mm Hg
HCO3- 26 mEq/L
Which of the following could explain this patient's presentation?

Answer Choices:

(A) Diabetic ketoacidosis
(B) Diuretic overdose
(C) Hyperventilation
(D) Opioid overdose

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/b0804e56-c523-48f7-be8e-6bbd7fb26ef7

OpenEvidence Explanation

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The answer is **D. Opioid overdose**.

This presentation is classic for opioid toxicity, characterized by the **toxidrome triad** of:

1. **Central nervous system depression** — unresponsive to voice/touch, flexor response to pain only
2. **Respiratory depression** — respiratory rate of 7/min with shallow breathing
3. **Miotic (constricted) pupils** — pinpoint pupils are a hallmark of opioid intoxication

ABG interpretation: The arterial blood gas shows a **primary respiratory acidosis** — low pH (7.26), markedly elevated PCO_2 (70 mmHg), and a near-normal HCO_3^- (26 mEq/L). The elevated PCO_2 with minimal bicarbonate compensation indicates an **acute** process, consistent with hypoventilation from opioid-induced respiratory depression. The CO_2 retention is a direct consequence of the depressed respiratory drive.

Why the other options are incorrect:

- **A. Diabetic ketoacidosis** — DKA produces a primary metabolic acidosis (low HCO_3^-, low PCO_2 from compensatory hyperventilation, Kussmaul respirations), not respiratory acidosis with CO_2 retention.
- **B. Diuretic overdose** — Diuretics (e.g., loop or thiazide) typically cause a metabolic alkalosis from volume contraction and electrolyte losses, not respiratory acidosis.
- **C. Hyperventilation** — Hyperventilation causes respiratory alkalosis (low PCO_2, elevated pH), which is the opposite of this patient's ABG findings.

The immediate management priority would be administration of **naloxone** (an opioid antagonist) along with airway protection and ventilatory support.

Would you like to explore the dosing strategies and monitoring considerations for naloxone in suspected opioid overdose, including the risk of re-sedation with long-acting opioids?

Question 999

A 40-year-old man is referred to an optometrist. He complains of mild vision impairment over the last 6 months. His vision has continued to slowly deteriorate and his condition is now affecting his night driving. Past medical history is significant for well-controlled schizophrenia. He takes a low-potency typical antipsychotics and a multivitamin every day. He has been compliant with his medication and has regular follow-up visits. What is the best first step in the management of this patient's symptoms?

> **Answer Choices:**
>
> (A) Decrease medication dosage
> (B) Reassurance
> (C) Ocular examination under anesthesia
> (D) Slit-lamp examination

> **Correct Answer:**
>
> **(D)**
>
> **OpenEvidence Response:**
>
> **(D)** ✓

OpenEvidence Link: https://openevidence.com/ask/29914bf2-1fc9-4258-95e5-8fb0611de849

OpenEvidence Explanation

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The best first step is **D. Slit-lamp examination**.

This patient on a **low-potency typical antipsychotic** (such as chlorpromazine or thioridazine) presenting with progressive vision impairment and difficulty with night driving should undergo a **slit-lamp examination** to evaluate for drug-induced ocular toxicity. Low-potency phenothiazines are well-known to cause corneal and lenticular pigmentary deposits, cataracts, and pigmentary retinopathy — all of which can be identified on slit-lamp examination.[1][2]

Why slit-lamp examination is the correct answer:

- Chlorpromazine and thioridazine, the classic low-potency typical antipsychotics, cause deposition of fine particulate matter in the lens and cornea, with more advanced cases showing star-shaped lenticular opacities. These changes are best visualized on slit-lamp examination.[2][3]
- Cataractous changes from antipsychotics, particularly with prolonged use, frequently cause lenticular opacifications that can impair vision.[1]
- The FDA label for chlorpromazine specifically recommends that long-term patients on moderate to high dosage levels have **periodic ocular examinations**.[2]
- A consensus panel on physical health monitoring in schizophrenia similarly recommended that patients with schizophrenia receive **regular visual examinations**.[4]

Why the other options are incorrect:

- **A. Decrease medication dosage** — Adjusting the dose without first confirming the diagnosis would be premature. The etiology of the visual symptoms must be established before making medication changes, especially in a patient with well-controlled schizophrenia.
- **B. Reassurance** — Progressive vision loss affecting night driving is not benign and warrants investigation, particularly given the known ocular toxicity profile of low-potency antipsychotics.
- **C. Ocular examination under anesthesia** — This is unnecessarily invasive. The patient is a cooperative adult who can undergo a standard slit-lamp examination without anesthesia.

Would you like to explore the specific management approach if pigmentary deposits or retinopathy are confirmed on slit-lamp examination in this patient?

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Question 1000

A 65-year-old man presents with a 6-month history of repeated falls, postural dizziness, progressive fatigue, generalized weakness and a 13.6 kg (30 lb) weight loss. He is a vegetarian. The patient's family says that he had been high functioning but has had significant behavioral changes over the past year. The patient denies any smoking history, alcohol consumption, or illicit drug use. No significant family history. His vital signs include: blood pressure 90/50 mm Hg without postural changes, pulse 92/min, respiratory rate 16/min, temperature 37.0°C (98.6°F). Physical examination reveals a poorly groomed, disheveled, thin man. He is irritable, paranoid, and delusional but denies any hallucinations. An unstable, wide-based ataxic gait is noted. Laboratory results are significant for the following:
Hb 6.1 g/dL
MCV 109 fL
Platelets 90,0000/mm3
Total count 3,000/mm3
Reticulocyte count 0.8%
A peripheral blood smear demonstrates hypersegmented neutrophils. Anti-intrinsic factor antibodies are negative. Which of the following is the most likely cause of this patient's condition?

Answer Choices:

(A) Hypothyroidism
(B) Folate deficiency
(C) Vitamin B12 deficiency
(D) Parvovirus infection

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/a0a17d7d-e631-45e5-9511-8d2187537704

OpenEvidence Explanation

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The correct answer is **C. Vitamin B12 deficiency**.

This patient presents with classic findings of **vitamin B12 (cobalamin) deficiency**: megaloblastic anemia (Hb 6.1 g/dL, MCV 109 fL), **pancytopenia** (low platelets, leukopenia), low reticulocyte count, **hypersegmented neutrophils** on peripheral smear, and prominent **neuropsychiatric symptoms** (behavioral changes, paranoia, delusions) along with a **wide-based ataxic gait** — all hallmarks of severe B12 deficiency.[1][2]

Why not the other options?

- **Folate deficiency (B):** While folate deficiency also causes megaloblastic anemia with hypersegmented neutrophils, it does **not** produce the neuropsychiatric and neurological manifestations seen here (paranoia, delusions, ataxia). Neurologic symptoms occur in B12 deficiency but not in folate deficiency.[1]
- **Hypothyroidism (A):** Can cause macrocytosis but does not produce hypersegmented neutrophils, pancytopenia, or this degree of neuropsychiatric deterioration.
- **Parvovirus infection (D):** Causes pure red cell aplasia with reticulocytopenia but does not produce macrocytosis, hypersegmented neutrophils, or neuropsychiatric symptoms.

Why B12 deficiency despite negative anti-intrinsic factor antibodies?

The negative anti-intrinsic factor antibodies effectively rule out pernicious anemia as the mechanism, but the patient is a **vegetarian** — a well-established risk factor for dietary B12 deficiency. Vitamin B12 is found exclusively in animal-

source foods.[3][4] Pure nutritional B12 deficiency occurs in strict vegans and vegetarians; a cross-sectional analysis found B12 deficiency in 7% of vegetarians and 52% of vegans.[5] Additionally, approximately 20% of patients with biopsy-proven autoimmune gastritis are seronegative for anti-intrinsic factor antibodies, so pernicious anemia cannot be entirely excluded by serology alone.[5] However, the dietary history is the most parsimonious explanation in this case.

Would you like to explore the recommended repletion strategies and monitoring parameters for severe B12 deficiency with neuropsychiatric involvement?

Relevant images

(CONTENT OMITTED)

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Question 1001

A 42-year-old man presents to establish care with a family physician after having progressively worsening back pain. He has recently migrated from Sweden and has not had any checkups in the last 3 years. He first started having back pain 3 years ago, but his pain has begun to be excruciating in the mornings. He is no longer able to get relief with over the counter medications. He also feels stiff every morning and this usually lasts between 30 minutes and an hour. Both of his knees are also very painful, particularly upon standing up from a seated position. His pain improves when he moves around, so he tries to be somewhat physically active. He also reports that he cannot use his hands for long periods of time due to joint pain and stiffness. His father and sister also have joint issues, and his mother was recently diagnosed with osteoporosis. He has been a smoker for 13 years. Upon physical examination, his wrist and proximal interphalangeal (PIP) joints are warm and swollen. Which of the following is the next best step in management?

Answer Choices:

(A) Testing for serum Ca and PTH
(B) Calcium and Vitamin D prescription
(C) Testing for serum ESR and autoantibodies
(D) Testing for serum ferritin

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/9d24d987-ba6e-4abd-9bac-331d613d64d6

OpenEvidence Explanation

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The correct answer is **C. Testing for serum ESR and autoantibodies**.

This patient's presentation is classic for **inflammatory arthritis**, most likely **rheumatoid arthritis (RA)**. Key features pointing to this diagnosis include:

- **Morning stiffness lasting 30–60 minutes** that improves with activity
- **Warm, swollen wrist and PIP joints** (synovitis of small joints of the hands)
- Polyarticular involvement (back, knees, hands)
- Progressive course over 3 years
- Family history of joint disease

The 2010 ACR/EULAR classification criteria for RA require at least one clinically swollen joint, and the scoring system incorporates joint distribution, **autoantibody status (rheumatoid factor and anti-cyclic citrullinated peptide antibodies)**, **acute phase reactants (ESR and CRP)**, and symptom duration.[1][2] The recommended initial laboratory workup for suspected RA includes ESR, CRP, rheumatoid factor, and anti-CCP antibodies.[1][3] A score ≥6 on the ACR/EULAR criteria is classified as definite RA.[2]

Why the other options are incorrect:

- **A (Serum Ca and PTH):** This would evaluate for hyperparathyroidism or metabolic bone disease, which does not present with warm, swollen joints or inflammatory morning stiffness.
- **B (Calcium and Vitamin D):** This addresses osteoporosis prevention/treatment. While the patient's mother has osteoporosis, the acute clinical priority is the inflammatory joint disease, not empiric osteoporosis therapy.
- **D (Serum ferritin):** This could screen for hemochromatosis-associated arthropathy, which can cause joint disease but typically affects the 2nd and 3rd MCP joints with a non-inflammatory pattern and does not present with

warm, swollen PIP joints and prolonged morning stiffness as the predominant features.

Early diagnosis is critical, as treatment within a **3- to 6-month window of opportunity** from symptom onset is associated with less joint damage and higher rates of remission.[4]

Would you like to explore the initial treatment approach with DMARDs once RA is confirmed, including the role of early methotrexate initiation?

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Question 1004

A 66-year-old man presents to the emergency department due to a productive cough. His cough has been increasing in frequency and severity over the course of 3 days, and his sputum production has increased in volume. The color of his sputum is yellow-green. He denies any chest pain or palpitations but has experienced worsening shortness of breath with exertion and at rest, which is above his baseline. He has not noticed any changes in his weight or edema in his lower extremities. He denies any recent history of long travel. Medical history is significant for hypertension, hyperlipidemia, and chronic obstructive pulmonary disease (COPD). He has been hospitalized four times for similar symptoms within the last year. He has smoked approximately 1 pack of cigarettes per day for the past 45 years. His temperature is 102°F (38.9°C), blood pressure is 156/94 mmHg, pulse is 101/min, and respirations are 26/min with an oxygen saturation of 85% on room air. On physical exam, the patient has difficulty speaking, and there is asynchronous motion between the chest and abdomen with respiration. Wheezing is appreciated on pulmonary auscultation. An ECG demonstrates normal sinus rhythm. A chest radiograph is obtained, and he is administered supplemental oxygen. He is started on ipratropium, albuterol, and methylprednisolone. Which of the following should be added to this patient's treatment regimen?

Answer Choices:

(A) Cefazolin
(B) Ceftriaxone
(C) Levofloxacin
(D) Penicillin

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/7f6c47f0-a2da-4762-a442-b1795834b1f6

OpenEvidence Explanation

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The correct answer is **C. Levofloxacin**. This patient presents with a **severe acute exacerbation of COPD (AECOPD)** characterized by all three Anthonisen cardinal symptoms (increased dyspnea, increased sputum volume, and increased sputum purulence), along with fever, significant hypoxemia (SpO_2 85%), tachypnea, and signs of impending respiratory failure (abdominal paradox, difficulty speaking). Critically, he has had **four hospitalizations in the past year** for similar symptoms, placing him in the category of patients with repeated exacerbations and suspected bacterial resistance.

Why levofloxacin over the other options:

For patients with repeated COPD exacerbations or suspected bacterial resistance, **respiratory fluoroquinolones** (e.g., levofloxacin, moxifloxacin) or amoxicillin/clavulanate are recommended over first-line agents such as macrolides, doxycycline, or trimethoprim-sulfamethoxazole.[1] A JAMA review notes that while first-line oral antibiotics are appropriate for initial presentations, "quinolones or ampicillin plus clavulanate are considered for patients with repeated exacerbations or suspected bacterial resistance".[1] Additionally, in patients with severe COPD at risk for Pseudomonas colonization, fluoroquinolones such as levofloxacin or ciprofloxacin are specifically recommended.[2]

Why the other choices are incorrect:

- **A. Cefazolin** — A first-generation cephalosporin with a narrow gram-positive spectrum; it does not adequately cover the typical AECOPD pathogens (H. influenzae, M. catarrhalis) or Pseudomonas.

- **B. Ceftriaxone** — A third-generation cephalosporin that would be appropriate for community-acquired pneumonia but lacks anti-pseudomonal activity and is not the standard recommendation for severe AECOPD with frequent exacerbations.

- **D. Penicillin** — Too narrow in spectrum; resistance among COPD-associated pathogens (particularly beta-lactamase–producing H. influenzae and M. catarrhalis) makes penicillin alone inadequate.[2]

The combination of severe exacerbation, multiple recent hospitalizations (raising concern for resistant organisms including Pseudomonas), and the need for broad-spectrum empiric coverage makes **levofloxacin** the most appropriate addition to this patient's regimen.

Would you like to explore the role of non-invasive positive pressure ventilation in this patient given his signs of impending respiratory failure (abdominal paradox, accessory muscle use)?

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Question 1005

A 55-year-old man presents with bloody nasal secretions and shortness of breath. He reports he has lost 4 kg (8.8 lb) in the last two months with no changes in his diet. He has also been suffering from mild to moderate joint pain in the left knee for the last year. His past medical history is unremarkable. His vitals include: blood pressure 120/70 mm Hg, temperature 37.0°C (98.6°F), pulse 70/min, respiratory rate 14/min. Physical examination is significant for nasal ulcers. Diffuse crackles are present over all lobes of the lung bilaterally. Laboratory findings are significant for the following:
Hemoglobin 12.9 g/dL
Hematocrit 37.7%
Leukocyte count 5500/mm3
Neutrophils 65%
Lymphocytes 30%
Monocytes 5%
Mean corpuscular volume 82.2 µm3
Platelet count 190,000/mm3
Erythrocyte sedimentation rate 35 mm/h
C-reactive protein 14 mg/dL
Creatinine 3.09 mg/dL
The patient is prescribed a corticosteroid nasal spray and oral antibiotics but returns in 2 weeks without any clinical improvement. Which of the following would most likely confirm the diagnosis in this patient?

Answer Choices:

(A) Anti-citrullinated protein antibodies
(B) Erythrocyte sedimentation rate
(C) Anti-histone bodies
(D) Antineutrophil cytoplasmic antibodies

Correct Answer:

(D)

> **OpenEvidence Response:**
>
> **(D)** ✓

OpenEvidence Link: https://openevidence.com/ask/2eb4dc89-35a0-4286-b603-37c8f551e2ab

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OpenEvidence Explanation

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The answer is **D. Antineutrophil cytoplasmic antibodies (ANCA)**. This clinical presentation — bloody nasal secretions, nasal ulcers, diffuse pulmonary crackles (suggesting alveolar hemorrhage), elevated creatinine (renal impairment), weight loss, arthralgias, elevated ESR/CRP, and failure to respond to antibiotics — is classic for **granulomatosis with polyangiitis (GPA)**, an ANCA-associated vasculitis.

Why ANCA testing confirms the diagnosis:

GPA characteristically involves the triad of upper respiratory tract disease (nasal ulcers, bloody discharge), lower respiratory tract disease (pulmonary infiltrates/hemorrhage), and pauci-immune glomerulonephritis. Approximately **90% of patients** with GPA have circulating ANCA, most commonly cytoplasmic ANCA (c-ANCA) directed against proteinase 3 (PR3).[1] The 2022 ACR/EULAR classification criteria assign the highest weight (+5 points) to c-ANCA/anti-PR3 positivity among all criteria items for GPA.[2] The KDIGO 2024 guidelines emphasize that in a clinical presentation compatible with small-vessel vasculitis, positive MPO- or PR3-ANCA serology supports the diagnosis and should prompt initiation of immunosuppressive therapy even before biopsy results are available.[1]

Why the other options are incorrect:

- **A. Anti-citrullinated protein antibodies (anti-CCP)** — These are specific for rheumatoid arthritis, which does not explain the nasal ulcers, pulmonary involvement, or renal failure.

- **B. ESR** — Already elevated in this patient (35 mm/h) and is a nonspecific inflammatory marker that cannot confirm a specific diagnosis.
- **C. Anti-histone antibodies** — These are associated with drug-induced lupus, which does not fit this clinical picture of destructive upper airway disease and renal failure.

Would you like to explore the recommended induction therapy regimens for GPA, including the role of rituximab versus cyclophosphamide?

Relevant images

(CONTENT OMITTED)

References

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Question 1007

A 3-day-old male is evaluated in the hospital nursery for delayed passage of meconium. His mother is breastfeeding and has started to produce milk. The patient has been feeding well every two hours and is urinating over eight times per day. The patient was born at 35 weeks gestation to a 27-year-old gravida 4. The patient is of Ashkenazi Jewish descent, and the patient's parents denied all prenatal genetic testing. The pregnancy was uncomplicated until the patient's mother had spontaneous rupture of membranes at 35 weeks gestation. The patient's three older siblings are all healthy. In the hospital nursery, the patient's temperature is 98.2°F (36.8°C), blood pressure is 48/32 mmHg, pulse is 164/min, and respirations are 48/min. On physical exam, he appears to be in moderate distress. He has no dysmorphic features, and his abdomen is distended and non-tender. Bowel sounds are absent.

Which of the following is the best next step in management?

Answer Choices:

(A) Abdominal radiograph
(B) Contrast enema
(C) Upper gastrointestinal series
(D) Sweat testing

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/acb91be9-57d3-4798-915a-69abe80c6379

OpenEvidence Explanation

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The best next step in management is **A. Abdominal radiograph**.

This 3-day-old neonate presents with delayed passage of meconium, abdominal distension, absent bowel sounds, and moderate distress — a clinical picture consistent with **distal intestinal obstruction**. The differential includes Hirschsprung disease, meconium ileus (associated with cystic fibrosis, and notably more common in Ashkenazi Jewish populations), meconium plug syndrome, and intestinal atresia.[1][2][3]

Why abdominal radiograph first: An abdominal radiograph is the appropriate initial imaging study in the evaluation of neonatal bowel obstruction. It can confirm the presence of obstruction and help distinguish proximal from distal obstruction based on the pattern of bowel dilation and gas distribution.[4][5] The ACR Appropriateness Criteria explicitly state that there is no literature to support performing a contrast enema as the initial study prior to obtaining an abdominal radiograph.[6] The radiograph findings then guide the selection of subsequent studies — a contrast enema would be the appropriate next step if the radiograph confirms a distal obstruction pattern.[6]

Why not the other options:

- **Contrast enema (B)** — While ultimately likely needed to evaluate for Hirschsprung disease or meconium ileus, it should follow the initial radiograph, not replace it.[6]
- **Upper GI series (C)** — Indicated when proximal obstruction (e.g., malrotation with volvulus) is suspected, which is not the primary concern here given the clinical presentation of distal obstruction.[7]
- **Sweat testing (D)** — While cystic fibrosis should be considered (especially given Ashkenazi Jewish descent and the possibility of meconium ileus), sweat testing is not the immediate next step in a neonate with signs of acute obstruction; the obstruction must be evaluated and managed first.[2][8]

Would you like to explore the diagnostic workup algorithm after the abdominal radiograph confirms distal bowel obstruction, including the role of contrast enema and rectal biopsy?

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Official Clinical Practice Journal of the American Gastroenterological Association. 2026;:S1542-3565(26)00159-X. doi:10.1016/j.cgh.2026.03.003.

Question 1008

A 78-year-old woman presents to the office for an annual health check-up with her family physician accompanied by her daughter. She has no complaints during this visit but her daughter states that she is having difficulty locating objects such as the television remote, car keys, and her purse. Her medical history is significant for Alzheimer's dementia, coronary artery disease, diabetes mellitus, hypothyroidism, congestive heart failure, osteoarthritis and centrilobular emphysema. The patient takes memantine, atorvastatin, metformin, levothyroxine, lisinopril, aspirin, albuterol, and ipratropium. The patient's vitals are within normal limits today. Physical exam reveals an elderly female in no acute distress, oriented to person, place and year, but not to month or day of the week. She has a 3/6 holosystolic murmur at the left sternal border along with an S3 gallop. There are mild crackles at the lung bases. The remainder of the exam is normal. A previous urine culture reports growth of > 100,000 CFU of Enterobacter. Urinalysis findings are offered below:
Leukocyte esterase positive
WBCs 50-100 cell/HPF
Nitrites positive
RBCs 2 cell/HPF
Epithelial cells 2 cell/HPF
Urine pH 5.7
Which of the following is the most appropriate next step?

Answer Choices:

(A) TMP-SMX
(B) Nitrofurantoin
(C) Levofloxacin
(D) No treatment is necessary

Correct Answer:

(D)

OpenEvidence Response:

> **(D)** ✓

OpenEvidence Link: https://openevidence.com/ask/8a15189e-7425-4b64-ba8f-7698d11ff647

OpenEvidence Explanation

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The correct answer is **D. No treatment is necessary**.

This patient has **asymptomatic bacteriuria (ASB)**, which does not warrant antimicrobial therapy. Despite the positive urine culture (>100,000 CFU of Enterobacter) and abnormal urinalysis (positive leukocyte esterase, pyuria, positive nitrites), the patient has **no urinary symptoms** — no dysuria, urgency, frequency, suprapubic pain, or fever. The difficulty locating objects is consistent with her known Alzheimer's dementia, not an acute change suggesting UTI. Vitals are within normal limits, and there are no systemic signs of infection.

Why not treat?

The 2019 IDSA Clinical Practice Guideline for the Management of Asymptomatic Bacteriuria makes a **strong recommendation** against antimicrobial treatment of bacteriuria in older, cognitively impaired patients without localizing genitourinary symptoms or systemic signs of infection (e.g., fever, hemodynamic instability).[1] The guideline emphasizes that there is high certainty of harm (Clostridioides difficile infection, antimicrobial resistance, adverse drug effects) and low certainty of any benefit from treating ASB in this population.[1] Prospective studies in long-term care residents with advanced dementia found that antimicrobial therapy conferred no survival benefit (adjusted HR for death 1.09; 95% CI 0.43–2.75).[1]

The American Geriatrics Society Choosing Wisely campaign similarly recommends against using antimicrobials to treat bacteriuria in older adults unless specific urinary tract symptoms are present, noting that treatment has

been associated with adverse drug reactions and reinfection with more resistant organisms.[2]

Key distinctions in this case:

- ASB prevalence in community-dwelling older women ranges from 6–16%, and up to 50% in institutionalized settings — it is an expected finding, not an indication for treatment.[2][3]
- Pyuria accompanying ASB is common in older adults and does not change the management; it does not distinguish ASB from symptomatic UTI.[4]
- The only populations in whom ASB screening and treatment are recommended are **pregnant women** and patients undergoing **endourological procedures** with anticipated mucosal bleeding.[3][4]

Would you like to explore the specific criteria that distinguish asymptomatic bacteriuria from symptomatic UTI in cognitively impaired elderly patients?

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Question 1010

A 25-year-old woman presents to her primary care provider for evaluation of a painful mass in my left groin. She says that her symptoms began 4 days ago as a painful mass that slowly enlarged, ruptured, and ulcerated. However, she denies fever, chills, dysuria, or hematuria. Three weeks prior to her current symptoms she noted a small, painless ulcer on her labium majorum that resolved after a few days. She admits to having unprotected sex with a male partner a month ago while she was traveling in Southeast Asia. Temperature is 99°F (37.2°C), blood pressure is 139/84 mmHg, pulse is 76/min, and respirations are 18/min. Physical examination is significant for left-sided, tender, ulcerative lymph nodes with a dark discoloration. Which of the following is most likely to be seen in this patient's condition?

Answer Choices:

(A) Gram-negative rods in school of fish formation on Gram stain
(B) PCR positive for Chlamydia trachomatis
(C) Positive RPR, VDRL, and FTA-ABS
(D) Tzanck smear with multinucleated giant cells

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/a79bbd66-381e-4499-b621-b8d3180aa066

OpenEvidence Explanation

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The correct answer is **B. PCR positive for Chlamydia trachomatis**.

This clinical presentation is classic for **lymphogranuloma venereum (LGV)**, caused by *Chlamydia trachomatis* serovars L1–L3. The key features that point to this diagnosis include:

- A **small, painless, self-limited genital ulcer** (the primary stage) on the labium majorum that resolved spontaneously after a few days — approximately 3 weeks before the current presentation
- Subsequent development of **painful, tender, unilateral inguinal lymphadenopathy** with bubo formation that enlarged, ruptured, and ulcerated (the secondary stage), occurring 2–6 weeks after the primary lesion[1][2]
- **Travel to Southeast Asia**, where LGV is endemic
- Unprotected sexual contact approximately one month prior

LGV is characterized by three stages: (1) a small, painless, transient ulcer at the site of inoculation; (2) large, tender inguinal lymph nodes appearing 2–6 weeks later, with approximately 30% spontaneously perforating; and (3) if untreated, chronic scarring that may lead to lymphedema and genital elephantiasis.[1] Diagnosis is based on a positive *C. trachomatis* NAAT (PCR), which detects the organism but cannot distinguish LGV serovars from D–K serovars without additional genotyping.[2][3]

Why the other options are incorrect:

- **A. Gram-negative rods in "school of fish" formation** — This describes *Haemophilus ducreyi* (chancroid), which presents with **painful** genital ulcers from the outset (not a painless primary ulcer that self-resolves), and the Gram stain pattern has limited diagnostic accuracy.[4]
- **C. Positive RPR, VDRL, and FTA-ABS** — Primary syphilis presents with a painless chancre, but the associated lymphadenopathy is characteristically **nontender**, and the chancre is typically indurated with a clean base rather than a transient papule. Additionally, serologic tests may be nonreactive in up to 30% of primary syphilis cases.[1][5]

- **D. Tzanck smear with multinucleated giant cells** — This indicates herpes simplex virus, which presents with **grouped vesicles** on an erythematous base that ulcerate, rather than a painless primary ulcer followed by suppurative lymphadenopathy weeks later.

Would you like to explore the recommended treatment regimens for LGV and how they differ from treatment of non-LGV chlamydial infections?

Relevant images

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Question 1013

A 46-year-old man presents with worsening pain in multiple joints for the past 2 weeks. He says the pain is most severe in the proximal parts of his fingers and his wrists, but it has now spread to his elbows, and, occasionally, his knees. He says the joint involvement is symmetric. He also complains of morning joint stiffness that improves with activity and reports feeling fatigued during the day. He started taking ibuprofen 2 months ago for the pain which initially subsided, but, over the last few weeks, it has worsened despite the medication. He was diagnosed with type 2 diabetes mellitus 1 year ago and has had difficulty controlling his blood glucose levels. The patient denies any smoking history, alcohol, or recreational drug use. A review of systems is significant for a weight loss of 3.0 kg (6.6 lb) over the last 3 months despite no change in diet or activity level. Which of the following is the most likely 1st-line medication in this patient?

Answer Choices:

(A) Infliximab
(B) Anakinra
(C) Methotrexate
(D) High-dose prednisone for 60 days

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/803d411d-29ed-4f81-8c3b-ec41a1c25fb5

OpenEvidence Explanation

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The correct answer is **C. Methotrexate**.

This patient presents with a classic picture of **rheumatoid arthritis (RA)**: symmetric polyarthritis involving the proximal interphalangeal joints and wrists with spread to larger joints, prolonged morning stiffness that improves with activity, fatigue, and unintentional weight loss. The first-line disease-modifying antirheumatic drug (DMARD) for RA is **methotrexate**.

Why methotrexate is first-line:

Both the ACR (2021) and EULAR (2025) guidelines strongly recommend methotrexate monotherapy as initial therapy for DMARD-naive patients with moderate-to-high disease activity.[1][2][3] Methotrexate is considered the "anchor drug" in RA management due to its established efficacy, favorable safety profile, and low cost compared to biologic agents.[1][4] Approximately 25–40% of patients achieve substantial improvement with methotrexate alone.[4] Biologic or targeted synthetic DMARDs are reserved for patients with an inadequate response to conventional synthetic DMARDs.

Why the other options are incorrect:

- **A. Infliximab** — A TNF-α inhibitor (biologic DMARD) used as second-line therapy after failure of methotrexate, not as initial treatment.[3]
- **B. Anakinra** — An IL-1 receptor antagonist rarely used in RA; it is not first-line and has limited efficacy compared to other biologics.
- **D. High-dose prednisone for 60 days** — Glucocorticoids may be used as short-term bridging therapy alongside methotrexate, but prolonged high-dose prednisone is not appropriate first-line treatment. This is especially concerning in this patient with poorly controlled type 2 diabetes, as glucocorticoids worsen hyperglycemia.[5]

Regarding the coexisting diabetes: Methotrexate is not contraindicated in diabetes. In fact, a meta-analysis found that RA patients on methotrexate had a *lower* risk of developing type 2 diabetes (RR 0.48) compared to those not on

methotrexate.[6] However, diabetes is a risk factor for methotrexate-associated hepatic steatosis and fibrosis, so closer hepatic monitoring is warranted.[7]

Would you like to explore the specific monitoring protocols and dose escalation strategies for methotrexate initiation in patients with comorbid diabetes and potential hepatic steatosis?

Relevant images

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Question 1014

A previously healthy 29-year-old woman, gravida 1, para 0, at 35 weeks' gestation comes to the physician for a routine prenatal visit. Current medications include folic acid and a multivitamin. A rectovaginal swab culture grows bacitracin-resistant colonies of gram-positive cocci with surrounding areas of clear hemolysis. Which of the following is the most appropriate intervention to decrease vertical transmission of this organism?

> **Answer Choices:**
>
> (A) Abstain from breastfeeding
> (B) Administer ampicillin intrapartum
> (C) Perform amniocentesis at 37 weeks
> (D) Administer intravenous immune globulin postpartum

> **Correct Answer:**
>
> **(B)**
>
> **OpenEvidence Response:**
>
> **(B)** ✓

OpenEvidence Link: https://openevidence.com/ask/d27a6ec3-9cf4-47a5-b8c5-836c23c57b98

OpenEvidence Explanation

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The answer is **B. Administer ampicillin intrapartum**.

The culture findings describe **Group B Streptococcus (GBS)** — *Streptococcus agalactiae* — which is a gram-positive coccus that is bacitracin-resistant and beta-hemolytic (clear hemolysis = beta-hemolysis). These features distinguish GBS from Group A Streptococcus, which is bacitracin-sensitive.

Intrapartum antibiotic prophylaxis (IAP) with intravenous penicillin G or ampicillin is the standard of care to prevent vertical transmission and neonatal early-onset GBS disease. ACOG, AAP, and CDC guidelines all recommend universal prenatal rectovaginal screening at 36 0/7–37 6/7 weeks' gestation, with IAP administered to all GBS-colonized women at the onset of labor.[1][2][3] Intrapartum ampicillin crosses the placenta rapidly, achieving cord-blood levels above the GBS minimum inhibitory concentration within 1–2 hours, and prevents neonatal surface colonization in ~97% of cases when given ≥2 hours before delivery.[1][2]

Why the other options are incorrect:

- **A (Abstain from breastfeeding):** GBS is not transmitted through breast milk, and breastfeeding is not contraindicated.
- **C (Amniocentesis at 37 weeks):** Amniocentesis has no role in GBS prevention and would introduce unnecessary procedural risk.
- **D (IVIG postpartum):** Intravenous immune globulin is not part of GBS prophylaxis guidelines.

Would you like to explore the recommended approach for GBS prophylaxis in penicillin-allergic patients, including the role of allergy testing during pregnancy?

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Question 1016

An 18-year-old male is brought in by fire rescue. The patient was an unrestrained passenger in a motor vehicle crash and was ejected from the vehicle after collision. Upon arrival to the trauma bay, the patient has a Glasgow coma scale (GCS) of 6. He is rapidly intubated, and vitals are a temperature of 99.5°F (37.5°C), pulse of 130 bpm, and blood pressure of 83/64 mmHg. He is noted to have multiple ecchymoses over his body, as well as petechiae and purpura. He has a laceration over his clavicle that continues to bleed despite a pressure bandage. Radiographs of his lower extremity show multiple long bone fractures. Two large bore IV lines are placed, and the patient oozes from around the sites of venepuncture. Labs are notable for a WBC of 20,000/mm^3, Hb of 10.1g/dL, platelets of 48,000/mm^3, and prolongation of the PT and aPTT. This patient's presentation can best be explained by which of the following diagnoses?

Answer Choices:

(A) Air embolization
(B) Tension pneumothorax
(C) Disseminated intravascular coagulation
(D) Coagulopathy of trauma

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/59025cbb-4781-4eb9-9644-64005be87be9

OpenEvidence Explanation

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The answer is **C. Disseminated intravascular coagulation (DIC)**.

This patient's presentation — severe trauma with **thrombocytopenia** (platelets 48,000), **prolonged PT and aPTT**, **petechiae and purpura**, **diffuse oozing from venipuncture sites**, and **uncontrolled bleeding from a laceration** — is the classic clinical picture of DIC with a hemorrhagic (fibrinolytic) phenotype triggered by massive tissue injury.[1][2][3]

Why DIC is the best answer:

DIC is an acquired, systemic activation of coagulation that leads to consumption of platelets and clotting factors, resulting in both thrombocytopenia and prolongation of PT/aPTT.[3] The hallmark clinical features seen here — petechiae, purpura, oozing from IV sites, and uncontrolled surgical bleeding — are characteristic of the consumptive coagulopathy of DIC.[4] Severe tissue injury from multiple long bone fractures and ejection from a vehicle releases tissue factor, triggering widespread thrombin generation and subsequent consumption of coagulation factors and platelets.[2]

Why not the other options:

- **A. Air embolization** — Would present with acute cardiovascular collapse (hypotension, tachycardia, hypoxia) but would not explain the thrombocytopenia, prolonged coagulation times, petechiae/purpura, or diffuse oozing from venipuncture sites.
- **B. Tension pneumothorax** — Would present with hypotension, tracheal deviation, absent breath sounds, and distended neck veins. It does not cause coagulopathy or thrombocytopenia.
- **D. Coagulopathy of trauma (trauma-induced coagulopathy, TIC)** — This is the most important distractor. While TIC and DIC share overlapping pathophysiology in trauma, the question stem specifically highlights features of a consumptive process: thrombocytopenia, prolonged PT/aPTT, petechiae, purpura, and oozing from puncture sites. Some authors argue

that early traumatic coagulopathy is essentially DIC with a fibrinolytic phenotype. However, TIC as classically described emphasizes dilutional and hypothermia/acidosis-driven coagulopathy, whereas the constellation of findings here — particularly the petechiae, purpura, and consumption of both platelets and clotting factors — points specifically to DIC as the named diagnosis.[3][5][6][7]

The ISTH diagnostic scoring system for overt DIC incorporates platelet count, PT prolongation, elevated fibrin markers (D-dimer), and fibrinogen level, and this patient would score highly given the thrombocytopenia and PT/aPTT prolongation in the setting of a known underlying trigger.[7][8]

Would you like to explore the evidence-based management approach for trauma-associated DIC, including the role of tranexamic acid, damage control resuscitation, and component therapy?

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Question 1018

A 31-year-old man with a history of schizophrenia is brought to the emergency department by police after being found agitated and attempting to steal from a grocery store. His past medical history is only notable for a recent office note from his primary care doctor for treatment of seasonal allergies. His temperature is 101°F (38.3°C), blood pressure is 173/97 mmHg, pulse is 105/min, respirations are 16/min, and oxygen saturation is 98% on room air. Physical exam is notable for a man who is very irritable and restless. He is not cooperative with exam or history and becomes combative requiring intramuscular medications and security restraining him. After this event, the rest of his exam is notable for 7 mm pupils which are equal and reactive to light, spontaneous movement of all limbs, normal sensation, and warm and sweaty skin. The patient is answering questions and states he wants to kill himself. Which of the following substances was most likely used by this patient?

Answer Choices:

(A) Alcohol
(B) Cocaine
(C) Diphenhydramine
(D) Haloperidol

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/70ac21b3-88af-4cf6-ade3-f9fde9a287b5

OpenEvidence Explanation

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The answer is **B. Cocaine**.

This patient presents with a classic **sympathomimetic toxidrome**, which is the hallmark of cocaine intoxication. The key distinguishing features are:

- **Agitation, combativeness, and psychomotor hyperactivity**
- **Hypertension** (173/97 mmHg) and **tachycardia** (105/min)
- **Hyperthermia** (101°F / 38.3°C)
- **Mydriasis** (7 mm pupils, equal and reactive)
- **Diaphoresis** (warm and sweaty skin)
- Suicidal ideation (neuropsychiatric manifestation)

Cocaine produces a sympathomimetic toxidrome through catecholamine reuptake inhibition, resulting in tachycardia, hypertension, hyperthermia, diaphoresis, increased psychomotor activity, and mydriasis.[1][2] The DSM-5 criteria for stimulant intoxication include pupillary dilation, perspiration, tachycardia, hypertension, and psychomotor agitation — all present in this patient.[3]

Why not the other options:

- **Alcohol (A):** Alcohol intoxication causes CNS depression, not sympathetic hyperactivation. It would not explain the hypertension, tachycardia, mydriasis, or diaphoresis seen here.
- **Diphenhydramine (C):** This is a critical distractor given the patient's history of seasonal allergies (suggesting access to diphenhydramine). Diphenhydramine overdose produces an **anticholinergic** toxidrome with mydriasis and agitation, but the skin would be **hot and dry** — not diaphoretic. The classic mnemonic is "blind as a bat, dry as a bone, red as a beet, hot as a hare, mad as a hatter." The presence of **diaphoresis** (warm

and sweaty skin) rules out an anticholinergic toxidrome and points toward a sympathomimetic cause.[4][5][6]

- **Haloperidol (D):** Haloperidol is a dopamine antagonist that would cause sedation, extrapyramidal symptoms, and potentially neuroleptic malignant syndrome — not the sympathomimetic picture seen here.

The critical differentiating feature between cocaine (sympathomimetic) and diphenhydramine (anticholinergic) in this case is the **diaphoresis** — sympathomimetic toxidromes cause sweating, while anticholinergic toxidromes cause dry skin.[6][7]

Would you like to explore the acute management approach for sympathomimetic toxicity in the emergency department, including the role of benzodiazepines and avoidance of specific antihypertensives?

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Question 1019

A 40-year-old obese man presents to his primary care provider with a history of excessive daytime somnolence and easy fatigability. Upon further questioning, it is found that although his sleeping hours are adequate, he does not feel refreshed in the morning. His wife complains that he snores loudly all night. After ruling out common medical disorders and possible drug abuse, he is advised an overnight polysomnogram that records 12 episodes of apnea and 30 episodes of hypopnea during a 7-hour sleep. Which of the following statements best describes this patient's condition?

Answer Choices:

(A) This patient's apnea-hypopnea index (AHI) is more than 5.
(B) Episodes of apnea and hypopnea are more likely to occur during deeper stages of non-rapid eye movement sleep.
(C) Mouth opening during sleep breaks the seal between the tongue and the teeth and relieves airway obstruction.
(D) Gynoid obesity is associated with apnea and hypopnea more frequently as compared to android obesity.

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/19d337a2-7c2e-468d-9904-1e9b6e0c70db

OpenEvidence Explanation

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The correct answer is **A. This patient's apnea-hypopnea index (AHI) is more than 5.**

The AHI is calculated as the total number of apneas and hypopneas per hour of sleep. This patient had 12 apneas + 30 hypopneas = 42 events over 7 hours, yielding an **AHI of 6 events/hour**, which is indeed greater than 5.[1][2] An AHI ≥5 events/hour defines the presence of obstructive sleep apnea, with 5–15 classified as mild OSA.[1][2][3]

Why the other options are incorrect:

- **B. Episodes occur during deeper stages of NREM sleep** — This is false. Apneas and hypopneas are more frequent during **lighter NREM sleep (stages 1 and 2) and REM sleep** rather than during slow-wave (deep) NREM sleep. One study found the AHI was 39/hr in NREM stages 1–2 compared to only 11/hr in slow-wave sleep.[4]

- **C. Mouth opening relieves airway obstruction** — This is false. Mouth opening during sleep actually **worsens** upper airway obstruction. Mandibular rotation associated with mouth opening shifts the tongue and soft palate posteriorly, narrowing the airway and increasing collapsibility. Open-mouth breathing has been shown to create a more elongated and narrow upper airway, aggravating OSA severity.[5][6]

- **D. Gynoid obesity is more associated with OSA** — This is false. **Android (central/visceral) obesity** is more strongly associated with OSA than gynoid (peripheral) obesity. Central adiposity increases pharyngeal collapsibility through mechanical effects on pharyngeal soft tissues and lung volume. Greater peripheral adiposity in women may actually be protective against developing OSA.[7][8][9]

Would you like to explore the treatment options and CPAP titration strategies for mild obstructive sleep apnea?

Relevant images

(CONTENT OMITTED)

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Question 1021

Two hours following an elective cholecystectomy, a 43-year-old woman has fever and chills. The patient received cephalexin for antibiotic prophylaxis and one unit of packed red blood cells during the procedure. She underwent a hysterectomy 9 years ago for leiomyomata uteri. She has a 5-year history of hypertension treated with lisinopril. Her temperature is 39.5°C (102.3°F), pulse is 90/min, respirations are 18/min, and blood pressure is 125/90 mm Hg. Examination shows a mildly tender abdominal wound without erythema. The lungs are clear to auscultation. Cardiac examination shows no abnormalities. She had a Foley catheter and peripheral line access placed at the time of the procedure. Which of the following is the most likely cause of this patient's symptoms?

Answer Choices:

(A) Adverse effect of medication
(B) Malignant hyperthermia
(C) Urinary tract infection
(D) Transfusion reaction

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/b52f647d-82ac-4e6e-bc5a-16cbe9e7a19a

OpenEvidence Explanation

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The most likely cause of this patient's symptoms is **D. Transfusion reaction**.

This patient presents with **fever (39.5°C) and chills occurring 2 hours after surgery** during which she received one unit of packed red blood cells. This acute presentation is most consistent with a **febrile non-hemolytic transfusion reaction (FNHTR)** or, less commonly, an acute hemolytic transfusion reaction. Key reasoning:

- **Timing**: Transfusion reactions typically present within minutes to hours of transfusion, fitting this 2-hour postoperative window perfectly. Febrile non-hemolytic reactions are common, occurring in approximately **1–3% per unit transfused**, and present with a temperature rise ≥1°C accompanied by chills, rigors, and discomfort. The patient's prior hysterectomy is also relevant — previous transfusions or pregnancies can sensitize patients to donor leukocyte antigens, increasing the risk of both FNHTR and hemolytic reactions.[1][2]

- **Why not the other options**:

- **Adverse effect of medication (A)**: Drug fevers from cephalexin are possible but typically present later and are less acute in onset. Drug fever is usually a diagnosis of exclusion.[3]

- **Malignant hyperthermia (B)**: This is a hypermetabolic reaction to volatile anesthetic agents or succinylcholine, presenting with muscle rigidity, rapidly rising temperature (often >40°C), tachycardia, hypercarbia, and metabolic acidosis — none of which are described here.[4]

- **Urinary tract infection (C)**: UTIs from Foley catheterization typically take longer to develop (usually >48–72 hours) and would not present this acutely at 2 hours postoperatively.[3][5]

The classic mnemonic for postoperative fever — "Wind, Water, Wound, What did we do?" — places **blood product reactions** squarely in the iatrogenic ("What did we do?") category, which is the most relevant consideration in this early postoperative timeframe.[3]

Would you like to explore the workup and management algorithm for distinguishing febrile non-hemolytic transfusion reactions from acute hemolytic transfusion reactions?

Relevant images

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Question 1022

The first 24 hours after delivery, a 2888 g (6.37 lb) male newborn is not feeding well, has a high-pitched cry, and is diaphoretic. He was born at 38 weeks' gestation to a 30-year-old woman, gravida 2, para 1, after an uncomplicated labor and delivery. Apgar scores were 8 and 9 at 1 and 5 minutes, respectively. The mother did not receive prenatal care. She takes codeine syrup frequently for dry cough. The infant's temperature is 37.8°C (100°F), pulse is 165/min, and blood pressure is 83/50 mm Hg. Examination shows hyperreflexia, tremors, and an excessive startle response. The baby is swaddled to prevent excoriations, and fluid resuscitation is initiated. Complete blood count and serum levels of glucose, bilirubin, and calcium are within normal limits. What is the most appropriate next step in treatment of this newborn?

Answer Choices:

(A) Oral morphine therapy
(B) Intravenous ampicillin and gentamicin combination therapy
(C) Oral methimazole therapy
(D) Dextrose infusion

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/5a1ce3af-3bfe-4ed0-9ecc-e13bc268ea9d

OpenEvidence Explanation

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The answer is **A. Oral morphine therapy**. This newborn is presenting with classic signs of **neonatal opioid withdrawal syndrome (NOWS)** — poor feeding, high-pitched cry, diaphoresis, hyperreflexia, tremors, and excessive startle response — in the context of maternal codeine use during pregnancy without prenatal care. Nonpharmacologic measures (swaddling) have already been initiated, and common metabolic causes (hypoglycemia, hypocalcemia, hyperbilirubinemia) and infection have been effectively ruled out by normal labs.

Why oral morphine is correct:

Per the American Academy of Pediatrics (AAP) guidelines, **opioids should be used as first-line pharmacotherapy** for severe NOWS when nonpharmacologic interventions are insufficient.[1] Oral morphine is the most commonly used first-line agent in the United States.[1][2] It acts as a full mu-opioid receptor agonist that replaces the opioid the infant was exposed to in utero, thereby controlling withdrawal symptoms and allowing a gradual, controlled wean.[2]

Why the other options are incorrect:

- **B. IV ampicillin and gentamicin** — While neonatal sepsis can present with irritability and temperature instability, the CBC is normal, and the constellation of high-pitched cry, tremors, hyperreflexia, and excessive startle response in the setting of maternal opioid use is far more consistent with NOWS than infection.
- **C. Oral methimazole** — This would treat neonatal hyperthyroidism, which can cause tachycardia and irritability. However, there is no maternal history of Graves disease, and the full clinical picture (tremors, hyperreflexia, startle response with maternal codeine use) points to opioid withdrawal.
- **D. Dextrose infusion** — This would treat hypoglycemia, which has already been ruled out by normal serum glucose.

Would you like to explore the comparative efficacy of morphine versus methadone versus buprenorphine as first-line agents for NOWS, including recent trial data on symptom-based dosing approaches?

Relevant images

(CONTENT OMITTED)

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Question 1024

A 64-year-old man presents with severe respiratory distress. This has onset over the past 3 weeks, progressively worsening. Past history involves congestive heart failure (CHF). Due to concerns of concurrent pneumonia, sputum studies are ordered. Microscopic examination of his sputum demonstrates heart failure cells (hemosiderin-containing macrophages). Which of the following cellular organelles is significant in the formation of these cells?

Answer Choices:

(A) Endoplasmic reticulum (ER)
(B) Ribosomes
(C) Lysosomes
(D) Mitochondria

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/1c483179-7abf-4816-b47e-97f277964186

OpenEvidence Explanation

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The answer is **C. Lysosomes**.

Lysosomes are the organelles most significant in the formation of heart failure cells (hemosiderin-containing macrophages). In congestive heart failure, elevated pulmonary capillary pressures cause red blood cells to leak into the alveolar spaces. Alveolar macrophages phagocytose these extravasated erythrocytes, forming phagolysosomes where hemoglobin is degraded.[1][2] Within the **phagolysosome**, hemoglobin is broken down and heme is released, then transported to the cytosol via the heme transporter HRG1.[1][3] Heme oxygenase-1 subsequently degrades heme into free iron, biliverdin, and carbon monoxide.[4][5]

The liberated iron is partially stored as ferritin, and over time, excess iron aggregates within lysosomes to form **hemosiderin** — an insoluble, partially degraded iron-storage complex.[6][7] Lysosomes occupy a central position in intracellular iron homeostasis, serving as the primary site for iron recycling from phagocytosed material and for hemosiderin accumulation.[6][8] Classic electron microscopy studies demonstrated that hemosiderin granules are situated inside membrane-bound cytoplasmic organelles consistent with lysosomes (termed "siderosomes"), containing aggregated ferritin-derived iron micelles.[7]

These hemosiderin-laden alveolar macrophages — the "heart failure cells" — are a hallmark finding in sputum or BAL fluid from patients with chronic pulmonary congestion due to CHF, with hemosiderin staining first detectable approximately 3 days after hemorrhage and peaking around day 7.[9]

Would you like to explore the diagnostic utility and limitations of hemosiderin-laden macrophages in distinguishing pulmonary congestion from other causes of alveolar hemorrhage?

Relevant images

(CONTENT OMITTED)

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Question 1025

A previously healthy 52-year-old woman is brought to the emergency department after sustaining burns over 45% of her body in a house fire. On arrival, she is in acute distress but is fully oriented. Aggressive intravenous fluid resuscitation is begun and the patient is transferred to the intensive care unit of a burn center. 20 hours later, she has several large, tarry black stools and develops hypotension and tachycardia. Despite appropriate lifesaving measures, she dies. Which of the following is the most likely underlying cause of the patient's tarry black stools?

Answer Choices:

(A) Decreased prostaglandin synthesis
(B) Erosion of tortuous submucosal arteriole
(C) Bacterial colonization of the gastric antrum
(D) Decreased gastric blood flow

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/16402de5-6e3c-4c81-83cd-ab5d68d96735

OpenEvidence Explanation

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The correct answer is **D. Decreased gastric blood flow**.

This patient developed **Curling ulcers** — stress-related mucosal disease classically associated with severe burns (>35% total body surface area). The tarry black stools (melena) indicate upper GI bleeding from these stress ulcers, which developed within 24 hours of the burn injury.

Pathophysiology of stress ulcers in burn patients:

The primary underlying mechanism is **decreased gastric mucosal blood flow** due to splanchnic hypoperfusion. In critically ill burn patients, hypovolemia, decreased cardiac output, catecholamine-mediated vasoconstriction, and proinflammatory cytokines all converge to reduce splanchnic and mucosal perfusion.[1] This ischemia leads to reduced bicarbonate secretion, impaired mucosal defense, acid back-diffusion, and ultimately mucosal erosion and ulceration.[2][3] Reperfusion injury after prolonged hypoperfusion further compounds the damage.[1][4]

Why not the other options?

- **A. Decreased prostaglandin synthesis** — While reduced prostaglandin levels do occur during stress ulcer formation, this is a downstream consequence of mucosal ischemia, not the primary initiating mechanism. Decreased prostaglandin synthesis is the hallmark mechanism of NSAID-induced ulcers, not stress ulcers.[1][4][5]
- **B. Erosion of tortuous submucosal arteriole** — This describes a **Dieulafoy lesion**, a rare cause of GI bleeding unrelated to burns or critical illness.
- **C. Bacterial colonization of the gastric antrum** — This describes *H. pylori*-associated peptic ulcer disease, which is a chronic process and not the mechanism in acute stress ulceration following burns.[1]

Burns over >35% TBSA are a well-established major risk factor for stress-related mucosal disease, and prophylaxis with acid suppression (PPIs or H2RAs) is recommended in these patients.[1][4]

Would you like to explore the current evidence comparing PPIs versus H2 receptor antagonists for stress ulcer prophylaxis in critically ill patients?

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Question 1028

A 45-year-old man presents to a surgeon with painless swelling over his right leg. He noticed the swelling 6 months ago, but he ignored it because it was painless. However, he is now concerned as the swelling has been increasing in size over the last 6 months. He also mentions that his father and brother have lipomas over the extremities. On physical examination, the swelling is well-circumscribed and non-tender, measuring approximately 4 x 5 cm. After evaluation, the surgeon performs a surgical resection of the tumor and sends the tissue for histopathological examination. The pathologist reports the tumor to be a liposarcoma rather than a lipoma. Which of the following enzymes is most likely to show increased activity in the cells of this patient's tumor?

Answer Choices:

(A) Alkaline phosphatase
(B) RNase
(C) Superoxide dismutase
(D) Telomerase

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/acb171e9-3e69-4743-8a98-636a35df10b3

OpenEvidence Explanation

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The correct answer is **D. Telomerase**.

Telomerase is the enzyme most likely to show increased activity in liposarcoma cells. Telomerase is a reverse transcriptase that maintains telomere length at chromosome ends, enabling unlimited replicative potential — one of the hallmarks of cancer.[1][2] In normal somatic cells, telomerase is repressed, leading to progressive telomere shortening and eventual replicative senescence. However, telomerase is reactivated in **85–90% of all human cancers**, conferring cellular immortality.[3][4]

Specifically in soft tissue sarcomas and liposarcomas, telomerase activity has been well documented:

- Telomerase activity was detected in **52% of sarcomas** but in **none of the benign soft tissue tumors** in one study, with activity correlating with clinical aggressiveness.[5]
- In another series, **81% of primary sarcomas** were telomerase-positive, compared to only 1 of 7 benign lesions and none of 12 normal tissue controls.[6]
- In liposarcomas specifically, elevated telomerase activity and hTERT expression are associated with tumor progression from low-grade to higher-grade malignancy. A parallel increase of telomerase activity and malignancy has been observed in adipose tissue lesions.[7][8][9]

Why not the other options?

- **Alkaline phosphatase (A):** Elevated in osteoblastic activity and certain liver/bone diseases, not a hallmark enzyme of malignant transformation.
- **RNase (B):** A degradative enzyme with no established role as a marker of malignancy.
- **Superoxide dismutase (C):** An antioxidant enzyme that neutralizes reactive oxygen species; not characteristically upregulated as a driver of cancer cell immortalization.

The key concept tested here is that malignant cells acquire replicative immortality through telomerase reactivation, distinguishing them from benign tumors like lipomas.

Would you like to explore the alternative lengthening of telomeres (ALT) pathway, which is used by a subset of sarcomas that maintain telomeres independently of telomerase?

Relevant images

(CONTENT OMITTED)

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Question 1029

A 24-year-old woman presents to her primary care physician for a wellness visit. She says that she has been generally healthy but has noticed difficulty concentrating, becoming increasingly fatigued, and a 15-pound weight increase over the course of a few months. She also reports mild constipation and joint pain. Approximately 6-months ago, she experienced palpitations, increased stool frequency, and a hand tremor. Her past medical history is significant for asthma. Her father is not living and had Parkinson disease, and her mother has poorly controlled rheumatoid arthritis. She is currently sexually active in a monogamous relationship and uses contraception consistently. She denies cigarette smoking and occasionally drinks wine. She experimented once with lysergic acid diethylamide 6 years ago. Her temperature is 99°F (37.2°C), blood pressure is 127/98 mmHg, pulse is 55/min, and respirations are 13/min. On physical exam, the patient has slow speech and movement. She has tenderness to palpation of her wrist and ankle joints. She has delayed relaxation of deep tendon reflexes. Which of the following will most likely be found in this patient?

Answer Choices:

(A) Elevated TSH
(B) High Patient Health Questionnaire-9 (PHQ-9) score
(C) Positive anti-CCP antibodies
(D) Positive urine toxicology

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/a6ef80b9-6d38-4acd-9b9f-30d8b325531d

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OpenEvidence Explanation

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The answer is **A. Elevated TSH**.

This patient's presentation is classic for **hypothyroidism**, most likely due to **Hashimoto thyroiditis**. The current symptoms — fatigue, difficulty concentrating, weight gain, constipation, joint pain, bradycardia (55/min), slow speech and movement, diastolic hypertension (127/98 mmHg), and **delayed relaxation of deep tendon reflexes** — are hallmark features of hypothyroidism.[1][2] Delayed relaxation of ankle reflexes has a sensitivity of ~77% and specificity of ~93% for hypothyroidism.[2]

Critically, the history of **palpitations, increased stool frequency, and hand tremor 6 months ago** is consistent with an initial **hashitoxicosis phase** — a transient thyrotoxic state caused by destructive inflammation of thyroid follicles releasing stored thyroid hormone, which then progresses to hypothyroidism as the gland is destroyed.[3][4] This biphasic course (hyperthyroid → hypothyroid) is characteristic of Hashimoto thyroiditis.

The family history of maternal rheumatoid arthritis further supports an autoimmune etiology, as autoimmune thyroid disease and RA frequently coexist and cluster in families, sharing genetic susceptibility.[5][6]

Why not the other options:

- **B. High PHQ-9 score** — While depression can occur in hypothyroidism, the constellation of physical findings (bradycardia, delayed reflexes, diastolic hypertension) points to an organic thyroid disorder rather than primary depression.
- **C. Positive anti-CCP antibodies** — Although the mother has RA and the patient has joint pain, hypothyroidism itself causes arthralgias and joint

tenderness. The systemic features are better explained by thyroid disease. [1]

- **D. Positive urine toxicology** — LSD use was 6 years ago and would not explain the current clinical picture. LSD is also not typically detected on standard urine drug screens.

Would you like to explore the diagnostic workup and management approach for suspected Hashimoto thyroiditis, including the role of thyroid antibodies and levothyroxine initiation?

Relevant images

(CONTENT OMITTED)

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Question 1034

A 34-year-old woman presents to the plastic surgery office 3 months following a rhinoplasty procedure. The patient has been recovering well. However, she has noticed a small whistling noise when she respires through her nose, which you appreciate on physical exam. Which of the following is the most likely cause of this phenomenon?

> **Answer Choices:**
>
> (A) Post-operative swelling
> (B) A septal hematoma causing a perforation
> (C) A deviated septum that is now straight, resulting in altered nasal airflow
> (D) Excessive columellar show resulting in increased nasal airflow

> **Correct Answer:**
>
> **(B)**
>
> **OpenEvidence Response:**
>
> **(B)** ✓

OpenEvidence Link: https://openevidence.com/ask/965aed78-3e95-49c3-8374-256fd19cc49a

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OpenEvidence Explanation

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The most likely cause of a whistling noise during nasal respiration 3 months after rhinoplasty is **B. A septal hematoma causing a perforation**.

Septal perforation is a recognized complication of rhinoplasty, occurring in up to 2.6% of cases.[1] The pathophysiology involves a septal hematoma that develops during or after surgery; if unrecognized or untreated, the hematoma compresses the septal cartilage, leading to avascular necrosis and eventual perforation of the nasal septum.[2][3]

A **whistling sound during nasal breathing** is one of the hallmark symptoms of nasal septal perforation, along with crusting, epistaxis, nasal obstruction, and dryness.[4][5] Computational fluid dynamics studies have demonstrated that airflow exchange through a septal perforation — particularly small, anteriorly located perforations — generates turbulence and cross-flow between the nasal passages, which produces the characteristic whistling noise.[6][7] Smaller and more anterior perforations tend to be more symptomatic, with a statistically significant negative correlation between perforation size and whistling symptoms (i.e., smaller perforations whistle more).[8]

Why the other options are less likely:

- **A. Post-operative swelling** — Swelling at 3 months post-rhinoplasty would be largely resolved and would more likely cause congestion or obstruction rather than a discrete whistling sound.[2]
- **C. A deviated septum that is now straight** — Correction of a deviated septum improves airflow and would not produce a whistling noise; altered laminar flow from straightening does not generate this phenomenon.
- **D. Excessive columellar show** — This is a cosmetic concern related to the external appearance of the nose and does not cause whistling during respiration.

Would you like to explore the management options for small symptomatic septal perforations, including prosthetic buttons versus surgical repair techniques?

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Question 1035

A 43-year-old woman comes to the physician because of a 1-day history of rash on the trunk and lower extremities. Three days ago, she visited a spa resort with multiple swimming pools and whirlpools. A friend of hers who also visited the spa has developed a similar rash. She does not smoke or drink alcohol and takes no medications. She appears well. Her vital signs are within normal limits. Examination shows multiple erythematous, excoriated papules and pustules over the trunk and upper thighs. The inflammation seen in this patient's condition most likely originated in which of the following parts of the skin?

Answer Choices:

(A) Superfical epidermis
(B) Hair follicles
(C) Papillary dermis
(D) Eccrine sweat glands

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/1839212f-b0db-4cca-abd1-679651cf72b8

OpenEvidence Explanation

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The answer is **B. Hair follicles**. This clinical presentation is classic for **"hot tub" folliculitis** (Pseudomonas folliculitis), in which the inflammation originates in the **hair follicles**.

Key clinical reasoning:

The history of spa/whirlpool exposure followed 1–3 days later by pruritic, erythematous papules and pustules on the trunk and proximal extremities — with a similarly affected contact — is the hallmark presentation of Pseudomonas aeruginosa folliculitis. This condition typically develops **8 to 48 hours** after exposure to contaminated water in hot tubs, whirlpools, or swimming pools.[1][2] The eruption characteristically involves areas covered by swimwear (trunk, buttocks, upper thighs) and spares the head and neck.[2]

Why hair follicles? Folliculitis is, by definition, inflammation of the hair follicle. Pseudomonas aeruginosa enters the skin through the follicular openings, and histopathology demonstrates acute suppurative folliculitis with neutrophilic infiltration of the pilar canal.[1][3] The pilosebaceous unit — specifically the infundibulum (superficial portion of the follicle) — is the site of initial inflammation.[4]

Why not the other options?

- **Superficial epidermis** — would suggest impetigo or contact dermatitis, not the follicular-based papulopustules seen here.
- **Papillary dermis** — would suggest urticaria or dermatitis herpetiformis.
- **Eccrine sweat glands** — eccrine-based inflammation (e.g., neutrophilic eccrine hidradenitis) is a distinct and much rarer entity, typically associated with chemotherapy or systemic illness, not recreational water exposure.[5][6]

The condition is generally self-limited, resolving within 7–10 days without treatment.[1][2]

Would you like to explore the management approach for cases of hot tub folliculitis that fail to resolve spontaneously?

Relevant images

(CONTENT OMITTED)

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Question 1036

A 19-year-old man is brought to the emergency department because of severe right shoulder pain and inability to move the shoulder after a fall while climbing outdoors. Examination shows the right upper extremity is externally rotated and slightly abducted. There is loss of the the normal rounded appearance of the shoulder. The right humeral head is palpated below the coracoid process. Sensation to pinprick over which of the following skin areas is most likely to be reduced?

Answer Choices:

(A) Medial aspect of the upper arm
(B) Lateral aspect of the shoulder
(C) Skin above the clavicle
(D) Dorsal aspect of forearm and hand

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/933c67a9-7779-4303-91c0-7b372ea268d7

OpenEvidence Explanation

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The answer is **B. Lateral aspect of the shoulder**.

This presentation — external rotation, abduction, loss of the normal shoulder contour, and humeral head palpable below the coracoid process — is classic for an **anterior glenohumeral dislocation**. The nerve most vulnerable to injury in this setting is the **axillary nerve** (C5–C6), which courses inferior to the glenohumeral joint and is stretched or compressed by the dislocating humeral head.[1][2]

The axillary nerve provides sensory innervation to the "**regimental badge" area** — the lateral aspect of the shoulder and proximal deltoid region — via the superior lateral cutaneous nerve of the arm.[1] The AAFP guidelines on acute shoulder injuries specifically recommend assessing axillary nerve function by **testing sensation to the lateral shoulder** and deltoid muscle strength both before and after reduction.[3] The axillary nerve is injured in up to 9–40% of anterior shoulder dislocations, making it the most commonly affected nerve in this injury.[1][2][4]

The other answer choices correspond to different nerves:

- **A (Medial upper arm)** — medial cutaneous nerve of the arm (T1–T2)
- **C (Skin above the clavicle)** — supraclavicular nerves (C3–C4)
- **D (Dorsal forearm and hand)** — radial nerve / posterior cutaneous nerve of the forearm

Would you like to explore the recommended reduction techniques for anterior shoulder dislocation and the evidence comparing their success rates?

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Question 1037

A 25-year-old girl is brought to the emergency room after a suicide attempt. Her mother states that she found a large empty pill bottle next to her. The patient is conscious and tearful. She is currently complaining of severe abdominal pain but refuses to give any other history. She has a blood pressure of 135/86, respiratory rate of 18/min, and heart rate of 86/min. On examination, her abdomen is exquisitely tender with evidence of crepitus in the epigastric region. Abdominal CT reveals a gastric perforation. Which of the following is the most likely cause?

Answer Choices:

(A) Decreased production of PGE2
(B) Buildup of a toxic metabolite due to kidney disease
(C) Increased stimulation of the vagus nerve
(D) Hypovolemia

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/a2f930d7-7ff9-4b7c-ae22-3a1778277ff5

OpenEvidence Explanation

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The answer is **A. Decreased production of PGE2**.

This clinical scenario describes a young woman who attempted suicide by ingesting a large quantity of pills, now presenting with gastric perforation. The most likely ingested medication is an **NSAID** (such as aspirin or ibuprofen), which causes gastric mucosal injury primarily through **inhibition of cyclooxygenase (COX) enzymes**, leading to decreased production of prostaglandin E2 (PGE2).

Why PGE2 matters: PGE2 is a key cytoprotective prostaglandin in the gastric mucosa. It promotes mucus and bicarbonate secretion, maintains mucosal blood flow, and supports epithelial cell integrity. NSAIDs inhibit COX-1 (and COX-2), dramatically reducing PGE2 synthesis, which removes these protective mechanisms and leaves the mucosa vulnerable to acid-mediated injury.[1][2] In massive overdose, this can progress from erosions to frank ulceration and perforation.

Why not the other options:

- **B (Buildup of a toxic metabolite due to kidney disease):** This would suggest acetaminophen toxicity via NAPQI accumulation. However, acetaminophen's primary toxicity target is the liver, not the stomach. Studies show acetaminophen does not significantly alter gastric mucosal barrier function, ionic fluxes, or potential difference, even at supratherapeutic doses. Gastric perforation is not a recognized complication of acetaminophen overdose.[1][3]

- **C (Increased vagus nerve stimulation):** Vagal stimulation increases gastric acid secretion but is not a mechanism associated with drug overdose-induced gastric perforation.

- **D (Hypovolemia):** While hypovolemia can cause stress-related mucosal injury, the patient's vital signs (BP 135/86, HR 86) do not suggest hemodynamic compromise, and this would not explain perforation in the context of pill ingestion.

The presence of epigastric crepitus (subcutaneous emphysema from free air) and CT-confirmed gastric perforation in the setting of a large pill ingestion is classic for massive NSAID overdose causing severe gastric mucosal injury through prostaglandin depletion.[1][4]

Would you like to explore the acute management of NSAID-induced gastric perforation, including surgical versus conservative approaches?

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Question 1038

A 32-year-old male presents to the ED with acute-onset chest pain. His blood pressure is 157/90 mmHg and his his pulse is 116/min. He appears anxious and agitated and a careful exam reveals dilated pupils and a perforated nasal septum. An EKG reveals ST segment elevation so he is urgently taken for cardiac intervention. Upon review, this patient reveals that he has not had care from a physician since he graduated from college. In the interim he has been largely unemployed and admits that he has recently been homeless. When asked directly, the patient admits to alcohol and marijuana use but denies illicit drug use. Which of the following best describes the mechanism of action of the agent most likely responsible for this patient's presentation?

Answer Choices:

(A) Blocking reuptake of dopamine and norepinephrine
(B) Inhibiting breakdown of biogenic amines
(C) Antagonizing the NMDA receptor
(D) Inhibiting the GABA receptor

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/197ff173-dc3f-4d9a-a462-1527f2e34d66

OpenEvidence Explanation

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The answer is **A. Blocking reuptake of dopamine and norepinephrine**.

This clinical vignette describes a young male with classic signs of **cocaine use**: hypertension, tachycardia, agitation, dilated pupils, **nasal septal perforation** (pathognomonic for chronic intranasal cocaine use), and ST-segment elevation myocardial infarction (STEMI). Despite denying illicit drug use — which is common among patients with substance use disorders — the constellation of findings is unmistakable for cocaine toxicity.

Cocaine's primary mechanism of action is blocking the presynaptic reuptake of catecholamines — specifically **dopamine, norepinephrine, and serotonin** — leading to their accumulation at postsynaptic receptors.[1][2][3] This produces a powerful sympathomimetic toxidrome characterized by tachycardia (via β_1-adrenergic stimulation), hypertension (via α_1-adrenergic stimulation), mydriasis, and psychomotor agitation.[1][4] The resulting increase in myocardial oxygen demand, combined with coronary vasoconstriction and a prothrombotic state, predisposes to acute myocardial ischemia and infarction — even in young patients without traditional risk factors.[5][6]

The following figure illustrates the multifactorial mechanisms by which cocaine induces myocardial ischemia, including supply-demand mismatch, coronary vasoconstriction, and accelerated thrombosis:

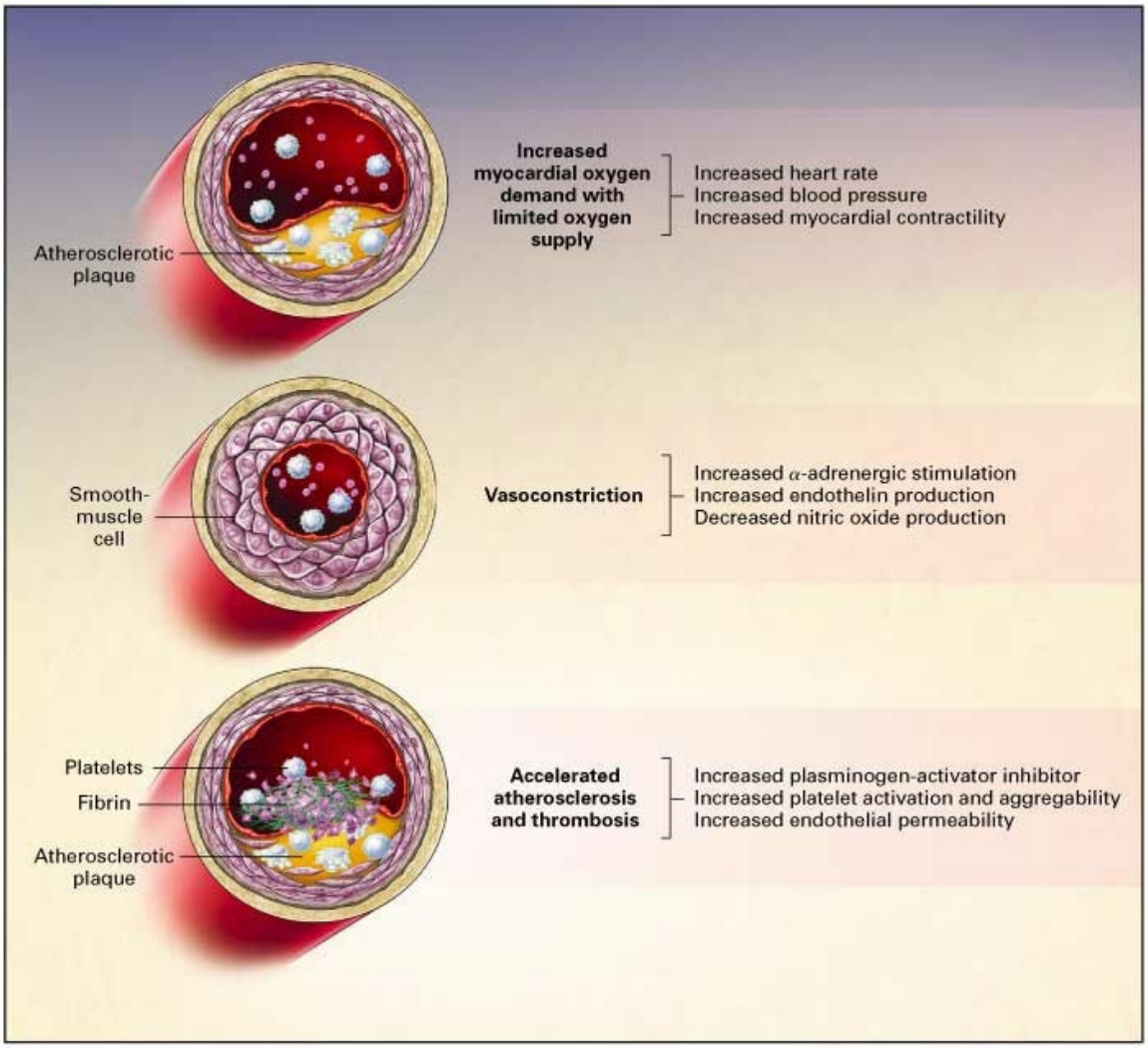


Figure 2. Mechanisms by Which Cocaine May Induce Myocardial Ischemia or Infarction.

Used under license from The New England Journal of Medicine.

Why the other options are incorrect:

- **B (Inhibiting breakdown of biogenic amines)** — This describes MAO inhibitors, which prevent enzymatic degradation of monoamines rather than blocking reuptake.
- **C (Antagonizing the NMDA receptor)** — This describes agents like ketamine or PCP, which produce dissociative effects rather than a sympathomimetic toxidrome.
- **D (Inhibiting the GABA receptor)** — This would produce CNS excitation but is not the mechanism of cocaine; GABA antagonism is associated with agents like flumazenil or picrotoxin.

Would you like to explore the specific management considerations for cocaine-associated STEMI, including the controversy around beta-blocker use in this setting?

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Question 1040

A 55-year-old woman is brought to the emergency department because of worsening upper abdominal pain for the past 8 hours. She reports that the pain radiates to her back and is associated with nausea. She has hypertension and hyperlipidemia, for which she takes enalapril, furosemide, and simvastatin. Her temperature is 37.5°C (99.5°F), blood pressure is 84/58 mm Hg, and pulse is 115/min. The lungs are clear to auscultation. Examination shows abdominal distention with epigastric tenderness and guarding. Bowel sounds are decreased. Extremities are warm. Laboratory studies show:
Hematocrit 48%
Leukocyte count 13,800/mm3
Platelet count 175,000/mm3
Serum
Calcium 8.0 mg/dL
Urea nitrogen 32 mg/dL
Amylase 250 U/L
An ECG shows sinus tachycardia. Which of the following is the most likely underlying cause of this patient's vital sign abnormalities?

Answer Choices:

(A) Abnormal coagulation and fibrinolysis
(B) Capillary leakage
(C) Decreased cardiac output
(D) Pseudocyst formation

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/4b155f67-6eb8-4f36-8654-dd8afc65773f

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OpenEvidence Explanation

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The answer is **B. Capillary leakage**.

This patient presents with acute pancreatitis (epigastric pain radiating to the back, elevated amylase, nausea) and vital sign abnormalities of **hypotension** (84/58 mmHg) and **tachycardia** (115/min) with warm extremities. The underlying cause of these hemodynamic derangements is **capillary leakage** — the systemic inflammatory response in acute pancreatitis causes marked endothelial injury and increased vascular permeability, leading to extravasation of fluid into the interstitial space and peritoneum (third-spacing).[1][2]

Several laboratory findings in this patient corroborate this mechanism:

- **Hemoconcentration** (hematocrit 48%) — as plasma leaks out of the intravascular space through permeable capillaries, the remaining blood becomes more concentrated.[3][4]
- **Elevated BUN** (32 mg/dL) — reflects decreased renal perfusion from intravascular volume depletion, a recognized marker of hypovolemia in acute pancreatitis.[2][5]
- **Warm extremities** — consistent with a distributive/vasodilatory hemodynamic pattern driven by systemic inflammation (SIRS), with decreased systemic vascular resistance rather than cardiogenic shock.[6][7]

A capillary permeability model of severe acute pancreatitis demonstrated that increased capillary permeability to plasma proteins predicts loss of oncotic pressure, reduced vascular volume, hypotension with prerenal azotemia, and organ dysfunction — all consistent with this patient's presentation.[3]

Why not the other options?

- **A. Abnormal coagulation and fibrinolysis** — DIC can occur in pancreatitis but is not the primary mechanism of early hypotension and tachycardia; the platelet count here is normal.
- **C. Decreased cardiac output** — Severe pancreatitis typically produces a hyperdynamic circulatory state (high cardiac output, low SVR) rather than low cardiac output, and warm extremities argue against cardiogenic shock. [6]
- **D. Pseudocyst formation** — Pseudocysts develop weeks after the onset of pancreatitis, not within 8 hours.

Would you like to explore the scoring systems (Ranson, BISAP, APACHE II) used to predict severity and guide management in acute pancreatitis?

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Question 1042

A 21-year-old man with a past medical history significant for Down syndrome presents to the outpatient primary care clinic for a routine follow up and high risk screening. He is relatively high functioning and currently has no additional significant medical conditions. He feels well and a physical examination shows that he is within normal limits. He denies any current tobacco use, alcohol use, or illicit drug use. His vital signs include: temperature, 36.7°C (98.0°F); blood pressure, 126/74 mm Hg; heart rate, 87/min; and respiratory rate, 17/min. When considering possible conditions for which this patient is predisposed, which of the following neoplasms is associated with Down syndrome?

Answer Choices:

(A) Gastric adenocarcinoma
(B) Astrocytoma and cardiac rhabdomyoma
(C) Esophageal adenocarcinoma
(D) Acute lymphocytic leukemia

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/cbb2e757-2bdf-46fc-ab51-50cd96546392

OpenEvidence Explanation

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The correct answer is **D. Acute lymphocytic leukemia**.

Down syndrome (trisomy 21) is strongly associated with **acute lymphocytic leukemia (ALL)**, with children having an approximately **20- to 30-fold increased risk** compared to the general population.[1][2][3] Leukemia develops in 2–3% of all patients with Down syndrome, with both ALL and acute myeloid leukemia (AML) occurring at significantly elevated rates.[1] A large Swedish population-based cohort study confirmed a 20-fold increased risk of ALL and nearly 500-fold increased risk of AML before age 5.[2] The NCCN Pediatric ALL Guidelines explicitly identify Down syndrome as "an important ALL predisposition syndrome".[4]

Regarding the other answer choices:

- **A. Gastric adenocarcinoma** – Not associated with Down syndrome. Epidemiologic data actually suggest that most solid tumors, including gastrointestinal cancers, occur at **lower** rates in individuals with Down syndrome.[2][5]
- **B. Astrocytoma and cardiac rhabdomyoma** – These are classic features of **tuberous sclerosis complex (TSC)**, not Down syndrome. Subependymal giant cell astrocytoma and cardiac rhabdomyoma are both major diagnostic criteria for TSC, caused by mutations in TSC1/TSC2 genes. Up to 90% of cardiac rhabdomyomas are associated with TSC.[6][7][8]
- **C. Esophageal adenocarcinoma** – Not associated with Down syndrome. Solid tumors in general are less prevalent in this population.[2][3]

Notably, while Down syndrome is protective against most solid tumors, **testicular cancer** is one exception, occurring at increased rates in males with Down syndrome.[2][9][10]

Would you like to explore the current recommended cancer screening and health surveillance guidelines for adults with Down syndrome?

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Question 1044

A 4-year-old boy presents to the pediatrician's office. His mother complains that he has been sleeping poorly, and she has noticed that he often scratches his perianal area. A scotch tape test is found to be positive and mebendazole is prescribed. Into which of the following subsets have the naïve T cells (TH0) developed due to the infection in this patient?

Answer Choices:

(A) TH1 cells
(B) TH2 cells
(C) TH17
(D) T0 cells

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/b1bb92bd-32fd-4ea3-a989-9a4b36af0591

OpenEvidence Explanation

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The answer is **B. TH2 cells**.

Enterobius vermicularis (pinworm) is a helminth (intestinal nematode), and helminth infections characteristically drive naïve CD4+ T cells (TH0) to

differentiate into **TH2 cells**. This is one of the most consistent immunological paradigms in parasitology.

The TH2 response to helminth infection is characterized by production of the canonical cytokines **IL-4, IL-5, IL-9, and IL-13**, which in turn drive elevated **IgE** production, **eosinophilia**, **mast cell activation**, and **goblet cell hyperplasia** — all of which contribute to parasite expulsion.[1][2] Pinworm infection specifically has been shown to induce a transient TH2-type immune response with elevated IL-4, IL-5, and IL-13 cytokine production and parasite-specific IgG1.[3] In contrast, TH1 responses (associated with intracellular pathogens), TH17 responses (associated with extracellular bacteria and fungi), and "T0 cells" (which is not a recognized effector subset) are not the predominant response to helminth infection.[4][5]

The following figure illustrates the differentiation pathways of naïve CD4+ T cells into distinct T helper cell subsets, including the TH2 pathway driven by STAT6 and GATA3:

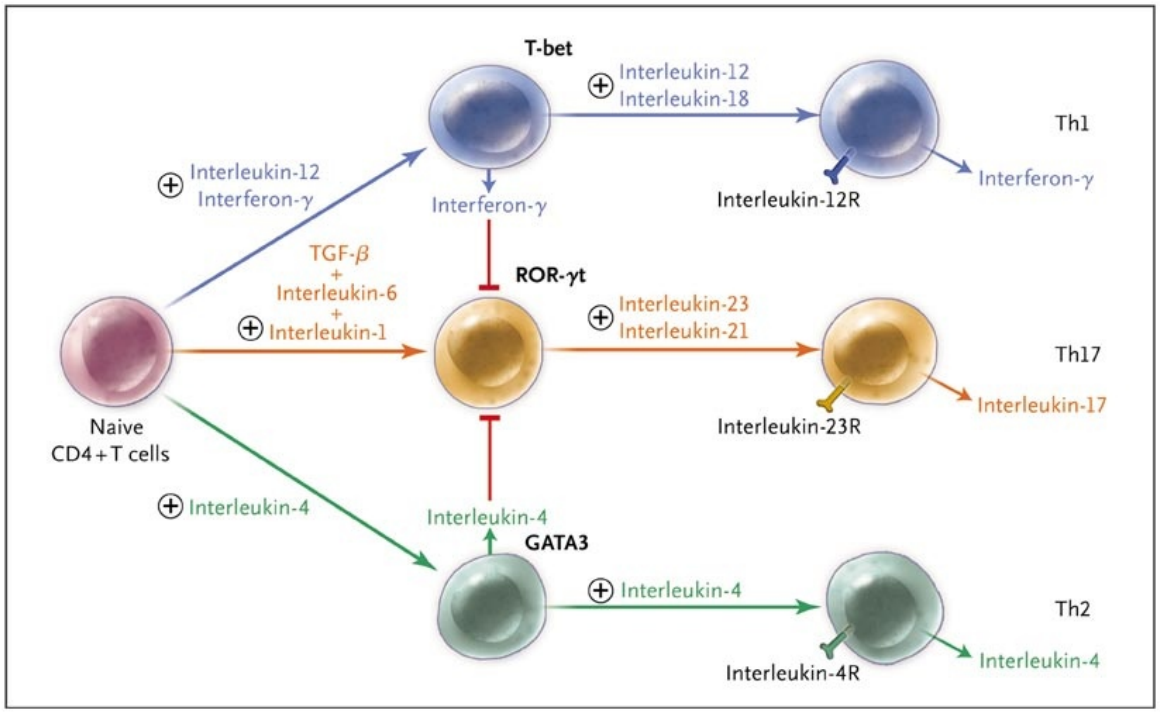


Figure 2. Differentiation of Mouse Th17 Cells.

Used under license from The New England Journal of Medicine.

Would you like to explore the specific mechanisms by which TH2 cytokines mediate worm expulsion in intestinal nematode infections?

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Question 1045

A 69-year-old right-handed man comes to the physician for a routine health maintenance examination. On questioning, he has had some difficulty speaking for 3 months. During a conversation, he often has difficulty repeating what his interlocutor has said. He has hypertension and takes hydrochlorothiazide. His vital signs are within normal limits. The patient speaks fluently in full sentences and demonstrates normal comprehension. When asked to say the word “kindergarten,” he replies with, “Sintelmarvin... no, that's wrong...kinterflargin, no that isn't it either...kantolargen...no? How about, kindergarten?” The most likely cause of the patient's symptoms is occlusion of a branch of which of the following arteries?

Answer Choices:

(A) Left middle cerebral
(B) Right vertebral
(C) Left posterior inferior cerebellar
(D) Left penetrating

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/0309ed85-6a5d-4f1f-99e6-d8152c84388a

OpenEvidence Explanation

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The answer is **A. Left middle cerebral artery**.

This patient presents with classic **conduction aphasia**, characterized by:

- **Fluent speech** with preserved comprehension
- **Impaired repetition** (difficulty repeating what others say)
- **Phonemic paraphasias** with successive self-correction attempts ("Sintelmarvin… kinterflargin… kantolargen… kindergarten") — a phenomenon known as **conduite d'approche**, where the patient recognizes errors and progressively approximates the target word[1][2]

Conduction aphasia results from damage to the left temporoparietal region, specifically the **supramarginal gyrus** (Brodmann area 40), the arcuate fasciculus, and/or the posterior planum temporale (area Spt), which are critical for phonological assembly and auditory-motor integration.[1][3] These structures lie within the vascular territory of the **left middle cerebral artery (MCA)**.[4][5] A case report of conduction aphasia following stroke confirmed a left MCA infarction involving the parietal lobe that engulfed the arcuate fasciculus on MR tractography.[4]

The other options are incorrect:

- **Right vertebral artery** — supplies the posterior fossa; would not produce a dominant-hemisphere language deficit
- **Left posterior inferior cerebellar artery (PICA)** — supplies the lateral medulla and inferior cerebellum; occlusion causes lateral medullary (Wallenberg) syndrome, not aphasia
- **Left penetrating arteries** — supply deep structures (basal ganglia, internal capsule, thalamus); occlusion would produce motor/sensory deficits or subcortical aphasia patterns, not the classic conduction aphasia pattern seen here

Would you like to explore how conduction aphasia is differentiated from other perisylvian aphasias such as Broca's and Wernicke's aphasia based on clinical examination findings?

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Question 1052

A 7-day-old infant boy presents to an emergency department due to poor feeding. His parents are recent immigrants to the United States. He was born in a traditional home birth and has never seen a medical provider. Mom had no prenatal care, has no medical issues, and is unvaccinated. The baby had been breastfeeding well until 24 hours ago when mom noticed he started having trouble latching. In the last 12 hours, he has completely refused to feed. He has had a decreased number of wet diapers and has stooled twice in the last 24 hours. His temperature is 98.6°F (37.0°C), pulse is 180/min, respirations are 52/min, and blood pressure is 70/50 mmHg. On exam, the infant has increased tone, a clenched jaw, no head lag, and clenched hands. Initial screening bloodwork is normal. What is the most likely organism causing this infant's presentation?

Answer Choices:

(A) Clostridium botulinum
(B) Clostridium tetani
(C) Group B streptococcus
(D) Listeria monocytogenes

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/77563607-8422-41d6-8787-2e6951b811e4

OpenEvidence Explanation

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The answer is **B. Clostridium tetani**.

This presentation is classic for **neonatal tetanus**. The key features pointing to this diagnosis include:

- **7-day-old infant** — the median incubation period for neonatal tetanus is 5–7 days after birth, with ~90% of cases developing symptoms between days 3–14 (most commonly days 6–8)[1][2]
- **Unvaccinated mother, no prenatal care, and traditional home birth** — these are the major risk factors for neonatal tetanus, as maternal tetanus toxoid vaccination provides ~94% protection against neonatal tetanus, and unhygienic cord care during home deliveries is the typical portal of entry for *C. tetani* spores[1][3]
- **Refusal to feed with trismus (clenched jaw)** — inability to suck due to trismus is the hallmark presenting symptom of neonatal tetanus[1][2]
- **Increased tone and clenched hands** — generalized hypertonia with clenched hands and dorsiflexion of the feet are characteristic findings, progressing to rigidity and opisthotonus[1][3]
- **Normal screening bloodwork** — tetanus is a clinical diagnosis; routine labs are typically normal because the toxin acts at the neuromuscular level without causing systemic inflammation or bacteremia[4]

Why not the other options:

- **Clostridium botulinum (A):** Infant botulism causes *flaccid* paralysis (hypotonia, "floppy baby"), constipation, and weak cry — the opposite of the hypertonia and rigidity seen here[5]
- **Group B streptococcus (C):** GBS neonatal sepsis/meningitis typically presents with fever, lethargy, respiratory distress, and hypotonia — not the hypertonic, afebrile presentation described
- **Listeria monocytogenes (D):** Neonatal listeriosis presents with sepsis, fever, and meningitis — again inconsistent with the afebrile, hypertonic picture with normal bloodwork

The critical distinguishing feature is **hypertonia with trismus** (spastic paralysis from tetanus toxin blocking inhibitory neurotransmitters GABA and glycine) versus the **hypotonia** that would be expected with botulism or bacterial sepsis/meningitis.[4]

Would you like to explore the acute management of neonatal tetanus, including the role of tetanus immunoglobulin, wound care, and supportive measures?

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Question 1055

A 9-year-old male visited his primary care physician for a check-up three months after a throat infection. Upon examination, the patient exhibits painless subcutaneous nodules on the back of the wrist, the outside elbow, and the front of the knees, as well as inflammation in the joints of the lower extremities. Which of the following symptoms is most likely to also be present in this patient?

Answer Choices:

(A) Renal failure
(B) Hepatomegaly
(C) Chorea
(D) Pleural effusion

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/8e0c9ee5-1b58-42ce-a76d-34fc4fdd8764

OpenEvidence Explanation

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The answer is **C. Chorea**.

This clinical presentation is classic for **acute rheumatic fever (ARF)** following a group A streptococcal (GAS) pharyngitis. The key features — painless

subcutaneous nodules over extensor surfaces (wrists, elbows, knees) and lower extremity arthritis occurring approximately 3 months after a throat infection in a school-aged child — fulfill major Jones criteria for ARF.[1][2]

Chorea (Sydenham chorea) is one of the five major manifestations of ARF, along with carditis, polyarthritis, erythema marginatum, and subcutaneous nodules.[1][2] It occurs in 10–30% of ARF cases and characteristically presents with purposeless, involuntary movements of the extremities and trunk, often accompanied by emotional lability and muscle weakness.[1][3] The typical latent period for chorea is 1–6 months after GAS infection, which aligns with this patient's timeline of 3 months post-pharyngitis.[3][4]

Notably, subcutaneous nodules are usually associated with carditis and are strongly linked to other major manifestations of ARF.[1] The other answer choices — renal failure, hepatomegaly, and pleural effusion — are not recognized major or minor manifestations of ARF per the Jones criteria.[2]

Would you like to explore the recommended workup and secondary prophylaxis regimen for a child presenting with acute rheumatic fever?

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Question 1056

A 29-year-old man diagnosed with schizophrenia 4 years ago presents for follow-up to discuss his medication. The patient was diagnosed with schizophrenia 4 years ago and has since tried several antipsychotic medications, none of which have been able to treat his negative symptoms. He has changed to clozapine 2 weeks ago and says that he does feel better. His physical exam is unremarkable, and he is responding appropriately to questioning. If this patient's current medication is to be continued, which of the following laboratory tests should be ordered at this time?

Answer Choices:

(A) Slit-lamp examination
(B) Electrocardiogram
(C) Prolactin level
(D) Complete blood count

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/46e40355-20ab-4665-b5fb-9c177eebccd1

OpenEvidence Explanation

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The answer is **D. Complete blood count**. Clozapine carries a well-known risk of **severe neutropenia and agranulocytosis**, a rare but potentially fatal adverse effect that requires mandatory hematologic monitoring throughout treatment.[1]

The FDA-mandated Clozapine REMS program requires obtaining a baseline **absolute neutrophil count (ANC)** prior to initiation and then monitoring ANC **weekly for the first 6 months**, every 2 weeks for the next 6 months, and monthly thereafter.[1][2] Since this patient is only 2 weeks into clozapine therapy, he falls within the highest-risk period — the risk of severe neutropenia is greatest during the **first 18 weeks** of treatment.[1][3] A complete blood count (CBC) with differential provides the ANC needed for this monitoring.

Why the other options are incorrect:

- **A. Slit-lamp examination** — This is associated with monitoring for corneal deposits or lens opacities seen with long-term use of certain antipsychotics (e.g., chlorpromazine, thioridazine), not clozapine.
- **B. Electrocardiogram** — While an ECG is recommended at baseline before clozapine initiation (to assess QTc interval), it is not the primary ongoing monitoring requirement.[4][5]
- **C. Prolactin level** — Prolactin elevation is more commonly associated with typical antipsychotics (e.g., haloperidol) and risperidone. Clozapine has relatively minimal effect on prolactin levels.

Would you like to explore the specific ANC thresholds and management protocols for clozapine-induced neutropenia, including when to hold or discontinue therapy?

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Question 1058

A 7-year-old boy is rushed to the emergency room after losing consciousness 30 mins ago at home. The patient's mother says that he has had a "running nose" for the past few days However, he did not receive any treatment for it, and his condition rapidly worsened today. He does not have any significant past medical history. His vaccination records are up to date. His temperature is 38.2°C (100.7°F), blood pressure is 90/50 mm Hg, heart rate is 120/min, and respiratory rate is 22/min. On physical examination, the patient is unresponsive. There is a petechial rash present on his chest, and he has some neck rigidity. Empiric intravenous antibiotics are started, and a lumbar puncture is performed. Which of the following is the most likely cause of this patient's low blood pressure?

Answer Choices:

(A) Human immunodeficiency virus infection
(B) Hypertrophic cardiomyopathy
(C) Adrenocortical insufficiency
(D) Pheochromocytoma

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/70ef6bd5-f094-4b2a-afaf-0380b774b482

OpenEvidence Explanation

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The answer is **C. Adrenocortical insufficiency**. This patient's presentation — acute onset of altered consciousness, petechial rash, neck rigidity, fever, and hypotension following a prodromal upper respiratory illness — is classic for **meningococcal meningitis/meningococcemia**. The most likely cause of his low blood pressure is **Waterhouse-Friderichsen syndrome**, which involves bilateral adrenal hemorrhage leading to acute adrenocortical insufficiency.

Waterhouse-Friderichsen syndrome is classically associated with fulminant meningococcal sepsis and presents with shock, petechial/purpuric rashes, and features of acute adrenal crisis.[1] The pathophysiology involves endotoxin-mediated hemorrhagic necrosis of the adrenal glands during overwhelming meningococcal bacteremia.[2] Studies of children with meningococcal septic shock have demonstrated that nonsurvivors have significantly lower cortisol-to-ACTH ratios, indicating inadequate adrenal function as a critical determinant of outcome.[3] Patients with fulminant meningococcal septicemia often develop adrenal hemorrhage, with higher corticotropin and lower cortisol levels in fatal cases compared to survivors.[4]

The clinical vignette highlights several key features pointing to this diagnosis:

- **Petechial rash** with a shock-like state is almost pathognomonic of meningococcemia (Waterhouse-Friderichsen syndrome)[5]
- Rapid progression from a prodromal URI to unconsciousness and hemodynamic collapse
- Neck rigidity consistent with meningeal irritation[6]

Why the other options are incorrect:

- **A (HIV):** Would not cause acute hypotension in this clinical context; HIV-related adrenal insufficiency is a chronic process
- **B (Hypertrophic cardiomyopathy):** Causes outflow obstruction and syncope, not septic shock with petechiae and meningismus
- **D (Pheochromocytoma):** Typically causes hypertension, not hypotension

Would you like to explore the evidence for stress-dose corticosteroid use in pediatric meningococcal septic shock?

References

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Question 1059

A chronic opioid abuser undergoes emergency surgery. Following the operation, the man is started on a patient controlled analgesia (PCA) thought to be dosed adequately to control his pain in the face of his opioid tolerance. He reports intense pain 6 hours after the conclusion of the surgery. Which agent could have been given intraoperatively to reduce this patient's risk of developing postoperative hyperalgesia?

Answer Choices:

(A) Ketamine
(B) Midazolam
(C) Propofol
(D) Etomidate

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/d4d5e830-9585-413b-80c5-907f3a6bb317

OpenEvidence Explanation

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The answer is **A. Ketamine**.

Ketamine, an **NMDA (N-methyl-D-aspartate) receptor antagonist**, is the agent that could have been given intraoperatively to reduce the risk of postoperative

hyperalgesia in this opioid-tolerant patient. NMDA receptors play a central role in the development of both opioid-induced hyperalgesia (OIH) and opioid tolerance through mechanisms involving central sensitization and the "wind-up" phenomenon in dorsal horn neurons.[1] Blockade of these receptors by ketamine attenuates these processes.

Why ketamine is the correct choice:

- In opioid-dependent patients, intraoperative ketamine has been shown to significantly reduce postoperative opioid consumption — by approximately 42 mg morphine equivalents in the first 24 hours in a randomized trial of opioid-dependent patients undergoing spinal fusion.[2]
- A systematic review and meta-analysis of 9 RCTs (802 opioid-using patients) confirmed a clinically relevant opioid-sparing effect (reduction of ~97 mg cumulative morphine at 24 hours) and concluded that ketamine is a "useful anti-hyperalgesic adjuvant" in this population.[3]
- The American Society for Enhanced Recovery consensus guidelines specifically recommend ketamine as a key multimodal adjunct, particularly in opioid-tolerant patients, supported by level-1 evidence.[4]
- The Society of Critical Care Medicine similarly recommends low-dose ketamine (0.5 mg/kg bolus followed by 1–2 μg/kg/min infusion) as an adjunct to opioids in postsurgical ICU patients to reduce opioid consumption.[5]

Why the other options are incorrect:

- **Midazolam (B):** A benzodiazepine with no anti-hyperalgesic properties. Long-term benzodiazepine use may actually worsen opioid-induced hyperalgesia.[6]
- **Propofol (C):** While propofol-based anesthesia may carry a slightly lower risk of OIH compared to volatile agents, it is not used as a targeted anti-hyperalgesic intervention.[7]
- **Etomidate (D):** An induction agent with no known role in preventing hyperalgesia or modulating NMDA-mediated central sensitization.

Would you like to explore specific ketamine dosing protocols and monitoring considerations for perioperative use in opioid-tolerant patients?

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Question 1061

A 37-year-old woman presents to the emergency department with confusion, anxiety, sweating, and episodes of vomiting. She is accompanied by her sister who says that her symptoms developed acutely and is unsure about what caused it. She is currently on methimazole, which she last took approximately 1 week ago. Approximately 5 days ago she developed an upper respiratory infection managed with bed rest and ibuprofen. Her temperature is 105°F (40.6°C), blood pressure is 95/68 mmHg, pulse is 145/min, and respirations are 23/min. On physical examination, the patient has altered mentation and is agitated and diaphoretic. The patient also has a goiter, exophthalmos, warm skin, and a hand tremor. She is started on intravenous fluids. Which of the following is the best treatment option for this patient?

Answer Choices:

(A) Antibiotics
(B) Carotid massage
(C) Clonazepam
(D) Propranolol

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/00bf2d8b-4619-4c2c-819f-e2b22906aafa

OpenEvidence Explanation

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The answer is **D. Propranolol**. This patient is presenting with **thyroid storm**, and **β-adrenergic blockade with propranolol** is a critical component of the acute management.

Clinical Presentation and Diagnosis

This patient has classic features of thyroid storm: high fever (105°F), tachycardia (145/min), altered mentation with agitation, diaphoresis, vomiting, and hypotension — all in the setting of known Graves' disease (goiter, exophthalmos, methimazole use). Two key precipitants are present: **discontinuation of antithyroid medication** (~1 week without methimazole) and an **intercurrent infection** (upper respiratory infection).[1][2] Thyroid storm is a clinical diagnosis characterized by multisystem decompensation in the setting of severe thyrotoxicosis, with mortality rates of 5–25% without rapid intervention.[1][3]

The Burch-Wartofsky Point Scale can help confirm the diagnosis:

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Computed value for Burch-Wartofsky Point Scale: 95 points

Computed value for Interpretation: Highly suggestive of thyroid storm

With a Burch-Wartofsky score of **95**, this is highly suggestive of thyroid storm (≥45 is highly suggestive).[2]

Why Propranolol?

Per the American Thyroid Association (ATA) guidelines, a multimodality treatment approach is recommended, including **β-adrenergic blockade, antithyroid drugs, inorganic iodide, corticosteroids**, and supportive care.[2] Among the answer choices, propranolol is the only appropriate therapy. Propranolol specifically is preferred among β-blockers because, in addition to controlling adrenergic symptoms (tachycardia, tremor, agitation, diaphoresis), it also **inhibits peripheral T4-to-T3 conversion** at high doses, dosed at 60–80 mg every 4 hours.[2][4]

Why Not the Other Options?

- **A. Antibiotics** — While treating the precipitating infection is part of supportive care, antibiotics alone do not address the underlying thyrotoxic crisis and are not the best initial treatment.
- **B. Carotid massage** — This is a vagal maneuver for supraventricular tachycardia, not appropriate here where the tachycardia is driven by thyroid hormone excess.
- **C. Clonazepam** — Benzodiazepines may be used adjunctively for agitation, but they do not address the underlying pathophysiology of thyroid storm.

Would you like to explore the full stepwise pharmacologic management protocol for thyroid storm, including the sequencing of thionamides, iodine, and glucocorticoids?

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Question 1062

A 13-year-old boy is brought to the emergency department because he was vomiting and seemed abnormally sleepy at home. On presentation, he is found to be confused and very lethargic. His parents said that he has had a fever and cough for several days prior to presentation and was given an over the counter medication. Physical exam of this patient reveals mild hepatomegaly and dry mucous membranes. Which of the following effects would the drug most likely also have on the nephron?

Answer Choices:

(A) Constriction of afferent arteriole and no effect on efferent arteriole
(B) Dilation of afferent arteriole and no effect on efferent arteriole
(C) No effect on afferent arteriole and constriction of efferent arteriole
(D) No effect on afferent arteriole and dilation of efferent arteriole

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/8782429d-3da0-46a8-94a3-b9461c966fed

OpenEvidence Explanation

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The answer is **A. Constriction of afferent arteriole and no effect on efferent arteriole**.

This clinical vignette describes **Reye syndrome** — a 13-year-old with encephalopathy (confusion, lethargy, vomiting) and hepatomegaly following a febrile viral illness treated with an over-the-counter medication. The implicated drug is **aspirin (acetylsalicylic acid)**, which is strongly associated with Reye syndrome when given to children during viral illnesses such as influenza or varicella.[1][2] Reye syndrome is characterized by encephalopathy and fatty degeneration of the liver, with a case fatality rate of approximately 31%.[1]

Renal effects of aspirin: Aspirin inhibits cyclooxygenase (COX), blocking the synthesis of vasodilatory prostaglandins (PGE2 and PGI2) in the kidney.[3][4] Under normal conditions, these prostaglandins maintain vasodilation of the **afferent arteriole** to preserve renal blood flow and GFR. When COX is inhibited by aspirin, the loss of prostaglandin-mediated vasodilation results in **unopposed constriction of the afferent arteriole**, leading to decreased renal blood flow and GFR.[3][5] Aspirin has **no direct effect on the efferent arteriole**, which is primarily regulated by angiotensin II rather than prostaglandins.

This mechanism is particularly pronounced in states of decreased renal perfusion (e.g., dehydration, as suggested by the dry mucous membranes in this patient), where renal prostaglandin synthesis is upregulated as a compensatory vasodilatory mechanism, and its inhibition can precipitate acute renal failure.[3][4]

Would you like to explore the pathophysiology and management of Reye syndrome in more detail, including the role of N-acetylcysteine and supportive care?

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1. Reye's Syndrome in the United States from 1981 through 1997. Belay ED, Bresee JS, Holman RC, et al.. The New England Journal of Medicine. 1999;340(18):1377-82. doi:10.1056/NEJM199905063401801.

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Question 1063

A 54-year-old woman presents with sudden onset, mild vaginal bleeding for the past day. She says she is postmenopausal, and her last menstrual period was 5 years ago. A detailed workup is performed, and several premalignant lesions are found in her uterus. The patient agrees to a hysterectomy. The surgical team decides to use an anesthesia protocol consisting of nitrous oxide, desflurane, and atracurium. Which of the following best describes the role of atracurium in this patient's anesthesia?

> **Answer Choices:**
>
> (A) It reduces neuron and muscle tissue excitability
> (B) It increases GABA linked chloride channel opening
> (C) It acts on the pain centers in the spinal cord and brain
> (D) It competes with acetylcholine for binding sites in the neuromuscular junction

> **Correct Answer:**
>
> **(D)**
>
> **OpenEvidence Response:**
>
> **(D)** ✓

OpenEvidence Link: https://openevidence.com/ask/e515285d-ae33-4506-92cc-534552678208

OpenEvidence Explanation

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The correct answer is **D. It competes with acetylcholine for binding sites in the neuromuscular junction**.

Atracurium besylate is a **nondepolarizing skeletal muscle relaxant** that antagonizes the neurotransmitter action of acetylcholine by **binding competitively with cholinergic (nicotinic) receptor sites on the motor end-plate** at the neuromuscular junction.[1][2] This competitive blockade prevents acetylcholine-induced depolarization and thereby inhibits skeletal muscle contraction, providing the muscle relaxation needed for endotracheal intubation and surgical procedures such as hysterectomy.[3]

The other answer choices describe mechanisms of different anesthetic agents:

- **A (reduces neuron and muscle tissue excitability)** — describes local anesthetics (e.g., lidocaine), which block voltage-gated sodium channels.
- **B (increases GABA-linked chloride channel opening)** — describes the mechanism of barbiturates and benzodiazepines, not neuromuscular blockers.
- **C (acts on pain centers in the spinal cord and brain)** — describes opioid analgesics, which act on central pain pathways.

Notably, atracurium's neuromuscular blockade is reversible and can be antagonized by acetylcholinesterase inhibitors such as neostigmine, edrophonium, or pyridostigmine, which increase acetylcholine concentration at the neuromuscular junction to overcome the competitive block.[1][2] Atracurium is also unique in that it undergoes organ-independent elimination via Hofmann degradation and nonspecific ester hydrolysis, making its duration of action independent of renal or hepatic function.[1][4]

Would you like to explore how the choice between different nondepolarizing neuromuscular blocking agents (e.g., atracurium vs. rocuronium vs. cisatracurium) is guided by patient comorbidities and surgical context?

References

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Question 1064

A 22-year-old woman presents with recurrent episodes of swelling in her face, hands, and neck with occasional abdominal pain. The symptoms usually resolve in 2 to 3 days. She has had these swelling events her whole life; however, they have become more debilitating recently. Last week she had an event that restricted her ability to eat and swallow. Past medical history is noncontributory. Her father is alive and well with no significant medical history. Her mother and her maternal aunt have a similar condition. Today, her physical exam is within normal limits. She brought a picture of her swollen hand as seen in the picture. The treating physician has a strong suspicion of an inherited disorder. C1-inhibitor levels are ordered and found to be extremely low. Which of the following is the most likely diagnosis of this patient?

Answer Choices:

(A) Chediak-Higashi syndrome
(B) Wiskott-Aldrich syndrome
(C) Paroxysmal nocturnal hemoglobinuria
(D) Hereditary angioedema

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/16664af6-f3ed-4138-8cd8-5f40cb367983

OpenEvidence Explanation

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The correct answer is **D. Hereditary angioedema (HAE)**.

Hereditary angioedema due to C1-inhibitor deficiency is an autosomal dominant disorder characterized by recurrent episodes of nonpitting, nonpruritic angioedema without urticaria, affecting the extremities, face, oropharynx, and gastrointestinal tract.[1] The clinical presentation in this vignette — lifelong recurrent swelling of the face, hands, and neck with abdominal pain, episodes lasting 2–3 days, worsening around young adulthood, a maternal family history, and extremely low C1-inhibitor levels — is classic for HAE type I.[1]

Key features supporting this diagnosis:

- **Autosomal dominant inheritance** — the patient's mother and maternal aunt are affected, consistent with the ~75% of HAE patients who have a positive family history. The father being unaffected is expected, as the mutation is carried on the maternal side.[1]
- **Onset in childhood with worsening around puberty/young adulthood** — HAE typically develops in childhood (mean onset 8–12 years) and frequently worsens during puberty.[1][2]
- **Episodic swelling lasting 2–3 days** — attacks are characteristically prolonged (>48 hours) and self-resolving.[1]
- **Abdominal pain** — submucosal intestinal edema is a hallmark feature and can mimic an acute abdomen.[1]
- **Laryngeal/oropharyngeal involvement** — the episode restricting eating and swallowing reflects upper airway edema, which occurs in >50% of patients during their lifetime and is the leading cause of HAE-related mortality.[1]
- **Low C1-inhibitor levels** — diagnostic for HAE type I (85% of cases), which presents with both low antigenic and functional C1-inhibitor levels.[1]

Why the other options are incorrect:

- **Chediak-Higashi syndrome (A)** — a rare autosomal recessive disorder of lysosomal trafficking causing partial oculocutaneous albinism, recurrent

pyogenic infections, and giant granules in leukocytes. It does not cause angioedema or C1-inhibitor deficiency.

- **Wiskott-Aldrich syndrome (B)** — an X-linked recessive immunodeficiency characterized by eczema, thrombocytopenia, and recurrent infections. It would not present in a female with this pattern and is unrelated to C1-inhibitor.

- **Paroxysmal nocturnal hemoglobinuria (D)** — an acquired disorder of complement regulation (GPI-anchor deficiency) causing hemolytic anemia, thrombosis, and hemoglobinuria. It involves complement dysregulation but does not cause C1-inhibitor deficiency or recurrent angioedema.

The following table from the NEJM summarizes the clinical and laboratory features distinguishing different types of bradykinin-mediated angioedema:

Table 1. Clinical and Laboratory Features of Bradykinin-Mediated Angioedema, According to Type.*

Variable	HAE-C1-INH†	HAE-nl-C1-INH‡	INHA	Acquired C1-INH Deficiency	ACE-Inhibitor–Induced HAE
Clinical features	Recurrent cutaneous and submucosal angioedema without urticaria Attacks prolonged (>48 hr) Physical prodrome of erythema marginatum in approximately one third of patients	Phenotypic presentation similar to HAE-C1-INH Absence of erythema marginatum Rare cutaneous hemorrhage May have more disease-free intervals than with HAE-C1-INH	Similar to HAE-C1-INH	Phenotypic presentation similar to HAE-C1-INH Associated antibodies to C1-INH§ Cancer (e.g., non-Hodgkin's B-cell lymphoma)§	More common in blacks and smokers Less common in patients with diabetes
Genetic features	AD, full penetrance Approximately 75% of patients have positive family history; 25% have de novo mutation (no family history)	AD, incomplete penetrance, female predominance (males can be silent carriers, particularly in subtype HAE-XII)	None	None	None
Attack location	Extremity and abdominal attacks more frequent than facial attacks	Facial attacks most frequent, then extremity attacks, then abdominal attacks More cutaneous and abdominal attacks in subtype HAE-FXII than in HAE-U Characteristic tongue swelling in subtype HAE-PLG	Face and periorbital areas	Facial attacks most frequent, followed by peripheral, abdominal, and oral attacks	Head (tongue) and neck
Age at onset	Childhood or young adulthood, worsening in puberty	Usually after childhood	Usually about 30–40 yr	Usually >40 yr	Usually >40 yr
Triggers	Often unpredictable; stress, trauma, infection, estrogen, fatigue	Often unpredictable; stress, trauma, infection, estrogen, fatigue; greater influence of estrogen in HAE-FXII than in HAE-U	Unknown	May be affected by underlying disorder Often unpredictable; stress, trauma, infection, estrogen, fatigue	ACE-inhibitor use; ARBs are usually associated with an acceptable side-effect profile
C4	Decreased	Normal	Normal	Decreased more than with HAE-C1-INH	Normal
Antigenic C1-INH	Subtype I, decreased; subtype II, normal	Normal	Normal	Decreased or normal	Normal
Functional C1-INH	Decreased	Normal	Normal	Decreased	Normal
C1q	Normal¶	Normal	Normal	Normal or decreased‖	Normal
C3	Normal	Normal	Normal	Normal or decreased	Normal

* Information in the table is modified from Wu et al.[30] ACE denotes angiotensin-converting enzyme, AD autosomal dominant, ARB angiotensin-receptor blocker, C1-INH C1 inhibitor, HAE hereditary angioedema, HAE-C1-INH HAE with low functional C1-INH, HAE-FXII HAE with coagulation factor XII mutation, HAE-KNG1 HAE with kininogen-1 mutation, HAE-nl-C1-INH HAE with normal C1-INH, HAE-PLG HAE with plasminogen mutation, HAE-U HAE with unknown mutation, and INHA idiopathic nonhistaminergic angioedema.
† Subtypes are HAE type I and HAE type II.
‡ Subtypes are HAE-U, HAE-FXII, HAE-PLG, HAE-ANGPT-1, and HAE-KNG1.
§ This feature is seen in some patients and should therefore be included in the evaluation.
¶ On rare occasions, a decrease in homozygous HAE occurs.[31-33]
‖ C1q may be normal in some patients.

Table 1. Clinical and Laboratory Features of Bradykinin-Mediated Angioedema, According to Type.*

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Would you like to explore the current acute and prophylactic treatment options for hereditary angioedema, including newer targeted therapies such as lanadelumab and berotralstat?

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Question 1067

A 27-year-old woman, gravida 1, para 0, at 38 weeks' gestation is admitted to the hospital for active labor. The pregnancy was complicated by gestational diabetes and fetal weight is estimated to be at the 90th percentile for gestational age. During delivery, there is an arrest in the second stage of labor, and a vacuum-assisted delivery is performed. Postpartum examination shows a third-degree laceration in the vagina extending into the perineum at the 6 o'clock position. This patient is most likely to experience which of the following complications?

Answer Choices:

(A) Urge incontinence
(B) Vesicovaginal fistula
(C) Fecal incontinence
(D) Stress incontinence

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/56166b80-86ac-4b7f-b5f0-468c092adf52

OpenEvidence Explanation

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The answer is **C. Fecal incontinence**.

A third-degree perineal laceration involves the **anal sphincter complex**, which is the defining feature that distinguishes it from a second-degree laceration (which involves only the perineal muscles without affecting the anal sphincter).[1] Because the anal sphincter is disrupted, the most likely complication is **fecal incontinence**.

Why fecal incontinence is the best answer:

- Obstetric anal sphincter injuries (OASIS), which include third- and fourth-degree tears, are the most important etiological factor in the pathogenesis of anal incontinence in women. Third-degree lacerations approximately **double the risk of fecal incontinence** at five years postpartum. Prospective data show fecal incontinence rates of 6–15% in women with third-degree tears and up to 26% in those with fourth-degree tears.[1][2][3]
- The prevalence of fecal incontinence increases with tear severity: 11.7% in women without sphincter injuries, 23.8% after one sphincter injury, and 36.1% after two sphincter injuries.[4]
- This patient had multiple risk factors for OASIS: nulliparity (OR 3.24), vacuum-assisted delivery (OR ~4.0), macrosomia (90th percentile), and prolonged second stage with arrest.[5][6]

Why the other options are less likely:

- **Urge incontinence (A)** and **stress incontinence (D)** are associated with pelvic floor dysfunction from vaginal delivery in general but are not the direct consequence of anal sphincter disruption. Stress incontinence relates more to urethral hypermobility and levator ani injury rather than a perineal laceration at the 6 o'clock position.
- **Vesicovaginal fistula (B)** is typically a complication of prolonged obstructed labor, pelvic surgery, or radiation — not a posterior midline perineal laceration.

Would you like to explore the evidence on optimal repair techniques for third-degree lacerations and their impact on long-term continence outcomes?

References

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Question 1069

A 45-year-old woman comes to the physician for the evaluation of a right breast mass that she noticed 3 weeks ago. It has rapidly increased in size during this period. She does not have pain. Vital signs are within normal limits. Examination shows large dense breasts; a 5-cm, nontender, multinodular mass is palpated in the right outer quadrant of the right breast. There are no changes in the skin or nipple. There is no palpable cervical or axillary adenopathy. Mammography shows a smooth polylobulated mass. Biopsy of the mass shows papillary projections of epithelial-lined stroma with hyperplasia and atypia. Which of the following is the most likely diagnosis?

Answer Choices:

(A) Phyllodes tumor
(B) Fibroadenoma
(C) Fibrocystic disease of the breast
(D) Invasive lobular carcinoma

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/f7cfd6b5-4e3e-4011-9922-c81e6b216e52

OpenEvidence Explanation

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The most likely diagnosis is **A. Phyllodes tumor**.

The clinical and histopathological features in this case are classic for a phyllodes tumor:

- **Rapid growth** over 3 weeks, **large size (5 cm)**, and a **smooth polylobulated mass** on mammography are hallmark clinical features of phyllodes tumors. NCCN guidelines specifically list palpable mass, rapid growth, and large size (>3 cm) as features raising clinical suspicion for phyllodes tumor.[1][2][3]
- **Age of presentation** at 45 years is consistent with the median age of 40–45 years for phyllodes tumors, which typically present 1–2 decades later than fibroadenomas.[3][4]
- The biopsy finding of **papillary projections of epithelial-lined stroma with hyperplasia and atypia** describes the characteristic leaf-like (phyllodes) architecture — hypercellular stromal fronds protruding into cystically dilated spaces, covered by epithelium — which is the defining histologic feature of phyllodes tumors. The presence of stromal atypia further supports this diagnosis.[3][5]

Why not the other options:

- **Fibroadenoma (B):** While fibroadenomas are also biphasic fibroepithelial lesions, they typically present at a younger age (median ~30 years), are smaller (average 2 cm), do not exhibit rapid growth, and lack the exaggerated intracanalicular leaf-like architecture with stromal atypia seen here.[3][6]
- **Fibrocystic disease (C):** This presents with diffuse breast changes (cysts, fibrosis, adenosis) rather than a discrete rapidly enlarging multinodular mass with the described histologic pattern.
- **Invasive lobular carcinoma (D):** This would show single-file infiltrating tumor cells with loss of E-cadherin expression, not the biphasic epithelial-stromal architecture with leaf-like projections described in this biopsy.

Would you like to explore the management approach and surgical margin recommendations for phyllodes tumors based on their histologic grade?

Relevant images

(CONTENT OMITTED)

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Question 1070

A 72-year-old Caucasian male presents to your office with dysphagia and halitosis. If this patient is also found to have cricopharyngeal muscle dysfunction, which of the following is the most likely cause of his presenting symptoms?

Answer Choices:

(A) Gastroesophageal reflux disease
(B) Esophageal candidiasis
(C) Meckel's diverticulum
(D) Zenker's diverticulum

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/843f9d67-c08c-4a68-98df-5ffc89a8c331

OpenEvidence Explanation

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The answer is **D. Zenker's diverticulum**. This is the classic presentation: an elderly male with **dysphagia**, **halitosis**, and **cricopharyngeal muscle dysfunction** — the triad most characteristic of Zenker's diverticulum.

Zenker's diverticulum is an acquired pulsion pseudodiverticulum that herniates through Killian's triangle (the area of weakness between the oblique fibers of the

thyropharyngeus and the horizontal fibers of the cricopharyngeus muscle).[1][2] The pathophysiology directly involves cricopharyngeal dysfunction — increased resting tone, reduced compliance, or incoordination of the cricopharyngeus leads to elevated intrabolus pressure and subsequent mucosal herniation.[3][4] The classic presenting symptoms are **dysphagia, halitosis, regurgitation of undigested food, and cough**.[1][3] It most commonly affects elderly individuals, with 50% of patients older than 70 years, and has a male predominance.[1][5]

Why the other options are incorrect:

- **A. GERD** — While GERD may be associated with Zenker's diverticulum formation, it does not itself cause cricopharyngeal muscle dysfunction or halitosis from food retention.[6]
- **B. Esophageal candidiasis** — Presents with odynophagia and dysphagia, typically in immunocompromised patients, and is not associated with cricopharyngeal dysfunction.
- **C. Meckel's diverticulum** — A congenital true diverticulum of the ileum (not the esophagus), presenting with GI bleeding or obstruction, and unrelated to cricopharyngeal dysfunction.

Diagnosis is confirmed by **modified barium swallow study** (videofluoroscopy), which is the criterion standard.[1][2] Treatment involves cricopharyngeal myotomy, performed either via open transcervical or endoscopic approaches.[5]

Would you like to explore the comparative outcomes of endoscopic versus open surgical approaches for Zenker's diverticulum repair?

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Question 1071

A 10-year-old boy is brought to the emergency department because he has not been able to walk since waking up that morning. His mother said that when he tried to get out of bed that he was unable to stand without support. He also complained of prickling in his hands and feet. Three weeks ago, he had a fever, dry cough, and a sore throat. The fever and sore throat subsided a week after they began, but the cough is persisting. He has no history of serious illness and takes no medication. His vital signs are within normal limits. The lungs are clear to auscultation. There is severe weakness in both lower extremities and mild sensory loss of the hands and feet. Knee and ankle jerk reflexes are absent. The remainder of the examination shows no abnormalities. Laboratory studies show:
Hemoglobin 12.0 g/dL
Leukocyte count 6000/mm3
Segmented neutrophils 64%
Eosinophils 2%
Lymphocytes 26%
Monocytes 7%
Platelet count 160,000/mm3
Erythrocyte sedimentation rate 27 mm/h
Serum
Na+ 138 mEq/L
Cl- 101 mEq/L
K+ 4.9 mEq/L
HCO3- 26 mEq/L
Ca2+ 9.7 mg/dL
Creatine kinase 93 U/L
A lumbar puncture is performed; cerebrospinal fluid analysis shows a leukocyte count of 2/mm3, a glucose concentration of 60 mg/dL, and a protein concentration of 91 mg/dL. Which of the following is the most appropriate next step in treatment?

Answer Choices:

(A) Intravenous immunoglobulin (IVIG)
(B) Prednisone

(C) Botulism antitoxin
(D) Gabapentin

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/bc74866f-ab46-4592-a49a-3652447704cb

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OpenEvidence Explanation

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The answer is **A. Intravenous immunoglobulin (IVIG)**.

This presentation is classic for **Guillain-Barré syndrome (GBS)**: acute ascending weakness with areflexia, distal paresthesias, and a preceding respiratory infection — likely *Mycoplasma pneumoniae* given the persistent dry cough.[1] The CSF demonstrates **albuminocytologic dissociation** (elevated protein at 91 mg/dL with a near-normal cell count of 2/mm³), which is the hallmark CSF finding in GBS.[2][3] Normal creatine kinase excludes a primary myopathic process, and the absence of cranial nerve findings or descending paralysis argues against botulism.

IVIG is the first-line treatment for pediatric GBS. Both IVIG and plasma exchange are equally effective in adults, but IVIG is preferred in children due to greater convenience, better tolerability, and technical difficulties with plasma exchange in pediatric patients.[4][5] The standard dose is **2 g/kg administered over 2–5 days**.[4][6] The AANEM consensus statement supports IVIG use in pediatric GBS based on consistent evidence showing accelerated recovery.[7]

Why the other options are incorrect:

- **Prednisone (B):** Corticosteroids alone are **not effective** in GBS and are not recommended as monotherapy.[4][8]
- **Botulism antitoxin (C):** Botulism presents with descending paralysis, cranial nerve involvement (diplopia, dysphagia), and autonomic dysfunction — none of which are present here. The CSF in botulism is typically normal.
- **Gabapentin (D):** While neuropathic pain is common in GBS and gabapentin may be used adjunctively for pain management, it does not treat the underlying disease and is not the most appropriate next step.[3]

Would you like to explore the prognostic factors and monitoring parameters for respiratory failure in pediatric GBS, including the use of the EGRIS score?

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Question 1072

A 27-year-old male presents to the psychiatrist requesting help with his compulsions as they are interfering with his life. He explains that he has this fear that something terrible will happen to his house if he does not check every appliance, outlet, window and door lock, faucet, and light fixture before he leaves. He states that he must check everything 7 times in a specific order and if he goes out of order he must start from the beginning and perform it all over. He has recently been fired from his job because he is always late and lost his fiancee as she could not deal with his habits anymore. The physician explained that cognitive-behavioral therapy may be of assistance and also prescribed clomipramine. Which of the following is the mechanism of reaction of clomipramine?

Answer Choices:

(A) Decreases the degradation of norepinephrine and serotonin
(B) Increases the release of norepinephrine and serotonin by alpha 2 receptor antagonism
(C) Blocks only norepinephrine reuptake
(D) Blocks reuptake of norepinephrine and serotonin

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/0aada1ca-0cdf-4a7a-a0a5-c2ed4fce900a

OpenEvidence Explanation

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The answer is **D. Blocks reuptake of norepinephrine and serotonin**.

Clomipramine is a **tricyclic antidepressant (TCA)** and the first FDA-approved pharmacotherapy for obsessive-compulsive disorder (OCD).[1][2] Its primary mechanism of action involves **inhibition of presynaptic reuptake of both serotonin (5-HT) and norepinephrine**.[3][4] Clomipramine itself is the strongest inhibitor of serotonin reuptake among the TCAs, while its major active metabolite,[3] **desmethylclomipramine**, preferentially inhibits norepinephrine reuptake.[4][5] Together, the parent compound and metabolite produce a dual reuptake inhibition profile.

Why the other options are incorrect:

- **A (Decreases degradation of norepinephrine and serotonin)** — This describes the mechanism of monoamine oxidase inhibitors (MAOIs), which prevent enzymatic breakdown of monoamines. Clomipramine does not inhibit MAO.
- **B (Alpha-2 receptor antagonism increasing release)** — This describes the mechanism of mirtazapine, which enhances noradrenergic and serotonergic transmission via presynaptic alpha-2 autoreceptor and heteroreceptor blockade.
- **C (Blocks only norepinephrine reuptake)** — This would describe selective norepinephrine reuptake inhibitors (e.g., desipramine, which is relatively NE-selective among TCAs). Clomipramine is notable precisely because it inhibits serotonin reuptake more potently than other TCAs, in addition to blocking norepinephrine reuptake.[3][6]

The anti-obsessional efficacy of clomipramine is thought to be primarily related to its serotonergic activity, which distinguishes it from other TCAs that are less effective in OCD.[1][2]

Would you like to explore how clomipramine compares to SSRIs in terms of efficacy and tolerability for OCD treatment?

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Question 1074

A 24-year-old man with chronic back pain comes to the physician to establish care after moving to Florida. He complains of anxiety, nausea, abdominal cramping, vomiting, and diarrhea for three days. He denies smoking, drinking alcohol, and using illicit drugs. He appears restless. His temperature is 37°C (98.6°F), pulse is 110/min, and blood pressure is 150/86 mm Hg. Physical examination shows dilated pupils, diaphoresis, and piloerection. His abdominal exam shows diffuse mild tenderness. There is no rebound tenderness or guarding. His hemoglobin concentration is 14.5 g/dL, leukocyte count is 8,000/mm, and platelet count is 250,000/mm3; serum studies and urinalysis show no abnormalities. Which of the following is the most appropriate pharmacotherapy?

Answer Choices:

(A) Lorazepam
(B) Naltrexone
(C) Methadone
(D) Naloxone

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/b5f8e964-cf4a-4884-90d5-24f20808a8a1

OpenEvidence Explanation

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The correct answer is **C. Methadone**.

This clinical presentation — a young man with chronic back pain (likely prescribed opioids), who recently moved and lost access to his medication, presenting with **anxiety, nausea, vomiting, diarrhea, tachycardia, hypertension, mydriasis, diaphoresis, and piloerection** — is classic for **opioid withdrawal syndrome**.[1][2] The constellation of autonomic hyperactivity (tachycardia, hypertension, diaphoresis, piloerection, mydriasis) combined with GI symptoms (nausea, vomiting, diarrhea, abdominal cramping) and neuropsychiatric symptoms (anxiety, restlessness) fulfills DSM-5 diagnostic criteria for opioid withdrawal.[2]

Why methadone is correct:

Opioid agonists — specifically **methadone** and buprenorphine — are the recommended first-line pharmacotherapy for opioid withdrawal management.[1][3][4] Methadone, a full μ-opioid receptor agonist, directly addresses the underlying pathophysiology by activating opioid receptors, relieving withdrawal symptoms, and is superior to both placebo and α2-adrenergic agonist-based regimens.[1][5] The ASAM guidelines recommend methadone or buprenorphine over abrupt cessation, noting that withdrawal management alone without ongoing treatment is not recommended.[4]

Why the other options are incorrect:

- **A. Lorazepam** — Benzodiazepines are only adjunctive agents for anxiety and insomnia during opioid withdrawal; they do not treat the underlying withdrawal syndrome.[1]
- **B. Naltrexone** — An opioid antagonist used for relapse prevention after detoxification is complete. Administering naltrexone during active withdrawal would precipitate or worsen withdrawal symptoms.[1]
- **D. Naloxone** — An opioid antagonist used to reverse opioid overdose. Like naltrexone, it would precipitate severe withdrawal if given to an opioid-dependent patient.[1]

Would you like to explore the practical differences between methadone and buprenorphine for opioid withdrawal management, including initiation protocols and outpatient considerations?

Relevant images

(CONTENT OMITTED)

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Question 1081

A 62-year-old woman comes to the physician because of a 6-month history of progressive pain and stiffness of the fingers of her right hand. The stiffness is worse at the end of the day. She recently retired after working for 28 years as a typist at a data entry firm. Physical examination shows swelling, joint-line tenderness, and decreased range of motion of the first metacarpophalangeal joint and the distal interphalangeal joints of the right hand. Discrete, hard, mildly tender nodules are palpated over the 2nd and 4th distal interphalangeal joints of the right hand. An x-ray of her right hand shows narrowing of the interphalangeal joint spaces with subchondral sclerosis and osteophytes. Which of the following is the most likely underlying mechanism of this patient's condition?

Answer Choices:

(A) Bacterial infection of the joint space
(B) Autoimmune-mediated cartilage erosion
(C) Calcium pyrophosphate dihydrate crystal precipitation in the joints
(D) Degenerative disease of the joints

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/25e279dd-f4c3-4c69-89d3-b98222839e4b

OpenEvidence Explanation

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D. Degenerative disease of the joints

This presentation is classic for **osteoarthritis (OA)**, a degenerative joint disease. Several key features point to this diagnosis:

- **Heberden's nodes** — the discrete, hard nodules over the distal interphalangeal (DIP) joints are pathognomonic for OA
- **DIP joint involvement** — OA characteristically affects DIP joints, first carpometacarpal (CMC) joints, and first MTP joints in the hand
- **Stiffness worse at the end of the day** — mechanical/usage-related stiffness that worsens with activity, in contrast to the prolonged morning stiffness of inflammatory arthritis
- **Radiographic findings** — joint space narrowing, subchondral sclerosis, and osteophytes are the hallmark radiographic triad of OA
- **Occupational history** — repetitive use of the hands over decades (typing) is a recognized risk factor for hand OA

The other options are less consistent:

- **A (Septic arthritis)** — would present acutely with warmth, erythema, and systemic signs, not a chronic 6-month course
- **B (Autoimmune/RA)** — rheumatoid arthritis typically affects MCP and PIP joints symmetrically, spares DIP joints, and causes morning stiffness (not end-of-day stiffness); erosions rather than osteophytes are seen on imaging
- **C (CPPD/pseudogout)** — typically affects large joints (knees, wrists) and shows chondrocalcinosis on X-ray, not osteophytes and subchondral sclerosis

The underlying mechanism in OA is progressive **degradation of articular cartilage** with secondary bony remodeling, driven by mechanical wear and impaired chondrocyte repair capacity.

Would you like to explore the current evidence on disease-modifying therapies for hand osteoarthritis?

Question 1085

A 3-year-old girl is brought to the emergency department by her mother 30 minutes after the sudden onset of shortness of breath, dizziness, abdominal pain, and urticaria. The symptoms began 5 minutes after she ate a peanut butter sandwich. Her respirations are 36/min and blood pressure is 84/50 mm Hg. There is stridor on auscultation of the chest. She is intubated and mechanical ventilation is begun. Intravenous fluid resuscitation and the appropriate pharmacotherapy are begun. The drug administered to this patient most likely has which of the following effects on cardiac pacemaker cells during an action potential?

Answer Choices:

(A) Increased Ca2+ influx in phase 4
(B) Increased Na+ influx in phase 3
(C) Decreased Ca2+ influx in phase 0
(D) Decreased K+ efflux during phase 3

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/86ada031-7055-42f4-97af-e01122a08c47

OpenEvidence Explanation

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The correct answer is **A. Increased Ca^{2+} influx in phase 4**.

This clinical scenario describes **anaphylaxis** from peanut allergy, and the drug administered is **epinephrine (adrenaline)**, the first-line treatment for anaphylaxis.[1][2]

Epinephrine's effect on cardiac pacemaker cells:

In sinoatrial node (SAN) pacemaker cells, epinephrine acts as a beta-1 adrenergic agonist, stimulating Gs-protein–coupled receptors → adenylyl cyclase activation → increased cAMP → protein kinase A (PKA) activation.[3][4] This cascade has two key effects on phase 4 (diastolic depolarization):

1. **Increased Ca^{2+} influx** — PKA phosphorylates L-type calcium channels and enhances ryanodine receptor (RyR)-mediated sarcoplasmic reticulum Ca^{2+} release during diastolic depolarization, increasing the slope of phase 4 and accelerating the pacemaker firing rate.[5][6]
2. **Activation of HCN (funny) channels** — cAMP directly binds to HCN channels, increasing the If current, which also steepens phase 4 depolarization.[3][4]

Together, these mechanisms increase the rate of diastolic depolarization (phase 4), producing the **positive chronotropic effect** (increased heart rate) characteristic of epinephrine.[3]

Why the other options are incorrect:

- **B (Increased Na^{+} influx in phase 3)** — Phase 3 is repolarization; Na^{+} influx does not play a significant role here in pacemaker cells.
- **C (Decreased Ca^{2+} influx in phase 0)** — Epinephrine actually increases (not decreases) Ca^{2+} influx during phase 0 in pacemaker cells.[3]
- **D (Decreased K^{+} efflux in phase 3)** — Epinephrine modestly increases (not decreases) K^{+} currents; decreasing K^{+} efflux would prolong repolarization, which is not the primary effect.[7]

Would you like to explore the detailed electrophysiology of how catecholamines modulate the coupled-clock mechanism (voltage clock and calcium clock) in sinoatrial node pacemaker cells?

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Question 1086

A 3-day-old boy is admitted to the neonatal intensive care unit for seizures. He was born to a 33-year-old woman at 31 weeks gestation via cesarean section. His birth weight was 1400 grams. Vital signs are significant for systemic hypotension, bradycardia, and hypoventilation. On physical exam, the patient has an altered level of consciousness with decreased spontaneous and elicited movements. The patient is hypotonic on motor testing, has bulging anterior fontanelle, and appears cyanotic. Which of the following is the best next step in management?

Answer Choices:

(A) Complete blood count
(B) Cranial ultrasonography
(C) Head CT
(D) MRI of the head

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/3143c792-5c81-4a8a-9713-fb5273f890cf

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OpenEvidence Explanation

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The best next step in management is **B. Cranial ultrasonography**.

This clinical scenario describes a **preterm neonate (31 weeks, 1400 g)** presenting with seizures, bulging anterior fontanelle, hypotension, bradycardia, hypotonia, and altered consciousness — a presentation highly concerning for **intraventricular hemorrhage (IVH)**, which is the most common cause of seizures in preterm infants.

Why cranial ultrasonography is the correct answer:

- Cranial ultrasonography is the **first-line neuroimaging modality** for neonates with seizures because of its ease of use and bedside accessibility, which is critical for acutely ill neonates who cannot be safely transported. It has **100% sensitivity and 93.3% specificity** for detecting intraventricular hemorrhages with ventricular enlargement.[1][2]
- The American Academy of Pediatrics recommends cranial ultrasonography as the primary screening tool for preterm infants ≤30 weeks, and for selected infants >30 weeks with risk factors such as hypotension or need for vigorous resuscitation. Screening before 7 days of age is indicated when clinical signs suggest significant brain injury.[3]
- **CT is no longer considered part of routine imaging** of the preterm brain due to ionizing radiation exposure and the availability of superior alternatives.[3]
- **MRI** provides superior anatomic detail and would ultimately be valuable, but it requires transport of an unstable neonate out of the NICU, sedation considerations, and longer acquisition times — making it impractical as the initial study in this acutely ill infant.[3]
- A **CBC** is part of the initial laboratory workup but does not address the immediate need to identify the structural cause of seizures in this presentation.[1]

The bulging fontanelle in a preterm infant with seizures and hemodynamic instability strongly suggests raised intracranial pressure from hemorrhage, and bedside cranial ultrasound is the fastest, safest way to confirm this diagnosis and guide urgent management.

Would you like to explore the grading system for intraventricular hemorrhage and how it guides subsequent management decisions in preterm neonates?

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Question 1087

A 39-year-old man seeks an evaluation in the emergency room due to an episode of syncope at work. He says that he has felt increasing shortness of breath while exercising over the past 6 months. He is a well-built man in mild distress. The vital signs include heart rate 98/min, respiratory rate 18/min, temperature 36.5°C (97.7°F), and blood pressure 135/90 mm Hg. The cardiac examination is significant for a harsh systolic ejection murmur at the left lower sternal border which is accentuated by forceful expiration against a closed airway. Palpation of the carotid artery shows 2 closely spaced pulses which occur during systole. Which of the following is most consistent with these findings?

Answer Choices:

(A) Aortic stenosis
(B) Cardiac tamponade
(C) Hypertrophic cardiomyopathy
(D) Third-degree heart block

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/9f68f3b9-0d9e-4d8d-9f30-609c47f84b91

OpenEvidence Explanation

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The answer is **C. Hypertrophic cardiomyopathy (HCM)**. The combination of findings in this young patient — syncope, exertional dyspnea, a harsh systolic ejection murmur at the left lower sternal border that increases with the Valsalva maneuver, and a **pulsus bisferiens** (two closely spaced systolic carotid pulses) — is classic for hypertrophic obstructive cardiomyopathy (HOCM).

Key distinguishing features pointing to HCM over the other options:

- **Murmur location and response to Valsalva:** The murmur of HCM is best heard at the left lower sternal border and characteristically **increases** with maneuvers that reduce preload, such as the Valsalva maneuver (forceful expiration against a closed airway). In contrast, the murmur of aortic stenosis (AS) is best heard at the right upper sternal border, radiates to the carotids, and **decreases** with Valsalva. This is because reduced preload decreases LV cavity size, worsening the dynamic LVOT obstruction in HCM, while in AS the fixed obstruction means less flow across the valve produces a softer murmur.[1][2][3]

- **Pulsus bisferiens vs. pulsus parvus et tardus:** The two closely spaced systolic carotid pulses described represent a **bisferiens pulse**, which is characteristic of HOCM with dynamic LVOT obstruction. This results from the initial rapid ejection before the obstruction develops, followed by a mid-systolic dip and then a second pressure wave. In aortic stenosis, the expected carotid finding is **pulsus parvus et tardus** — a single, slow-rising, diminished pulse.[4][5][6]

- **Patient demographics:** HCM commonly presents in younger patients and is the most common cause of sudden cardiac death in young athletes. A 39-year-old presenting with syncope and exertional dyspnea fits this profile. Calcific aortic stenosis typically presents in older adults (sixth to eighth decades for tricuspid valves, fourth to fifth decades for bicuspid valves).[7][8]

- **Cardiac tamponade** (B) would present with Beck's triad (hypotension, muffled heart sounds, JVD) and pulsus paradoxus, not a systolic ejection murmur. **Third-degree heart block** (D) would present with bradycardia and cannon A waves, not the findings described here.

The following figure illustrates the hemodynamic distinction between HOCM and AS, showing the characteristic "spike and dome" aortic pressure pattern in HOCM versus the delayed upstroke in AS:

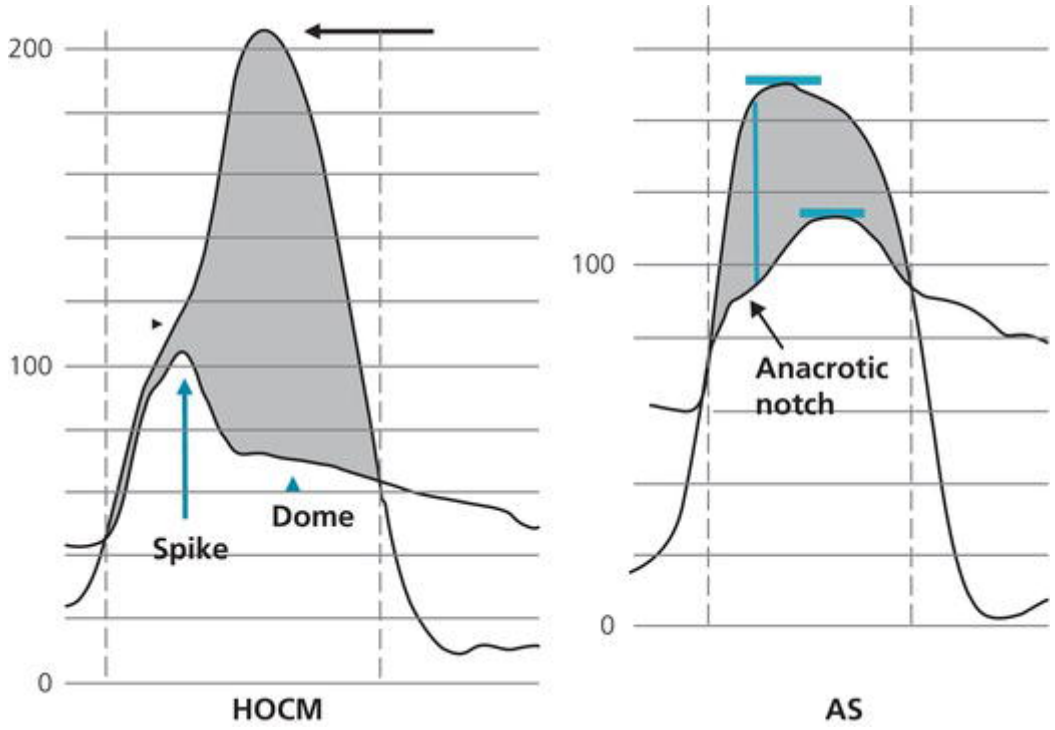


Figure 20. Contrast LV-aortic tracings in HOCM vs. AS. In HOCM, the aortic pressure peaks early while the LV pressure and the gradient peak late, after a bend (arrowhead). In AS, the LV pressure peaks early while the aortic pressure peaks late, after an anacrotic notch. Reproduced with permission of Demos Medical from Hanna and Glancy (2012).

Would you like to explore the current guideline-directed management of symptomatic obstructive HCM, including the role of newer agents like mavacamten?

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Question 1088

A 26-year-old nullipara presents to her physician for a routine check-up at 18 weeks gestation. She has no co-morbidities. Her only complaints are fatigability and a depressed mood for the past 2 weeks. Her vital signs are as follows: blood pressure, 125/80 mm Hg; heart rate, 87/min; respiratory rate, 14/min; and temperature, 36.7°C (98°F). The physical examination is unremarkable and the gynecologic examination is consistent with 18 weeks gestation. A thyroid profile s ordered to check for a possible cause of the fatigability and decreased mood:
Thyroid stimulating hormone (TSH) 0.3 mU/L
Total T4 160 nmol/L
Free T4 13 pmol/L
Corresponding to the obtained results, how should the patient be managed?

Answer Choices:

(A) Prescribe levothyroxine 50 mcg daily
(B) No specific management required
(C) Recommend additional anti-TPO test
(D) Recommend additional T3 assessment

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/366aa62a-bb22-4894-9133-8ad6cf0745de

OpenEvidence Explanation

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The answer is **B. No specific management required**. This patient's thyroid profile is consistent with **normal physiological changes of pregnancy**, and no treatment or additional testing is indicated.

Here is the interpretation of each lab value:

- **TSH 0.3 mU/L**: Mildly low but expected in pregnancy. During pregnancy, hCG directly stimulates the TSH receptor, causing a physiological downward shift in TSH. The lower reference range in pregnancy decreases by approximately 0.1–0.4 mU/L, and a TSH of 0.3 mU/L falls within or near the normal pregnancy range, particularly in the first and second trimesters. The ATA 2026 guidelines note a first-trimester reference interval of approximately 0.1–4.0 mU/L, with gradual normalization thereafter.[1][2][3]
- **Total T4 160 nmol/L**: Elevated compared to non-pregnant ranges but normal for pregnancy. After 16 weeks of gestation, the upper reference range for total T4 should be increased by approximately **50%** to account for the rise in thyroid-binding globulin (TBG). A typical non-pregnant upper limit of ~120 nmol/L adjusted by 1.5× yields ~180 nmol/L, making 160 nmol/L well within the expected range. One study found a second-trimester TT4 reference interval of 77–186 nmol/L.[1][4]
- **Free T4 13 pmol/L**: Normal. Second-trimester fT4 reference ranges are approximately 10.5–18.2 pmol/L, placing this value squarely within normal limits.[4]

Why the other options are incorrect:

- **A (Levothyroxine)**: There is no hypothyroidism — TSH is low-normal and free T4 is normal. Levothyroxine would be inappropriate and potentially harmful.
- **C (Anti-TPO testing)**: Anti-TPO testing is recommended when TSH is elevated (>2.5 mU/L) to guide management of subclinical hypothyroidism.

With a low-normal TSH and normal free T4, there is no indication for TPO antibody testing.[2]

- **D (T3 assessment)**: T3 measurement is useful when hyperthyroidism is suspected (e.g., suppressed TSH with normal free T4, to evaluate T3 thyrotoxicosis). Here, the mildly low TSH is physiologic, and free T4 is normal, so T3 assessment adds no clinical value.[5]

The ACOG Practice Bulletin explicitly states that subclinical hyperthyroidism in pregnancy "has not been associated with adverse pregnancy outcomes" and that "treatment of pregnant women with subclinical hyperthyroidism is not recommended".[1] Even if this were classified as subclinical hyperthyroidism (which it likely is not, given the physiologic TSH suppression of pregnancy), no intervention would be warranted.

Would you like to explore how to distinguish gestational transient thyrotoxicosis from Graves' disease when a pregnant patient presents with a more significantly suppressed TSH?

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Question 1090

A 15-year-old boy is brought to the physician by his mother. His mother reports multiple instances over the past month when she walked into his room while he was masturbating. She is worried he may be going through some sort of "problem." He is currently in 9th grade; his mother says that he is the captain of his high school wrestling team and does reasonably well in school. On examination, he seems embarrassed and avoids making eye contact. Physical examination shows no abnormalities. Which of the following is the most appropriate next step in management?

Answer Choices:

(A) Advise the patient to stop masturbating
(B) Measure serum testosterone level
(C) Reassure the mother
(D) Prescribe sertraline

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/867fdde1-553f-4a96-80de-96aed79bea34

OpenEvidence Explanation

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The most appropriate next step is **C. Reassure the mother**.

Masturbation is a normal part of adolescent sexual development and does not indicate a psychological or medical problem. This 15-year-old boy is functioning well — he is a team captain, performs adequately in school, and has a normal physical examination. There are no signs of compulsive behavior, social dysfunction, or underlying pathology.

Key reasoning for eliminating the other options:

- **Advising the patient to stop masturbating (A)** is inappropriate because masturbation is a normal, healthy behavior in adolescence. Discouraging it could induce unnecessary shame or guilt.
- **Measuring serum testosterone (B)** is not indicated. There is no clinical concern for a hormonal abnormality — his development and behavior are age-appropriate.
- **Prescribing sertraline (D)** would only be considered if there were evidence of obsessive-compulsive disorder or a compulsive sexual behavior disorder interfering with daily functioning, neither of which is present here.

The physician's role in this scenario is to **normalize the behavior** for the mother, educate her that this is a developmentally expected part of puberty, and perhaps counsel on respecting the adolescent's privacy (e.g., knocking before entering his room). The boy's embarrassment is itself a normal and expected reaction to the situation.

Would you like to explore guidelines on counseling parents about normal adolescent sexual development?

Question 1091

A 64-year-old man presents to the clinic with easy fatigability and breathlessness when climbing stairs for the last 2 weeks. He also mentions that he occasionally has bouts of cough at night after about 2–3 hours of sleep which is relieved when he sits upright. He denies shortness of breath at rest, palpitations, and loss of consciousness. He has had hypertension for the last 20 years and is on antihypertensive medications. On physical examination, his temperature is 36.9°C (98.4°F), pulse is 104/min, blood pressure is 122/82 mm Hg, and respirations are 18/min. Chest auscultation reveals crackles over the lung bases bilaterally. Examination of his abdomen reveals mildly tender hepatomegaly. Laboratory investigation results include a hemoglobin of 14.8 g/dL (9.18 mmol/L) and an elevated serum B-type natriuretic peptide. His two-dimensional echocardiogram reveals an enlarged left atrium and an ejection fraction of 55%. Which of the following novel drugs is most likely to benefit the patient in addition to valsartan?

Answer Choices:

(A) Etanercept
(B) Moxonidine
(C) Sacubitril
(D) Aliskiren

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/320ea992-36c2-445f-9fee-5048eb2d4a50

OpenEvidence Explanation

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The answer is **C. Sacubitril**.

This patient presents with heart failure with preserved ejection fraction (HFpEF) — evidenced by exertional dyspnea, paroxysmal nocturnal dyspnea, bibasilar crackles, hepatomegaly, elevated BNP, enlarged left atrium, and an **EF of 55%** — in the setting of longstanding hypertension. Among the listed options, **sacubitril** is the novel drug that would benefit this patient when combined with valsartan.

Why sacubitril? Sacubitril is a neprilysin inhibitor that, when combined with valsartan, forms the angiotensin receptor-neprilysin inhibitor (ARNI) sacubitril/valsartan (Entresto). Sacubitril inhibits neprilysin, the enzyme responsible for degrading natriuretic peptides, bradykinin, and other vasoactive peptides. This results in increased natriuresis, diuresis, and vasodilation while valsartan simultaneously blocks the deleterious effects of angiotensin II.[1][2] The PARAGON-HF trial evaluated sacubitril/valsartan versus valsartan alone in 4,822 patients with HFpEF (LVEF ≥45%) and showed a trend toward reduced HF hospitalizations and cardiovascular death (RR 0.87; 95% CI 0.75–1.01), with particular benefit in patients with LVEF between 45% and 57%.[3] The 2022 AHA/ACC/HFSA guidelines include ARNI as a Class IIb recommendation for HFpEF.[4][5]

Why not the other options?

- **Etanercept (A):** A TNF-α inhibitor used in rheumatologic diseases. Clinical trials (RECOVER and RENAISSANCE) showed no benefit and potential harm in heart failure, and TNF-α inhibitors are contraindicated in HF.
- **Moxonidine (B):** A centrally acting sympatholytic. The MOXCON trial in HF was terminated early due to increased mortality.
- **Aliskiren (D):** A direct renin inhibitor. The ASTRONAUT and ATMOSPHERE trials showed no benefit when added to standard HF therapy, and dual RAAS blockade (aliskiren + valsartan) increases the risk of hyperkalemia, hypotension, and renal dysfunction.

Would you like to explore the current evidence comparing SGLT2 inhibitors versus ARNI as add-on therapy in HFpEF management?

Relevant images

(CONTENT OMITTED)

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Question 1094

A 25-year-old female with Hodgkin's lymphoma presents with a several day history of edema. Lab studies show:

Serum Na+: 140 mmol/L
Serum K+: 3.5 mmol/L
Serum albumin: 1.9 g/dL
Total serum bilirubin: 1.0 mg/dL
Serum creatinine: 1.2 mg/dL

Urinalysis shows 4+ proteinuria and fatty casts. What is the most likely diagnosis?

> **Answer Choices:**
>
> (A) Focal segmental glomerulosclerosis
> (B) Membranous nephropathy
> (C) Minimal change disease
> (D) Amyloidosis

> **Correct Answer:**
>
> (C)
>
> **OpenEvidence Response:**
>
> (C) ✓

OpenEvidence Link: https://openevidence.com/ask/f81bb9a1-b60c-4c2d-8aa0-139227ae0850

OpenEvidence Explanation

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The correct answer is **C. Minimal change disease**.

This patient presents with classic features of **nephrotic syndrome** — edema, severe hypoalbuminemia (1.9 g/dL), heavy proteinuria (4+), and fatty casts — in the setting of Hodgkin's lymphoma. **Minimal change disease (MCD) is the most well-established paraneoplastic glomerular disease associated with Hodgkin's lymphoma**.[1][2][3]

Why minimal change disease?

The association between MCD and Hodgkin's lymphoma is one of the best-recognized paraneoplastic nephropathies in oncology. In a review of 76 cases of nephrotic syndrome associated with neoplasia, patients with lymphomas (particularly Hodgkin's disease) predominantly had lipoid nephrosis (minimal change disease) in approximately **60% of cases**, as opposed to solid tumors, which are more commonly associated with membranous nephropathy.[2] A retrospective French multicenter study of 21 patients with MCD and classical Hodgkin's lymphoma confirmed that MCD is a recognized paraneoplastic manifestation, with remission of nephrotic syndrome consistently achieved upon successful treatment of the lymphoma.[1]

The proposed pathogenesis involves **T-cell dysfunction** — Hodgkin's lymphoma is a malignancy of the lymphoid system, and products of tumor lymphocytes (including cytokines such as TNF-α and the c-mip protein) are thought to alter glomerular permeability, leading to podocyte foot process effacement without immune complex deposition.[4][5][6]

Why not the other options?

- **A. Focal segmental glomerulosclerosis (FSGS):** While FSGS is the most common cause of nephrotic syndrome in adults overall, it lacks the specific paraneoplastic association with Hodgkin's lymphoma.
- **B. Membranous nephropathy:** This is the classic paraneoplastic glomerular disease associated with **solid tumors** (carcinomas), not lymphomas.[2][7]
- **D. Amyloidosis:** Although amyloidosis can occur with Hodgkin's disease, it is far less common (0.1% vs. 0.4% for MCD in large series) and typically

presents with more chronic, progressive disease rather than as a paraneoplastic phenomenon.[3]

Would you like to explore the mechanisms by which treatment of Hodgkin's lymphoma leads to resolution of the associated nephrotic syndrome?

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Question 1096

A 7-year-old woman presents shortly after her birthday with red scaly plaques over both ears. Her mother reports that the patient recently received a pair of fashionable silver earrings from her older sister as a birthday present. Physical examination is only significant for erythema and tenderness over the lobules of the ears bilaterally. Her vital signs show a blood pressure of 121/73 mm Hg, heart rate of 72/min, and a respiratory rate of 21/min. Her medical history is non-significant. Of the following options, which is the mechanism of this reaction?

Answer Choices:

(A) Type I–anaphylactic hypersensitivity reaction
(B) Type III–immune complex-mediated hypersensitivity reaction
(C) Type IV–cell-mediated (delayed) hypersensitivity reaction
(D) Type III and IV–mixed immune complex and cell-mediated hypersensitivity reactions

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/e757c02a-dd93-4a16-a7fb-2c5bc23db76c

OpenEvidence Explanation

(CONTENT OMITTED)

The correct answer is **C. Type IV–cell-mediated (delayed) hypersensitivity reaction**.

This presentation describes **allergic contact dermatitis** (ACD) due to nickel exposure from costume/"silver" earrings, which is the classic example of a **Type IV (delayed-type) hypersensitivity reaction** mediated by T cells, not antibodies.

Why nickel contact dermatitis is Type IV:

Nickel contact allergy is a cell-mediated delayed-type hypersensitivity reaction to nickel ions.[1] The mechanism involves two phases:

1. **Sensitization phase**: Nickel ions penetrate the skin and bind directly to Toll-like receptor 4 (TLR4) on dendritic cells (including Langerhans cells), which then migrate to regional lymph nodes and present nickel to naive T cells via MHC II molecules, generating allergen-specific memory T cells.[1][2]

2. **Elicitation phase**: Upon re-exposure, nickel is captured by dendritic cells and presented to effector T cells, activating skin-resident memory T cells and recruiting circulating memory T cells, resulting in inflammation visible as erythematous, scaly plaques — typically within 48–72 hours.[1][2]

The following figure illustrates the two-phase pathogenesis of allergic contact dermatitis, showing Langerhans cell antigen presentation during sensitization and T cell–mediated inflammation during elicitation:

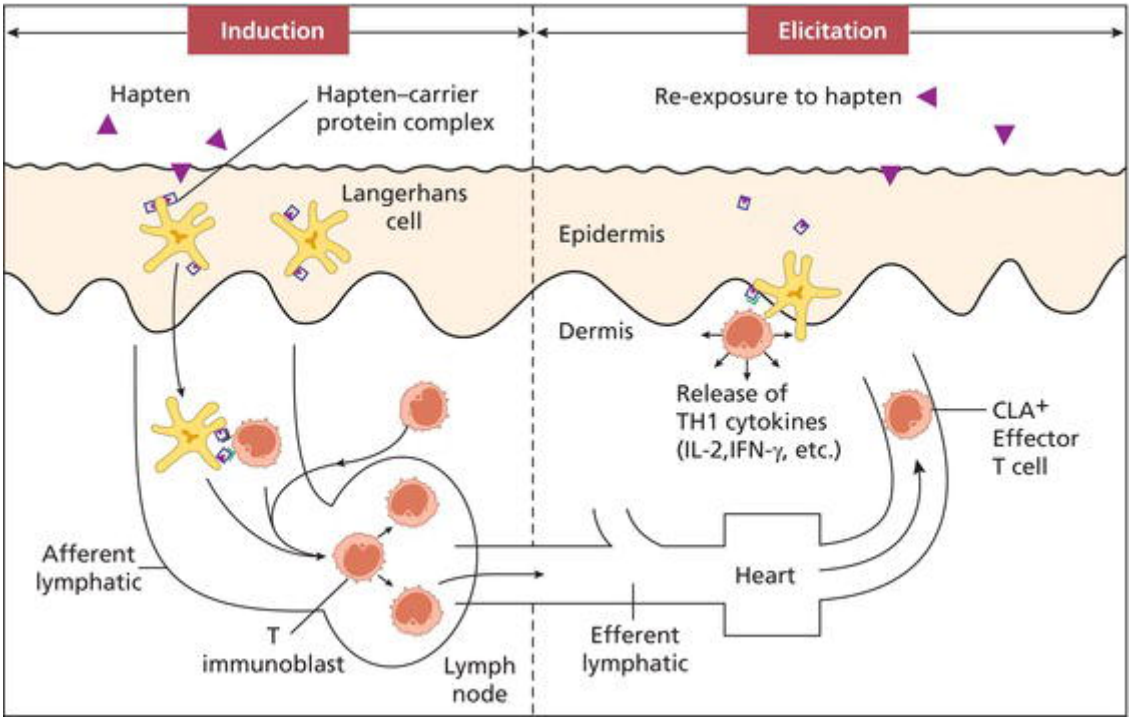


Figure 3. The pathogenesis of allergic contact dermatitis. Langerhans cells bind and present the hapten–carrier protein complex to T lymphocytes (T). Subsequent reexposure to the hapten triggers a T cell–mediated (type IV) hypersensitivity reaction in the skin. CLA, cutaneous lymphocyte-associated antigen; IFN, interferon; IL, interleukin.

Key clinical pearls:

- "Silver" costume jewelry frequently contains nickel, which is the most common contact allergen, with ~16.2% of patch-tested individuals reacting positively. Nickel allergy prevalence is even higher in children with piercings (up to 30–42%).[4][5]
- The bilateral ear involvement matching the site of earring contact is the hallmark distribution pattern of nickel ACD from earrings.[5]
- Although rare type I (IgE-mediated) reactions to nickel have been reported, the vast majority of nickel reactions — and certainly this classic presentation — are type IV.[5][6]

Why the other options are incorrect:

- **Type I (A)**: IgE-mediated, causes immediate reactions (urticaria, anaphylaxis) — not scaly plaques.
- **Type III (B)**: Immune complex–mediated (e.g., serum sickness, Arthus reaction) — not the mechanism of contact dermatitis.

- **Type III + IV (D)**: No immune complex component is involved in standard nickel ACD.

Would you like to explore the diagnostic approach to suspected nickel allergy, including the role of patch testing and dimethylglyoxime spot testing in pediatric patients?

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Question 1099

A 42-year-old woman comes to the clinic for a routine annual exam. She recently moved from New Jersey, and her medical records show a total colectomy. The patient reports that she has had annual colonoscopies since she was 10 years of age because her father had “a condition with his colon.” What is the genetic inheritance pattern of the patient’s disease?

Answer Choices:

(A) Autosomal dominant
(B) Autosomal recessive
(C) Multifactorial
(D) X-linked dominant

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/091a2ef6-0999-4daa-a688-dbb0dbc96452

OpenEvidence Explanation

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The answer is **A. Autosomal dominant**.

The clinical scenario describes a patient with **familial adenomatous polyposis (FAP)**, an **autosomal dominant** syndrome caused by germline pathogenic variants

in the APC tumor suppressor gene on chromosome 5q21. The key clinical clues are:

- **Total colectomy** — FAP progresses to colorectal cancer in nearly 100% of untreated patients, making prophylactic colectomy the standard of care.[1][2]
- **Annual colonoscopies beginning at age 10** — guidelines recommend initiating colonoscopic screening at age 10–15 years in at-risk individuals, consistent with FAP surveillance protocols.[2][3]
- **Affected father** ("a condition with his colon") — FAP is inherited in an autosomal dominant pattern, meaning only one copy of the altered APC gene is sufficient to cause the disorder, and each child of an affected parent has a 50% chance of inheriting the pathogenic variant.[1][4][5]

FAP has close to **100% penetrance**, and about half of patients develop adenomas by age 15, with 95% affected by age 35.[2][6] Approximately 20–30% of newly diagnosed cases represent de novo mutations without a family history, but in this case the paternal history confirms vertical transmission consistent with autosomal dominant inheritance.[1][7]

It is worth noting that a phenotypically similar but genetically distinct condition — MUTYH-associated polyposis (MAP) — follows **autosomal recessive** inheritance. However, MAP typically presents with fewer polyps (usually <100) and would not classically present with the severity requiring total colectomy and screening from age 10 as described here.[1][3][8]

Would you like to explore the extracolonic manifestations and ongoing surveillance recommendations for this patient following colectomy?

Relevant images

(CONTENT OMITTED)

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Question 1101

A 58-year-old man with hypertension and dyslipidemia comes to the physician for a routine health maintenance examination. He says he feels well. He is 180 cm (5 ft 11 in) tall and weighs 103 kg (227 lb); BMI is 32 kg/m2. His BMI last year was 27 kg/m2. When asked about his diet, he says, “Being overweight runs in my family. Rather than fight it, I just try to enjoy myself and eat what I want.” Which of the following defense mechanisms best describes the patient's response to the physician?

Answer Choices:

(A) Rationalization
(B) Fantasy
(C) Distortion
(D) Intellectualization

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/52599e5f-5abb-45aa-9a67-9482db0752fe

OpenEvidence Explanation

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The answer is **A. Rationalization**.

Rationalization is a defense mechanism in which a person constructs a seemingly logical or socially acceptable explanation to justify behavior that is actually driven by less acceptable motives.[1][2] In this case, the patient attributes his significant weight gain (BMI increase from 27 to 32 kg/m²) to genetics ("being overweight runs in my family") and uses this as justification for unhealthy eating habits ("I just try to enjoy myself and eat what I want"). He is offering a plausible-sounding reason to avoid confronting the real issue — his own dietary choices contributing to obesity in the setting of hypertension and dyslipidemia.

Key distinctions from the other options:

- **Fantasy** involves retreating into imaginary scenarios to avoid conflict or reality — the patient is not describing any wishful or imaginary thinking.
- **Distortion** involves grossly reshaping external reality to suit inner needs (e.g., grandiose delusions) — the patient is not misperceiving reality but rather offering a false justification.
- **Intellectualization** involves using abstract thinking or generalizations to distance oneself from the emotional aspects of a stressful situation — the patient is not analyzing his weight gain in detached, intellectual terms but rather excusing it with a convenient rationale.[2]

Rationalization is classified among the **disavowal-level defenses**, alongside denial and projection, and functions by allowing the individual to avoid acknowledging their own role in a problem by offering a conscious but incomplete or misleading explanation.[2]

Would you like to explore how motivational interviewing techniques can be used to address rationalization in patients resistant to lifestyle modification?

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Question 1102

A 27-year-old college student presents to his physician for constant fatigue. The patient states that for the past several weeks he has felt oddly fatigued and has struggled to complete his work. He is a foreign exchange student and is concerned he will fail out of his academic program. He has experienced some occasional nausea and vomiting which has caused him to lose weight. The patient is a first year college student, drinks alcohol regularly, smokes marijuana, and has unprotected sex with multiple partners. His temperature is 99.5°F (37.5°C), blood pressure is 127/68 mmHg, pulse is 90/min, respirations are 17/min, and oxygen saturation is 98% on room air. Laboratory values are ordered as seen below.

Serum:
Na+: 139 mEq/L
Cl-: 100 mEq/L
K+: 4.3 mEq/L
HCO3-: 25 mEq/L
BUN: 20 mg/dL
Glucose: 99 mg/dL
Creatinine: 1.1 mg/dL
Ca2+: 10.2 mg/dL
Total bilirubin: 2.0 mg/dL
AST: 85 U/L
ALT: 92 U/L

Urine
Color: Amber/brown
Marijuana: Positive
Amphetamines: Positive
Cocaine: Positive

The patient refuses an examination of his genitals. Which of the following is the best diagnostic test?

> **Answer Choices:**

(A) CAGE questions
(B) Uretheral swab and culture
(C) Viral core antibody
(D) Viral surface antibody

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/62ae49e0-fba9-4eda-8895-4480a48b10a9

OpenEvidence Explanation

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The best diagnostic test is **C. Viral core antibody** (anti-HCV antibody, also known as hepatitis C virus core antibody).

This patient presents with a clinical picture highly suggestive of **acute or early hepatitis C infection**: fatigue, nausea/vomiting, weight loss, low-grade fever, elevated transaminases (AST 85, ALT 92), and elevated total bilirubin (2.0 mg/dL) — all in the setting of significant risk factors including polysubstance use (marijuana, amphetamines, cocaine) and unprotected sex with multiple partners. [1]

Why viral core antibody (anti-HCV)?

The anti-HCV antibody test (which detects antibodies against the HCV core protein) is the standard initial screening test for hepatitis C infection, with sensitivity and specificity of approximately 99% using third-generation enzyme immunoassays.[2] The AASLD/IDSA and CDC recommend HCV antibody

screening with reflex HCV RNA testing as the initial diagnostic approach.[3] This patient's risk profile — illicit drug use and high-risk sexual behavior — combined with hepatocellular injury pattern (ALT > AST) and constitutional symptoms makes HCV the leading diagnostic concern.

Why not the other options?

- **A. CAGE questions** — While this patient drinks alcohol regularly, the CAGE questionnaire screens for alcohol use disorder and would not explain the elevated transaminases and systemic symptoms in this clinical context.
- **B. Urethral swab and culture** — The patient refuses a genital exam, making this impractical. Additionally, STIs such as gonorrhea or chlamydia would not explain the hepatitis picture.
- **D. Viral surface antibody** — Hepatitis B surface antibody (anti-HBs) indicates immunity to hepatitis B (from vaccination or prior resolved infection), not active infection. It would not be a diagnostic test for the current illness. To diagnose active hepatitis B, hepatitis B surface antigen (HBsAg) and/or IgM anti-HBc would be needed.[1][4]

Would you like to explore the approach to distinguishing acute from chronic HCV infection and the role of HCV RNA testing in confirming active viremia?

Relevant images

(CONTENT OMITTED)

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Question 1103

A 63-year-old woman comes to the physician because of a 6-month history of fatigue and shortness of breath on exertion in addition to a 1-month history of ankle swelling. She has a history of sleep apnea. Examination of the lower extremities shows bilateral pitting pedal and ankle edema. Cardiac examination shows a widely split S2 that varies with respiration. An ECG shows right bundle branch block. Which of the following is the most likely etiology of the patient's lower extremity edema?

Answer Choices:

(A) Localized lymphatic obstruction
(B) Thrombus formation in a deep vein
(C) Increased capillary hydrostatic pressure
(D) Decreased plasma oncotic pressure

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/a10c3c11-be9b-4fd1-8203-a904345717fd

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OpenEvidence Explanation

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The answer is **C. Increased capillary hydrostatic pressure**.

This patient presents with a clinical picture consistent with **right-sided heart failure** secondary to **cor pulmonale** from obstructive sleep apnea. The key findings include:

- **Fatigue and exertional dyspnea** (6 months) with progressive **bilateral pitting edema** (1 month) — classic signs of chronic right heart failure[1][2]
- **Widely split S2 varying with respiration** — indicates delayed pulmonic valve closure, consistent with right ventricular pressure/volume overload and pulmonary hypertension[3][4]
- **Right bundle branch block** on ECG — reflects right ventricular strain/conduction delay from chronic pressure overload[5]
- **History of sleep apnea** — a well-established cause of pulmonary hypertension leading to cor pulmonale[6]

The mechanism of edema in right heart failure is **increased capillary hydrostatic pressure** due to elevated central venous pressure (CVP). As the right ventricle fails, systemic venous pressures rise, which transmits backward to the peripheral capillary beds, increasing hydrostatic pressure and driving fluid into the interstitial space.[7][8] This is the fundamental Starling force responsible for the peripheral edema seen in right heart failure.

Why not the other options?

- **A (Lymphatic obstruction):** Would cause non-pitting, localized lymphedema — not bilateral pitting edema with systemic signs of heart failure.
- **B (Deep vein thrombosis):** Typically causes unilateral leg swelling and would not explain the cardiac findings (split S2, RBBB) or the systemic symptoms.
- **D (Decreased oncotic pressure):** Seen in nephrotic syndrome, liver failure, or malnutrition — there is no indication of hypoalbuminemia or protein loss in this presentation.

Would you like to explore the diagnostic workup and management of pulmonary hypertension secondary to obstructive sleep apnea?

Relevant images

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Question 1104

A 62-year-old man presents with bright red blood in his stool which occurred 2 times this week. He denies fever, weight loss, pain, pruritus or urinary symptoms. Past medical history is significant for gastroesophageal reflux disease, and recent appendicitis, status post laparoscopic appendectomy complicated by delirium tremens. His vitals are a temperature of 37.0°C (98.6°F), blood pressure of 130/80 mm Hg, pulse of 78/min, and respiratory rate of 12/min. Physical examination reveals a distended abdomen with shifting dullness on percussion. In addition, multiple purple spider web-like lesions are present on the chest and arms, which blanch when pressure is applied. Fecal occult blood test is negative. On anoscopy, a non-tender, dilated vascular protrusion is noted superior to the pectinate line. Which of the following is most likely true about this patient's current symptoms?

Answer Choices:

(A) This patient has peptic ulcer disease.
(B) The vascular protrusion drains into the superior rectal vein.
(C) The vascular protrusion drains into the inferior rectal vein.
(D) Fecal leukocytes and a stool culture are required for diagnosis.

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/febcf66f-806f-40e7-8842-767bdb2cc879

OpenEvidence Explanation

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The correct answer is **B. The vascular protrusion drains into the superior rectal vein.**

This patient has multiple clinical features pointing to **alcoholic liver cirrhosis with portal hypertension**: a history of delirium tremens (indicating alcohol use disorder), spider angiomas on the chest and arms (central arteriole with radiating vessels that blanch with pressure), and ascites (distended abdomen with shifting dullness).[1][2] On anoscopy, the non-tender, dilated vascular protrusion **superior to the pectinate (dentate) line** is an **internal hemorrhoid**.

Why answer B is correct: Internal hemorrhoids originate above the dentate line and drain into the **superior rectal vein**, which feeds into the inferior mesenteric vein and ultimately the portal venous system.[3][4] The American Society of Colon and Rectal Surgeons guidelines note that hemorrhoids "drain into the superior and inferior hemorrhoidal veins," with the internal hemorrhoidal plexus draining primarily via the superior rectal vein.[4] This portosystemic communication is precisely why portal hypertension exacerbates hemorrhoidal disease.[5]

Why the other answers are incorrect:

- **A (Peptic ulcer disease):** The fecal occult blood test is negative, and a visible vascular protrusion on anoscopy above the pectinate line explains the hematochezia. Peptic ulcer disease typically causes melena or hematemesis, not bright red blood per rectum with a negative FOBT.
- **C (Inferior rectal vein):** The inferior rectal vein drains the **external** hemorrhoidal plexus below the dentate line. Since this lesion is above the pectinate line, it drains via the superior rectal vein.[3][6]
- **D (Fecal leukocytes and stool culture):** These are used to evaluate infectious diarrhea, not hemorrhoidal bleeding. The clinical presentation is not consistent with an infectious etiology.

Notably, while anorectal varices and hemorrhoids can coexist in cirrhotic patients, they are distinct entities — anorectal varices appear as tortuous, bluish nonprolapsing veins in the distal rectum, whereas hemorrhoids present as soft, reddish-purple swollen veins.[7] The description in this case is consistent with an internal hemorrhoid.

Would you like to explore the differentiation between rectal varices and hemorrhoids in cirrhotic patients, including management considerations for hemorrhoidal disease in the setting of portal hypertension and coagulopathy?

Relevant images

(CONTENT OMITTED)

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Question 1105

A 55-year-old woman presents to the office because she has been feeling weak. For the past 2 years, she has been urinating a considerable volume every time she goes to the bathroom. She has no past medical history. Her heart rate is 86/min, respiratory rate is 15/min, temperature is 37.4°C (99.3°F), and blood pressure is 111/79 mm Hg. Laboratory studies are significant for the following:
Calcium 13.8 mg/dL
PTH 230 pg/mL
Her complete metabolic panel is otherwise within normal limits. Imaging studies show subperiosteal resorption and osteoporosis. Scintigraphy reveals the most common pathologic condition associated with the patient's diagnosis. Which of the following is the most likely diagnosis in this patient?

Answer Choices:

(A) Adenoma
(B) Carcinoma
(C) Decreased calcitriol concentration
(D) Phosphate retention

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/3c5b25a6-e697-4dd8-8ef3-beea1d04aedc

OpenEvidence Explanation

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The correct answer is **A. Adenoma**.

This patient presents with classic **primary hyperparathyroidism (PHPT)**: hypercalcemia (13.8 mg/dL), markedly elevated PTH (230 pg/mL), polyuria, weakness, subperiosteal resorption, and osteoporosis. The subperiosteal resorption is a pathognomonic skeletal feature of PHPT, part of the spectrum of osteitis fibrosa cystica.[1][2]

The question states that scintigraphy reveals "the most common pathologic condition" associated with this diagnosis. A **single parathyroid adenoma** accounts for approximately **80–85%** of all cases of PHPT, making it by far the most common etiology.[1][3][4] Sestamibi scintigraphy is a standard preoperative localization modality that identifies hyperfunctioning parathyroid tissue — in this case, a solitary adenoma.[5][6]

Why the other options are incorrect:

- **B. Carcinoma** — Parathyroid carcinoma accounts for well under 1% of PHPT cases and is rare.[1][3]
- **C. Decreased calcitriol concentration** — This is associated with secondary hyperparathyroidism (e.g., in chronic kidney disease), not primary hyperparathyroidism. The metabolic panel here is otherwise normal, arguing against renal failure.
- **D. Phosphate retention** — Also a feature of secondary hyperparathyroidism due to renal failure, not the primary form seen in this patient.

The following figure demonstrates the classic appearance of a parathyroid adenoma on sestamibi scintigraphy, showing persistent focal radiotracer uptake on delayed imaging with anatomic localization on fused SPECT/CT.

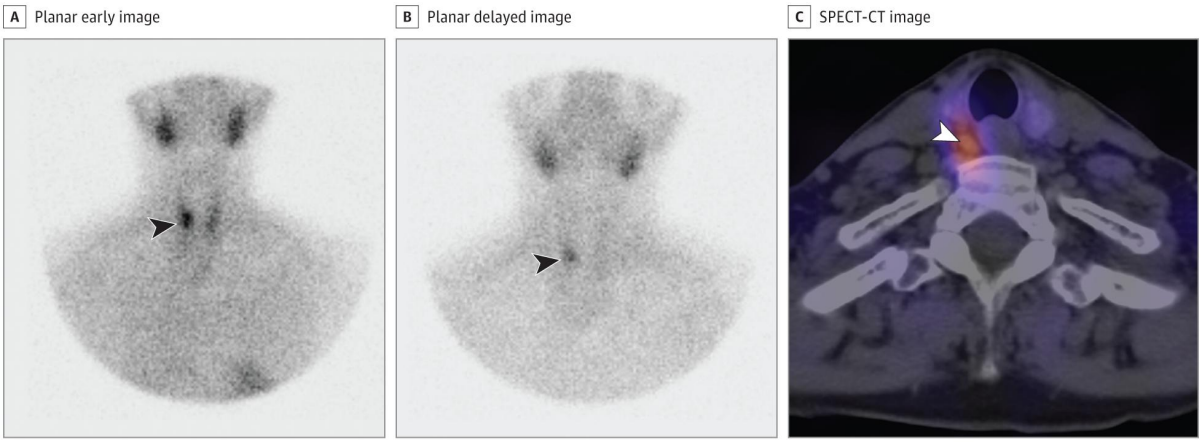


Figure 2. Classic Parathyroid Adenoma Sestamibi Scintigraphy Appearance

Used under license from JAMA Network.

Would you like to explore the current surgical indications and guidelines for parathyroidectomy in primary hyperparathyroidism?

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Question 1106

A 35-year-old woman presents to a psychiatrist for an initial consultation. She reports that for the past 3 years, she has experienced several periods of depressed mood. The episodes do not coincide with any specific life events and seem to resolve after 4-6 weeks. During these episodes, she experiences a depressed mood, sleep disturbances, and a poor appetite, but she at times is able to enjoy spending time with her children and husband but other times she is distressed and cannot enjoy time with them. Upon further questioning, she also reports experiencing occasional episodes of elevated mood over the past ten years. During these episodes, she is very productive at her work as a lawyer and requires less sleep than usual. Her past medical history is notable for obesity, type I diabetes mellitus, and rheumatoid arthritis. She is on insulin and takes methotrexate. She smokes marijuana occasionally. Her temperature is 99.2°F (37.3°C), blood pressure is 124/80 mmHg, pulse is 78/min, and respirations are 17/min. On exam, she is quiet with a flattened affect, but is cooperative and answers questions thoroughly. Which of the following is the most likely diagnosis in this patient?

Answer Choices:

(A) Bipolar I disorder
(B) Cyclothymic disorder
(C) Persistent depressive disorder
(D) Schizoaffective disorder

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/ffdef596-7fa2-4637-8b38-94202bdeb85d

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OpenEvidence Explanation

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The most likely diagnosis is **B. Cyclothymic disorder**.

This patient's presentation is characteristic of cyclothymic disorder based on the following DSM-5-TR criteria:[1]

- **Subsyndromal depressive episodes**: The depressive episodes last 4–6 weeks but do not meet full criteria for a major depressive episode. Critically, she retains the ability to enjoy time with her family during some of these episodes (inconsistent anhedonia), and only three depressive symptoms are described (depressed mood, sleep disturbance, poor appetite) — fewer than the five required for a major depressive episode.
- **Subsyndromal hypomanic symptoms**: The episodes of elevated mood with increased productivity and decreased need for sleep do not meet full criteria for a hypomanic episode (which requires ≥4 consecutive days of elevated mood plus ≥3 additional symptoms with a clear change in functioning). These are described as "occasional" and appear to enhance rather than impair her functioning at work.[2]
- **Duration ≥2 years**: Mood fluctuations have been present for at least 3 years (depressive symptoms) and up to 10 years (elevated mood episodes), well exceeding the 2-year minimum.[1]

Why the other options are less likely:

- **Bipolar I disorder** requires at least one full manic episode (≥1 week of elevated/irritable mood with marked functional impairment or psychotic features). This patient's elevated mood episodes are mild and ego-syntonic, without evidence of impairment.[2][3]

- **Persistent depressive disorder (dysthymia)** involves chronic depressed mood for ≥2 years but does not account for the episodes of elevated mood, which are a key feature here.[4]
- **Schizoaffective disorder** requires concurrent psychotic symptoms (delusions, hallucinations) alongside mood episodes. There is no evidence of psychotic features in this patient.[1]

Would you like to explore the treatment approach for cyclothymic disorder and the risk of progression to bipolar I or II?

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Question 1109

A 46-year-old man comes to the emergency department because of a 4-week history of fatigue and headache that have gotten progressively worse. He has allergic asthma treated with inhaled salbutamol. He immigrated to the USA from Thailand 9 years ago. He lives by himself and works as a waiter in a restaurant. He has had 6 lifetime male sexual partners and uses condoms inconsistently. He drinks 1–2 beers daily. His temperature is 38.2°C (100.8°F), pulse is 88/min, and blood pressure is 128/76 mm Hg. Examination of the mouth shows several white patches on the tongue and oral mucosa that can be easily scraped off with a tongue blade. On mental status examination, the patient is somnolent and has short-term memory deficits. The remainder of the examination shows no abnormalities.
Laboratory studies show:
Hemoglobin 13.6 g/dL
Leukocyte count 9,600/mm3
Segmented neutrophils 80%
Eosinophils 1%
Lymphocytes 17%
Monocytes 2%
CD4+ T-lymphocytes 80/mm3 (Normal ≥ 500)
Platelet count 328,000/mm3
Serum
pH 7.36
Na+ 135 mEq/L
Cl- 101 mEq/L
K+ 4.8 mEq/L
HCO3- 22 mEq/L
Glucose 95 mg/dL
Creatinine 0.9 mg/dL
BUN 16 mg/dL
Bilirubin, total 0.7 mg/dL
AST 13 U/L
ALT 15 U/L
Erythrocyte sedimentation rate 10 mm/hour
HIV test positive

A lumbar puncture is performed and an opening pressure of 150 mm H2O is noted. Cerebrospinal fluid analysis shows a leukocyte count of 25/mm3 (60% lymphocytes), protein concentration of 52 mg/dL, and a glucose concentration of 37 mg/dL. India ink stain shows organisms with prominent capsules. Blood cultures are drawn. Which of the following is the most appropriate pharmacotherapy for this patient's neurological symptoms?

> **Answer Choices:**
>
> (A) Pyrimethamine, sulfadiazine, and folinic acid
> (B) Amphotericin B and flucytosine
> (C) Fluconazole
> (D) Vancomycin and meropenem

> **Correct Answer:**
>
> **(B)**
>
> **OpenEvidence Response:**
>
> **(B)** ✓

OpenEvidence Link: https://openevidence.com/ask/1f8ccea0-39ce-4770-bd81-b6c79897a7c3

OpenEvidence Explanation

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The correct answer is **B. Amphotericin B and flucytosine**.

This patient presents with **cryptococcal meningitis** in the setting of advanced HIV/AIDS (CD4+ count of 80/mm³). The key diagnostic findings include:

- **Oral thrush** (white patches easily scraped off) indicating severe immunosuppression
- **Neurological symptoms** (somnolence, short-term memory deficits) with low-grade fever
- **CSF findings**: lymphocytic pleocytosis, elevated protein, low glucose — consistent with a subacute/chronic meningitis
- **India ink stain** showing encapsulated organisms, which is pathognomonic for **Cryptococcus neoformans**

Induction therapy with amphotericin B plus flucytosine is the standard of care for HIV-associated cryptococcal meningitis. Per the IDSA/NIH OI guidelines, an amphotericin B formulation (preferably liposomal in resource-available settings) combined with oral flucytosine for at least 2 weeks is recommended as induction therapy (AII).[1][2] This combination achieves more rapid CSF fungal clearance and improved survival compared to amphotericin B alone or amphotericin B with fluconazole.[2][3] After successful induction with clinical improvement and negative CSF cultures, consolidation therapy with fluconazole (800 mg/day for 8 weeks) is initiated, followed by long-term maintenance fluconazole (200 mg/day).[4]

Why the other options are incorrect:

- **A. Pyrimethamine, sulfadiazine, and folinic acid** — This is the treatment for **cerebral toxoplasmosis**, another AIDS-defining CNS infection, but toxoplasmosis typically presents with ring-enhancing lesions on imaging and would not show encapsulated organisms on India ink stain.
- **C. Fluconazole alone** — Fluconazole monotherapy is associated with approximately 50% mortality at 10 weeks and delayed CSF sterilization; it is reserved for consolidation/maintenance therapy, not induction.[2]
- **D. Vancomycin and meropenem** — This would target bacterial meningitis, which is inconsistent with the subacute presentation, CSF profile, and India ink findings.

Would you like to explore the management of elevated intracranial pressure in cryptococcal meningitis, which is a critical determinant of acute mortality in these patients?

Relevant images

(CONTENT OMITTED)

References

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Question 1110

A previously healthy 16-year-old boy comes to the physician because of a 5-day history of pain at the back of his left ankle. His mother had a myocardial infarction at 54 years. His BMI is 23 kg/m2. There is tenderness above the left posterior calcaneus and a firm, 3-cm, skin-colored nodule that moves with the left Achilles tendon. A photomicrograph from a biopsy of the nodule is shown. Serum studies in this patient are most likely to show increased levels of which of the following?

Answer Choices:

(A) Rheumatoid factor
(B) Angiotensin converting enzyme
(C) Low-density lipoprotein
(D) Triglycerides

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/d4bbeaf4-fba5-41b5-9279-c5b87e73dedb

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OpenEvidence Explanation

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The answer is **C. Low-density lipoprotein**.

This clinical presentation — a firm, skin-colored nodule that moves with the Achilles tendon in a young patient whose mother had a myocardial infarction at age 54 — is classic for an **Achilles tendon xanthoma** in the setting of **familial hypercholesterolemia (FH)**. The biopsy photomicrograph would show lipid-laden foamy macrophages (foam cells) within the tendon, which is the histological hallmark of xanthomas.[1][2]

Key clinical features pointing to FH:

- **Tendon xanthoma:** A firm, skin-colored nodule adherent to the Achilles tendon is nearly pathognomonic for FH. Xanthomas represent accumulation of cholesterol in macrophages within tendons, most commonly the Achilles and hand extensor tendons.[3][4]
- **Family history of premature cardiovascular disease:** The mother's MI at age 54 meets criteria for premature CAD in women (before age 65), which is a major diagnostic criterion for FH.[5]
- **Young age of presentation:** FH causes lifelong LDL-C elevation, and tendon xanthomas can appear in adolescence or young adulthood, particularly in more severe phenotypes.[6][7]

FH is characterized by markedly elevated **LDL cholesterol** with typically **normal triglyceride** levels.[5] This distinguishes it from hypertriglyceridemia, which is associated with eruptive xanthomas (small, yellowish papules on extensor surfaces and buttocks) rather than tendon xanthomas.[8][9] Rheumatoid factor (rheumatoid nodules) and ACE (sarcoidosis) can cause nodules but would not present as a firm mass moving with the Achilles tendon in this clinical context.

The following figure from the NEJM demonstrates the MRI and histopathological appearance of an Achilles tendon xanthoma in familial hypercholesterolemia, including the characteristic foamy macrophages on biopsy (Panel C).

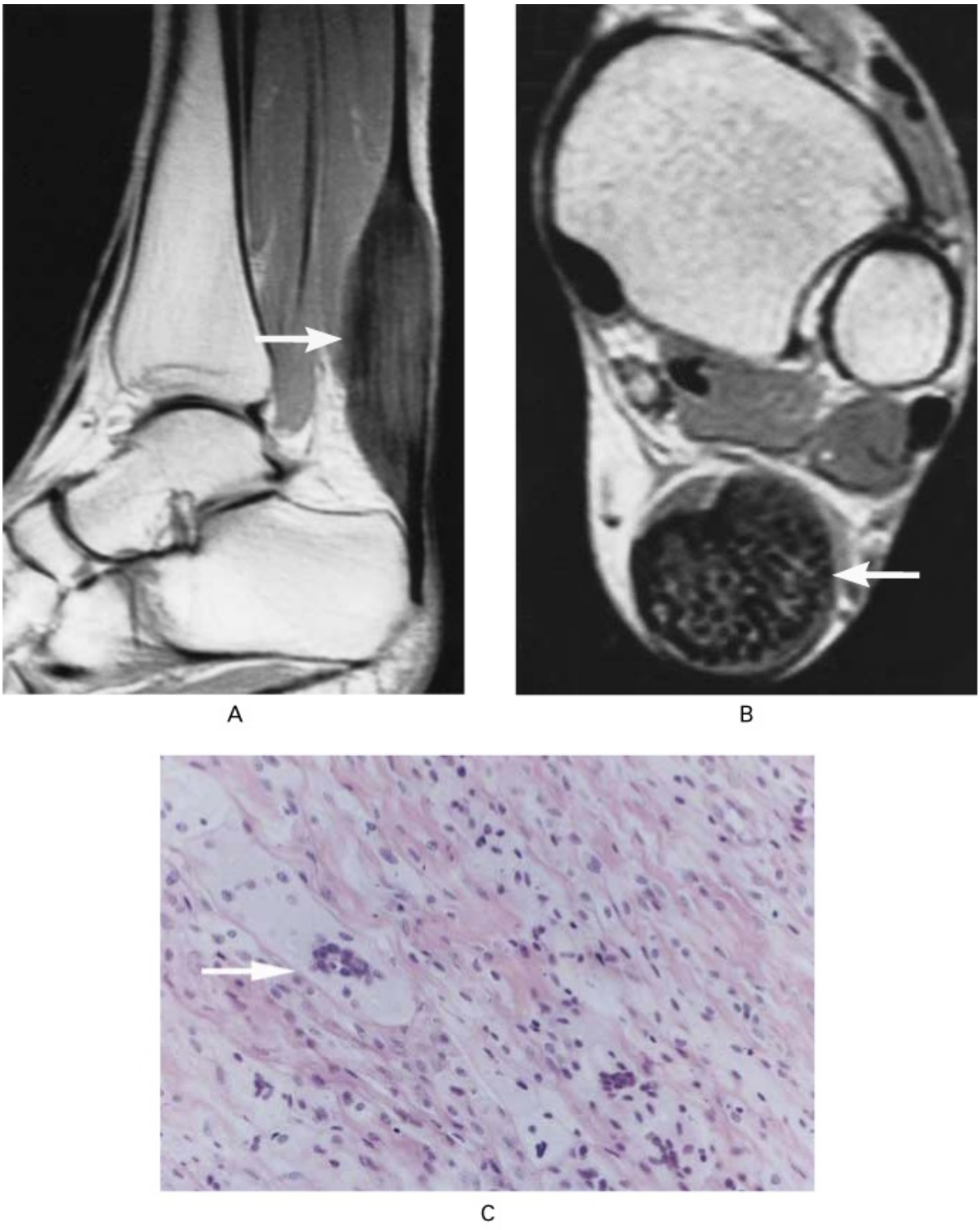


Figure 1.

Used under license from The New England Journal of Medicine.

Would you like to explore the current guideline-recommended screening criteria and treatment approach for familial hypercholesterolemia in adolescents?

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Question 1111

A 3-year-old boy presents with episodic diarrhea with malodorous stools, stunted growth, occasional abdominal cramps, and an itchy rash. His mother says that these symptoms developed approximately 2 years ago. The patient was exclusively breastfed up to the age of 7 months. Supplementary feeding was started with non-starchy vegetable followed by starchy vegetables, meat, fish, eggs, and bread. Bread and cookies were the last product to be introduced at the age of 12 months. The patient's mother tried to withdraw dairy products from the patient's diet because she heard that lactose can cause such symptoms, but it did not help. The patient's vital signs include: blood pressure 90/55 mm Hg, heart rate 101/min, respiratory rate 19/min, and temperature 36.3°C (97.3°F). His weight is 11 kg (24.2 lb, -2 SD) and height is 90 cm (2 ft 11 in, -1 SD). On physical examination, the patient's skin is pale with a papulovesicular rash on his abdomen and back. There are a few aphthous ulcers in the oral cavity. The abdomen is distended but no tenderness to palpation. No hepatosplenomegaly. An immunological assay is performed and shows positive anti-transglutaminase and anti-endomysial antibodies. Which of the following changes would you most likely expect to see on intestinal biopsy in this patient?

Answer Choices:

(A) Granulomas in the submucous tissue
(B) Crypt abscesses
(C) Villous atrophy and crypt hypertrophy
(D) Villous hyperplasia

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/5e7360ed-46c2-424d-b6a8-3773328bffcf

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OpenEvidence Explanation

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The correct answer is **C. Villous atrophy and crypt hypertrophy**.

This presentation — chronic malodorous diarrhea, failure to thrive, abdominal distension, papulovesicular rash (dermatitis herpetiformis), aphthous ulcers, and symptom onset after introduction of gluten-containing foods (bread/cookies at 12 months) — is classic for **celiac disease**. The positive **anti-tissue transglutaminase (anti-tTG)** and **anti-endomysial (EMA) antibodies** confirm the serologic diagnosis.[1][2][3]

The hallmark histologic findings on small intestinal biopsy in celiac disease are **villous atrophy, crypt hyperplasia (hypertrophy), and increased intraepithelial lymphocytes** — classified using the Marsh-Oberhuber system, where Marsh type 3 (3a–3c) represents the spectrum from partial to total villous atrophy with crypt hypertrophy.[1][4][5] Compensatory crypt hyperplasia develops in response to enterocyte loss driven by CD8+ cytotoxic T lymphocytes and the inflammatory cascade triggered by gluten-derived gliadin peptides.[6]

The following figure from an NEJM case illustrates the characteristic histopathology, comparing celiac disease mucosa (villous atrophy, crypt hyperplasia, intraepithelial lymphocytosis) with normal duodenal tissue:

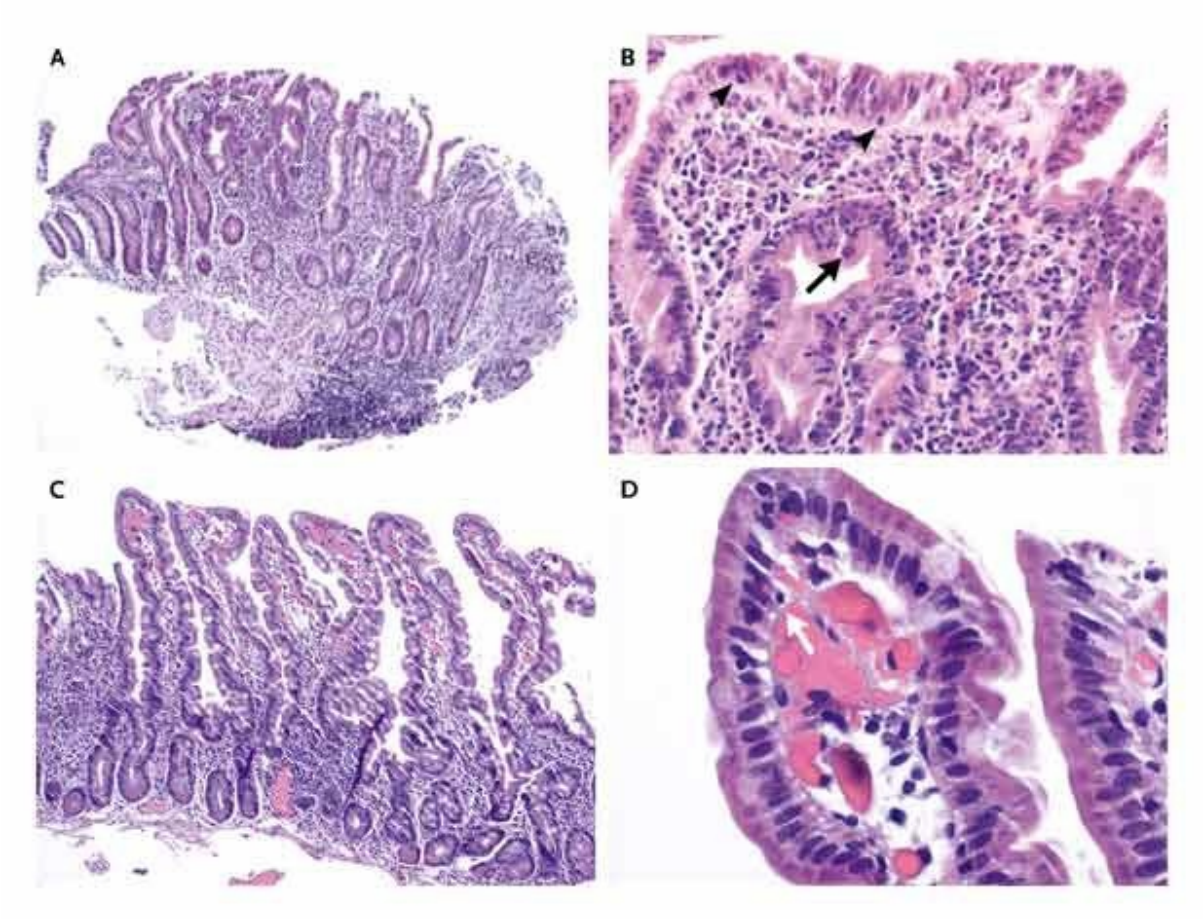


Figure 4. Duodenal-Biopsy Specimen (Hematoxylin and Eosin).

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Why the other options are incorrect:

- **A. Granulomas in the submucous tissue** — characteristic of Crohn's disease, not celiac disease.
- **B. Crypt abscesses** — a hallmark of ulcerative colitis (neutrophilic infiltration of crypts), not celiac disease.
- **D. Villous hyperplasia** — not a recognized feature of celiac disease; the villi undergo atrophy, not hyperplasia.

Would you like to explore the current guidelines on when duodenal biopsy can be omitted in pediatric celiac disease diagnosis (the ESPGHAN biopsy-avoidance strategy)?

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Question 1112

An 18-year-old patient is visiting the pediatrician with her mother for her annual exam before college starts. Her height and weight are appropriate for her age, and she is up to date on all her vaccinations and has no medical complaints. She is doing well in school and has a part-time job stocking shelves at a clothing store. She was offered a higher-paying job as a cashier at the store, but she declined. She is very shy and withdrawn with the physician. Afterwards, her mother asks to speak to the physician alone and expresses concern that her daughter is very socially isolated and feels lonely. She is also worried that her daughter is extremely sensitive to criticism, even from family. The daughter is interested in art and music, but hasn't participated in any extracurriculars because she says that she is untalented and thinks nobody wants to hang out with her. When her mother has encouraged her to invite friends over, the daughter bursts into tears and says, "Nobody wants to be friends with me, I am too lame and ugly and I just know I'll end up getting rejected." Which of the following is the most likely explanation for the daughter's behavior?

Answer Choices:

(A) Schizotypal personality disorder
(B) Generalized anxiety disorder
(C) Avoidant personality disorder
(D) Dependent personality disorder

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/e158d213-f785-40c0-9ab7-7e189c3f51a6

OpenEvidence Explanation

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The most likely explanation is **C. Avoidant personality disorder**.

This patient's presentation is a textbook match for avoidant personality disorder (AvPD), which is defined as a pervasive pattern of **social inhibition, feelings of inadequacy, and hypersensitivity to negative evaluation**.[1] Several specific features in the vignette map directly to DSM-5 diagnostic criteria:

- **Declining the cashier job** (more interpersonal contact) while keeping the shelf-stocking role aligns with Criterion 1: avoidance of work activities involving significant interpersonal contact due to fear of criticism or rejection.[1]
- **Extreme sensitivity to criticism**, even from family, corresponds to Criterion 4: preoccupation with being criticized or rejected.[1]
- **Low self-esteem** ("I am too lame and ugly," "I am untalented") matches Criterion 6: views self as socially inept, personally unappealing, or inferior.[1]
- **Social isolation despite desiring connection** — she wants friends but assumes rejection — reflects the core AvPD dynamic: craving acceptance while fearing judgment, leading to avoidance of relationships unless certain of being liked.[2]
- **Not participating in extracurriculars** despite genuine interest in art and music reflects Criterion 5: reluctance to engage in new activities involving interpersonal contact.[1]

Why not the other options:

- **Schizotypal personality disorder (A):** Characterized by cognitive/perceptual distortions, eccentric behavior, and a *lack of desire* for relationships. In AvPD, the desire for relationships is present but constrained by fear of rejection — a key distinguishing feature.[1][3]

- **Generalized anxiety disorder (B):** GAD involves excessive worry across multiple domains (health, finances, daily matters), not a pervasive pattern of social inhibition rooted in feelings of inadequacy and fear of negative evaluation.
- **Dependent personality disorder (D):** Characterized by an excessive need to be taken care of, resulting in submissive and clinging behavior. This patient is not clinging to others or seeking caretaking — she is *avoiding* relationships altogether.[3]

Would you like to explore the evidence-based psychotherapy approaches (such as cognitive-behavioral therapy or schema therapy) recommended for avoidant personality disorder?

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Question 1113

A 15-year-old girl comes to the physician because of a 2-week history of genital lesions. She has no history of serious illness. She is sexually active with 2 male partners and uses condoms inconsistently. Vital signs are within normal limits. Pelvic examination shows multiple hyperkeratotic exophytic papules over the vulva. The lesions turn white on application of 3% acetic acid. Which of the following is most likely to have prevented this patient's condition?

> **Answer Choices:**
>
> (A) Condoms
> (B) Anti-HIV prophylaxis
> (C) Spermicidal foam
> (D) Vaccination

> **Correct Answer:**
>
> **(D)**
>
> **OpenEvidence Response:**
>
> **(D)** ✓

OpenEvidence Link: https://openevidence.com/ask/91990a9c-7719-4a14-b4ff-366b02918fe8

OpenEvidence Explanation

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The answer is **D. Vaccination**.

The clinical presentation — multiple **hyperkeratotic exophytic papules** on the vulva that turn **white with acetic acid (acetowhite)** — is classic for **condylomata acuminata (genital warts)** caused by **human papillomavirus (HPV)**, most commonly types 6 and 11.[1][2]

HPV vaccination is the primary recommended modality for prevention of genital warts.[3][4] The 9-valent HPV vaccine (Gardasil 9) targets HPV types 6 and 11, which cause >90% of genital warts, and demonstrates **99% efficacy** against HPV 6/11-related genital warts in clinical trials.[5][6] ACIP recommends routine HPV vaccination for all adolescents at age 11–12 years, with catch-up vaccination through age 26.[2] Had this patient been vaccinated at the recommended age (before sexual debut), her condition would very likely have been prevented.

Why not the other options?

- **A. Condoms** — While condoms can reduce HPV transmission, evidence regarding their effect on genital warts is **conflicting**, and they do not fully protect because HPV can infect areas not covered by a condom. Condoms are not the most effective preventive measure.[2][4]
- **B. Anti-HIV prophylaxis** — Pre-exposure prophylaxis (PrEP) targets HIV, not HPV. It would have no role in preventing genital warts.
- **C. Spermicidal foam** — Spermicides have no demonstrated efficacy against HPV transmission.

Population-level data further support vaccination: US females aged 14–19 experienced an **88% decrease** in disease caused by HPV types 6, 11, 16, and 18 compared with the pre-vaccination era.[4]

Would you like to explore the recommended management and treatment options for genital warts in adolescents?

Relevant images

(CONTENT OMITTED)

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Question 1118

A 40-year-old obese man with a history of diabetes and chronic kidney disease presents with one day of excruciating pain, swelling, and redness in his greater toe. He denies any inciting trauma or similar prior episodes. Vital signs are stable. On examination, the right first toe is grossly erythematous and edematous, with range of motion limited due to pain. Deposition of which of the following is associated with the most likely underlying joint disorder?

Answer Choices:

(A) Calcium phosphate
(B) Calcium oxalate
(C) Monosodium urate
(D) Copper

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/a7b0d3dd-4c25-4daa-bc83-dc0368ef17ff

OpenEvidence Explanation

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The correct answer is **C. Monosodium urate**.

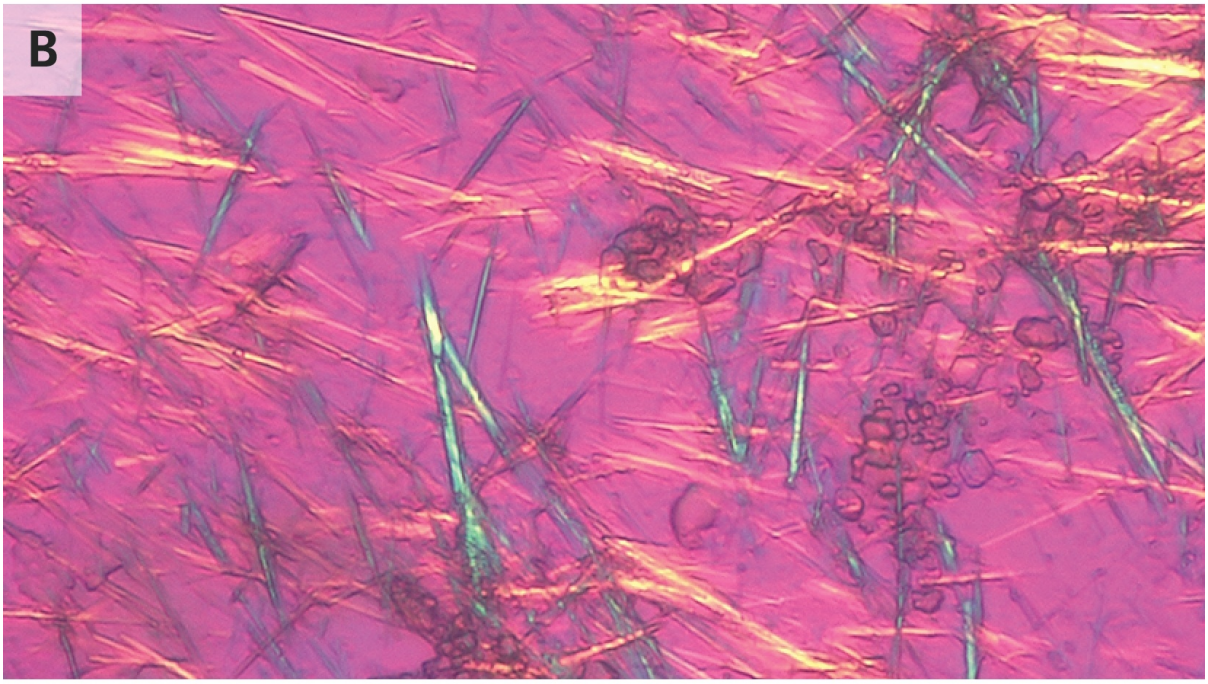
This presentation — acute onset of excruciating pain, swelling, and erythema of the **first metatarsophalangeal joint** (podagra) in an obese male with diabetes and chronic kidney disease — is classic for **gout**, which is caused by the deposition of **monosodium urate (MSU) crystals** in and around joints.[1][2]

Why gout is the most likely diagnosis:

- The first metatarsophalangeal joint is the most commonly affected site in gout, and rapid onset of monoarticular inflammation reaching peak intensity within 24 hours is characteristic.[1]
- Obesity, male sex, diabetes mellitus, and chronic kidney disease are all well-established risk factors for hyperuricemia and gout.[2][3][4]
- MSU crystals form when serum urate exceeds the solubility threshold (~6.8 mg/dL), triggering an intense innate immune response via NLRP3 inflammasome activation.[2][5]

The following figure from an NEJM review illustrates the clinical and diagnostic features of gout, including the classic podagra presentation and needle-shaped, negatively birefringent MSU crystals on polarized microscopy.


A


B

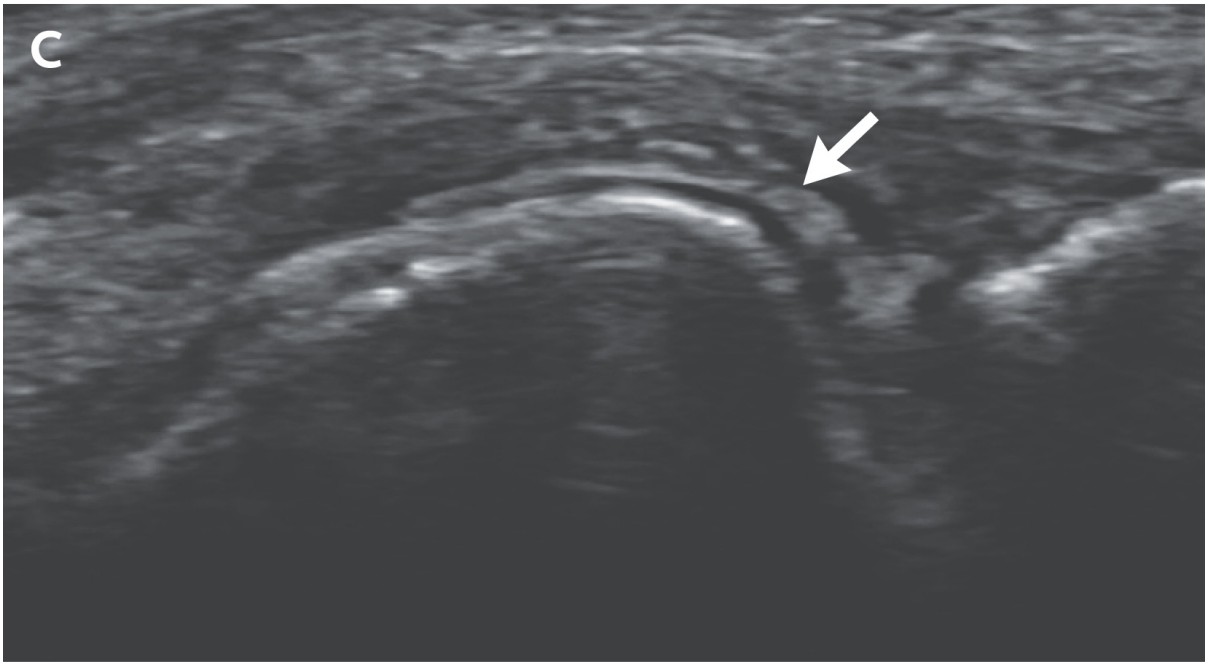

C

Figure 1. Clinical Findings in Gout.

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Why the other options are incorrect:

- **A. Calcium phosphate** — Basic calcium phosphate crystal deposition causes calcific periarthritis, most commonly affecting the shoulder, not the first toe.[2]
- **B. Calcium oxalate** — Calcium oxalate crystals are associated with nephrolithiasis and rarely with arthropathy (primarily in patients on dialysis or with primary hyperoxaluria), not with classic podagra.
- **D. Copper** — Copper deposition occurs in Wilson disease, which manifests with hepatic and neuropsychiatric disease, not acute monoarticular arthritis of the great toe.

Would you like to explore the recommended approach to acute gout flare management in patients with concurrent CKD, where NSAID and colchicine use may be limited?

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Question 1119

An obese 42-year-old female presents to her primary care physician with a complaint of left knee pain for the past 3 months. She describes the pain as affecting the inside part of the knee as well as the front of her knee, below the kneecap. She denies any inciting injury or trauma to the knee but reports that the pain is worse when she is climbing up stairs or rising from a chair. Physical examination is significant for localized tenderness to palpation over the left anteromedial proximal tibia, 6 cm inferior to the joint line. There is no joint effusion noted. Valgus stress testing is negative for any pain or instability of the knee joint. Radiographs of the left knee are obtained and reveal only mild arthritis, without evidence of any fractures or bony lesions. Which of the following is the most likely diagnosis in this patient?

Answer Choices:

(A) Stress fracture of proximal tibia
(B) Medial meniscus tear
(C) Medical collateral ligament (MCL) sprain
(D) Pes anserine bursitis

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/492b8824-c929-4af1-82a6-b43110301b9e

OpenEvidence Explanation

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The correct answer is **D. Pes anserine bursitis**.

The clinical presentation is classic for **pes anserine bursitis**: an obese female with localized tenderness over the **anteromedial proximal tibia, approximately 6 cm below the joint line**, pain worsened by stair climbing and rising from a chair, no history of trauma, and no joint effusion. The pes anserine bursa is located at the insertion of the sartorius, gracilis, and semitendinosus tendons on the medial proximal tibia, approximately 2 cm distal to the tibial plateau.[1] Pes anserine bursitis is an extra-articular condition and characteristically **does not cause joint effusions**; it is identified by local tenderness at the insertion site.[2]

Why the other options are less likely:

- **A. Stress fracture of proximal tibia** — Radiographs showed no fractures or bony lesions, and there is no history of repetitive high-impact activity or trauma to suggest a stress injury.
- **B. Medial meniscus tear** — Meniscal tears typically present with joint line tenderness (83% sensitivity, 83% specificity), not tenderness 6 cm below the joint line. Additionally, meniscal tears often follow a twisting injury and may present with mechanical symptoms (locking, catching) and effusion.[3]
- **C. MCL sprain** — Valgus stress testing was negative for pain or instability, effectively ruling out an MCL injury. MCL sprains also typically follow a traumatic mechanism.

Obesity is a well-recognized risk factor for pes anserine bursitis, and the condition is more common in **female patients**.[4][5] Notably, pes anserine bursitis can clinically mimic internal derangement of the knee, particularly medial meniscal tears, and accurate diagnosis can prevent unnecessary arthroscopy.[6][7]

Would you like to explore the evidence-based treatment options for pes anserine bursitis, including the role of corticosteroid injection versus conservative management?

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Question 1120

A 24-year-old woman comes to the physician's office with concerns about a recent pregnancy. She and her boyfriend had intercourse for the first time a few weeks ago. Two weeks ago she missed her menstrual period. She took several over the counter pregnancy tests that confirmed her pregnancy. She is tearful about the pregnancy and is very concerned. After extensive conversations with her physician and counseling, she decides she wants to medically abort her 6-week pregnancy. Which of the following drugs should be administered to this patient for this purpose?

Answer Choices:

(A) Tamoxifen
(B) Terbutaline
(C) Mifepristone
(D) Copper intrauterine device

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/04e9329e-3020-409d-9f3f-5be41b84b7fe

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OpenEvidence Explanation

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The correct answer is **C. Mifepristone**.

Mifepristone is the drug used to initiate medical abortion of an early intrauterine pregnancy. It is a selective progesterone receptor modulator that acts as an antiprogestin — binding the progesterone receptor with greater affinity than progesterone itself but without activating it. Its actions include decidual necrosis, cervical softening, and increased uterine contractility and prostaglandin sensitivity.[1] The FDA-approved regimen for medication abortion through 70 days of gestation is **200 mg oral mifepristone on Day 1**, followed 24–48 hours later by **800 mcg buccal misoprostol**.[1][2]

Combined mifepristone–misoprostol regimens achieve complete abortion rates of **95–97%**, with major complications occurring in fewer than 0.5% of cases.[1][3]

Why the other options are incorrect:

- **A. Tamoxifen** — A selective estrogen receptor modulator (SERM) used in breast cancer treatment. While it has been studied in combination with misoprostol as an alternative regimen, no definitive conclusions support its use, and it is not a standard or recommended agent for medical abortion.[4]
- **B. Terbutaline** — A beta-2 adrenergic agonist used as a tocolytic to suppress uterine contractions (i.e., to prevent preterm labor), which is the opposite of the desired effect here.
- **D. Copper intrauterine device** — Used as emergency contraception when placed within 5 days of unprotected intercourse. It is not effective once pregnancy is established and has no role in pregnancy termination.

Would you like to explore the specific contraindications and counseling considerations for medication abortion with mifepristone?

References

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Question 1121

A 25-year-old woman comes to the physician because of periodic painful double vision for 3 days. Her symptoms occur only when looking sideways. She has myopia and has been wearing corrective lenses for 10 years. Ten days ago, she lost her balance and fell off her bike, for which she went to a hospital. A CT scan of the head at that time showed no abnormalities and she was released without further treatment. Her only medication is an oral contraceptive. Her vital signs are within normal limits. The pupils are equal and reactive to light. Her best corrected visual acuity is 20/40 in each eye. She has an adduction deficit in the right eye and nystagmus in the left eye when looking left; she has an adduction deficit in the left eye and nystagmus in the right eye when looking right. Fundoscopy reveals bilateral disc hyperemia. Which of the following is the most likely cause of this patient's findings?

Answer Choices:

(A) Demyelination of the medial longitudinal fasciculus
(B) Compressive tumor of the pons
(C) Oxidative damage due to thiamine deficiency
(D) Infarction of the brainstem

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/5fd4e4a0-e26f-4cc1-a2f3-6c663bb747f7

OpenEvidence Explanation

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The correct answer is **A. Demyelination of the medial longitudinal fasciculus**.

This patient presents with classic **bilateral internuclear ophthalmoplegia (INO)** — bilateral adduction deficits with contralateral abducting nystagmus on lateral gaze in each direction. INO results from a lesion of the **medial longitudinal fasciculus (MLF)**, which connects the abducens nucleus on one side with the contralateral oculomotor nucleus to coordinate conjugate horizontal gaze.[1][2]

Why demyelination is most likely:

- In a **25-year-old woman**, the most common cause of INO is **demyelinating disease (multiple sclerosis)**, whereas in older patients, ischemic stroke predominates. In one large series of 410 INO cases, MS accounted for 34% and infarction for 38%, but bilateral INO was far more common in MS (73% bilateral) compared to infarction (87% unilateral).[1][3][4]
- The **bilateral disc hyperemia** (early papillitis/optic disc edema) is consistent with concurrent optic neuritis, a hallmark of MS that demonstrates dissemination in space.[5][6]
- The subacute onset over days, young age, and female sex are all classic for a first demyelinating event (clinically isolated syndrome).[6]
- The prior bike fall likely represented an early manifestation of neurological dysfunction (balance impairment) rather than a traumatic cause — the normal head CT at that time argues against traumatic INO.[7]

Why the other options are less likely:

- **B. Compressive tumor of the pons** — Tumors can cause INO but would typically present with additional brainstem signs and a more progressive course, not an acute/subacute presentation in a young woman.[4][7]
- **C. Oxidative damage due to thiamine deficiency (Wernicke encephalopathy)** — This requires risk factors such as alcoholism or

malnutrition and classically presents with the triad of ophthalmoplegia, ataxia, and confusion, none of which fit this otherwise healthy patient.[8]

- **D. Infarction of the brainstem** — Brainstem stroke is exceedingly rare in a 25-year-old and typically causes unilateral INO with acute onset and additional neurological deficits.[1][4]

Would you like to explore the diagnostic workup for a first demyelinating event, including MRI criteria and cerebrospinal fluid analysis for confirming multiple sclerosis?

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Question 1122

A 63-year-old man presents to the clinic for left calf pain when walking a distance of more than 200 m. He has had this pain for more than 8 months now, and he rates it as 7 out of 10. The pain subsides with rest. The patient has had a history of diabetes mellitus for the past 2 years which is well controlled. A percutaneous coronary intervention was performed in 2014. His current medications are insulin and aspirin. Family history is significant for coronary artery disease. He has an 80 pack-year history of smoking and currently smokes. He consumes 4 drinks per day of alcohol. On physical examination, his blood pressure is 144/89 mm Hg, the heart rate is 80/min and regular, the breathing rate is 25/min, and the pulse oximetry is 96%. Normal cardiac and lung sounds were heard on auscultation. Which of the following is the appropriate treatment to improve the patient's symptoms?

Answer Choices:

(A) Cilostazol
(B) Femoral embolectomy
(C) Femoral-to-popliteal bypass graft
(D) Interventional endovascular treatment

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/f2d137f0-9df4-42d9-84e6-28af02ccf650

OpenEvidence Explanation

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The answer is **A. Cilostazol**. This patient presents with classic **intermittent claudication** — exertional calf pain that occurs with walking and resolves with rest — consistent with chronic symptomatic peripheral artery disease (PAD). The appropriate initial pharmacologic treatment to improve symptoms is **cilostazol**, a phosphodiesterase III inhibitor.

Why cilostazol is correct:

The 2024 ACC/AHA PAD Guidelines give cilostazol a **Class I, Level of Evidence A** recommendation for patients with claudication to improve leg symptoms and increase walking distance.[1][2] A meta-analysis of 8 trials (2,247 patients) demonstrated cilostazol improved maximum treadmill walking distance by approximately 43 meters compared with placebo.[3] It is initiated at 50 mg twice daily and increased to 100 mg twice daily if tolerated. Notably, cilostazol is **contraindicated in heart failure** of any severity, which this patient does not have.[2]

Why the other options are incorrect:

- **B. Femoral embolectomy** — This is indicated for acute arterial occlusion (e.g., sudden onset of limb ischemia with the "6 Ps"), not chronic claudication with an 8-month history.
- **C. Femoral-to-popliteal bypass graft** — Surgical revascularization is reserved for patients with functionally limiting claudication who have had an **inadequate response to guideline-directed medical therapy** (GDMT), including structured exercise and pharmacotherapy. This patient has not yet received any medical therapy for claudication.[2]
- **D. Interventional endovascular treatment** — Similarly, endovascular revascularization is recommended only after an inadequate response to GDMT including structured exercise. It is not a first-line treatment.[2]

The stepwise approach per guidelines is: risk factor modification (smoking cessation, statin therapy, blood pressure control, diabetes management) → supervised exercise therapy → cilostazol → revascularization if symptoms persist despite adequate medical therapy.[2][4]

The following figure from the 2024 ACC/AHA PAD Guidelines illustrates the comprehensive medical therapy framework for PAD, including the role of cilostazol in chronic symptomatic disease.

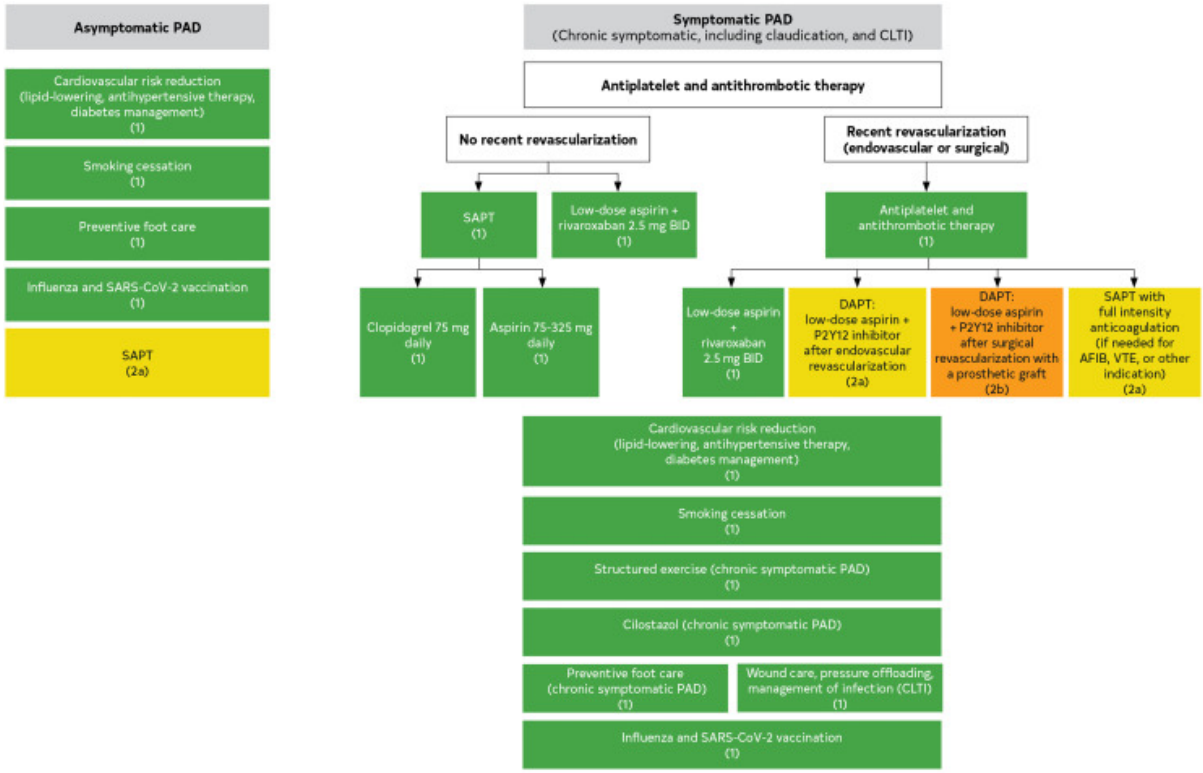


Figure 4. Medical Therapy and Foot Care for PAD

Would you like to explore the evidence comparing supervised exercise therapy versus endovascular revascularization for intermittent claudication outcomes?

References

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Question 1123

A 72-year-old woman comes to the physician because of a 1-month history of frequent headaches, double vision, fatigue, and myalgias. Physical examination shows pallor, tenderness to palpation over the temples, and inward deviation of the left eye. Laboratory studies show an erythrocyte sedimentation rate of 65 mm/h. Temporal artery biopsy shows transmural granulomatous inflammation and fragmentation of the internal elastic lamina. Treatment with high-dose intravenous corticosteroids is begun. The patient's condition puts her at greatest risk of developing which of the following complications?

Answer Choices:

(A) Pulmonary hypertension
(B) Lower extremity gangrene
(C) Palpable purpura
(D) Thoracic aortic aneurysm

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/61c7a712-2b31-4f2f-a061-16214e45b3d8

OpenEvidence Explanation

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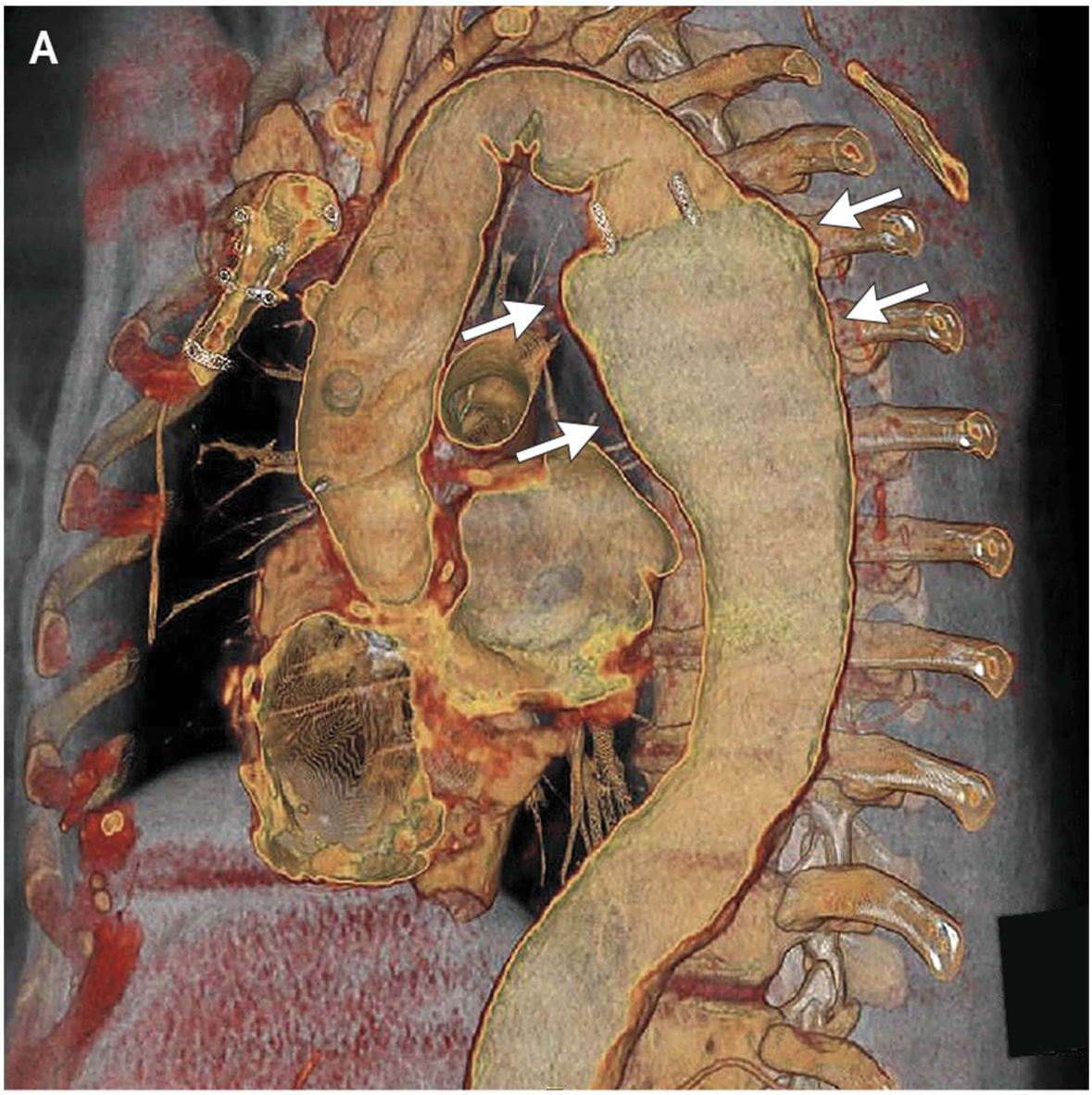
The answer is **D. Thoracic aortic aneurysm**. Giant cell arteritis (GCA) is a large-vessel vasculitis with a well-established predilection for the aorta, and **thoracic aortic aneurysm** is the most important long-term vascular complication of this disease.

This patient's presentation — new-onset headaches, diplopia (cranial nerve VI palsy causing inward deviation of the left eye), temporal tenderness, elevated ESR, and biopsy showing transmural granulomatous inflammation with internal elastic lamina fragmentation — is classic for GCA.

Why thoracic aortic aneurysm?

GCA preferentially affects the thoracic aorta and its branches. A large Danish population-based cohort study of 9,908 GCA patients found a **15-year relative risk of 11.2** (95% CI 7.41–16.9) for thoracic aortic aneurysm compared to the general population, with a median time to development of 7.5 years.[1] A separate study of over 7,000 patients with biopsy-proven GCA demonstrated a significantly higher 5-year risk of thoracic aortic aneurysm (2.23% vs 1.02%; aHR 2.01).[2] The 2022 ACC/AHA Guideline for Aortic Disease lists aortic aneurysms, dissection, and rupture among the potential complications of GCA.[3] Current recommendations emphasize that patients require **long-term monitoring for aortic aneurysms** even after therapy is discontinued.[4]

The following figure demonstrates the spectrum of large-vessel involvement in GCA, including thoracic aortic aneurysm and arterial stenosis.


A

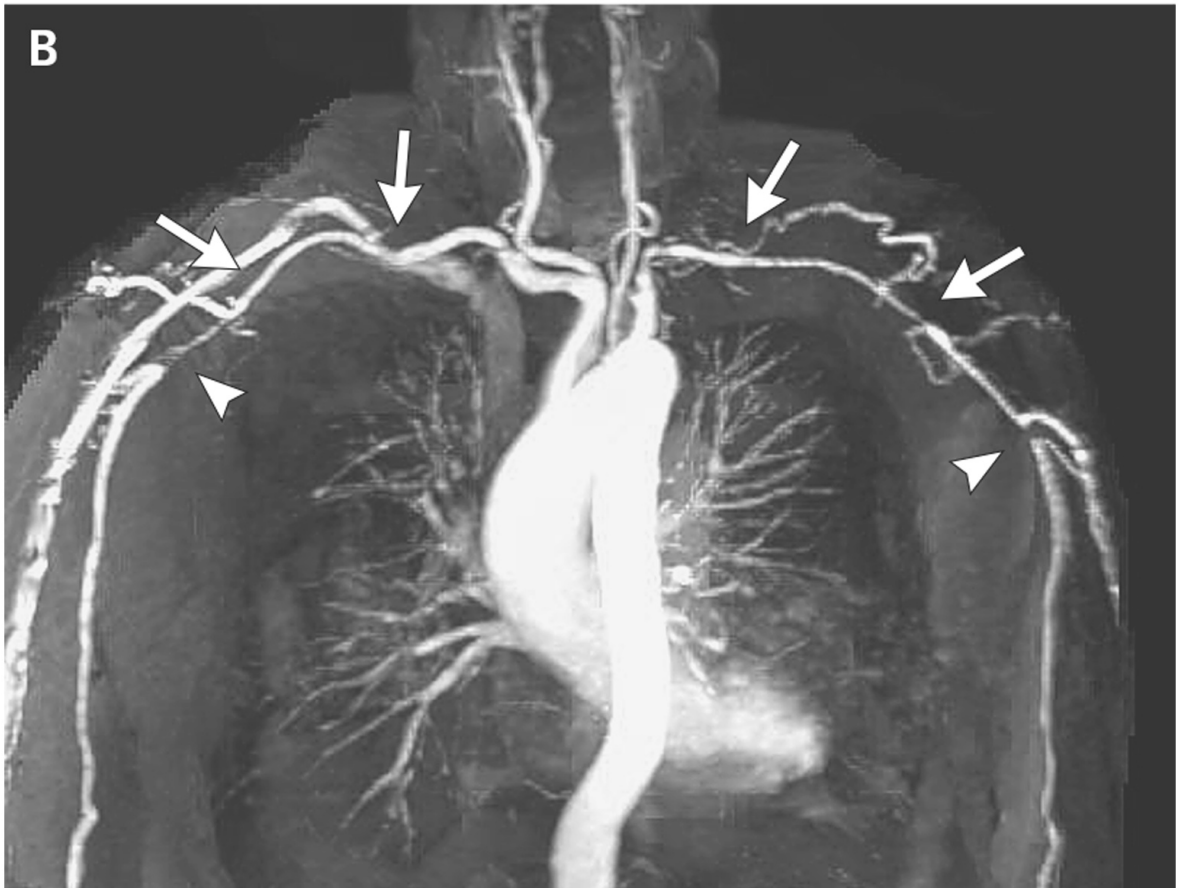

B

Figure 1. CTA and MRA of the Aortic Arch in Two Patients with Giant-Cell Arteritis.

Used under license from The New England Journal of Medicine.

Why not the other options?

- **Pulmonary hypertension** (A) — not a recognized complication of GCA.
- **Lower extremity gangrene** (B) — while limb claudication can occur, gangrene is not a characteristic complication; GCA predominantly affects the upper extremity vasculature (subclavian/axillary arteries).[6]
- **Palpable purpura** (C) — a feature of small-vessel vasculitides (e.g., IgA vasculitis, ANCA-associated vasculitis), not large-vessel vasculitis like GCA.

Would you like to explore the recommended screening intervals and imaging modalities for monitoring aortic aneurysm development in patients with GCA?

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Question 1128

A 74-year-old man was admitted to the intensive care ward due to progressive dyspnea, cough with pink sputum, and diaphoresis. He had 2 myocardial infarctions at the age of 66 and 69 years and suffers from chronic heart failure. At the time of presentation, his vital signs are as follows: blood pressure 90/50 mm Hg, heart rate 108/min, respiratory rate 29/min, and temperature 35.5°C (95.9°F). On physical examination, the patient sits upright. He is lethargic and cyanotic. Lung auscultation reveals widespread bilateral fine rales. Cardiac examination is significant for S3, accentuation of the pulmonic component of S2, and a systolic murmur heard best at the apex of the heart. Soon after hospitalization, the patient develops ventricular fibrillation and dies despite adequate resuscitation measures. Which microscopic finding would you expect to see in this patient on autopsy?

Answer Choices:

(A) Brownish inclusions in the pulmonary macrophages on H&E staining
(B) Positive Prussian-blue staining of the kidney tissue
(C) Ground-glass hepatocytes
(D) Positive Congo-red staining of the cardiac tissue

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/cdf8d63f-068b-4d0b-b19e-a9be7001d64e

OpenEvidence Explanation

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The correct answer is **A. Brownish inclusions in the pulmonary macrophages on H&E staining**.

This patient presents with decompensated chronic heart failure (history of two MIs, chronic HF, hypotension, tachycardia, pink frothy sputum, bilateral rales, S3 gallop, and mitral regurgitation murmur) culminating in cardiogenic shock and fatal ventricular fibrillation. The expected autopsy finding is **hemosiderin-laden macrophages** in the lungs, classically known as "**heart failure cells.**"

Pathophysiology: In chronic left-sided heart failure, elevated left atrial and pulmonary venous pressures cause chronic passive congestion of the lungs. This leads to stress failure of alveolar capillaries with microhemorrhages into the alveolar spaces.[1][2] Alveolar macrophages phagocytize the extravasated red blood cells and degrade hemoglobin, accumulating **hemosiderin** — an iron-storage pigment that appears as **golden-brown granular inclusions on H&E staining**.[1][3] These hemosiderin-laden macrophages (siderophages) are a hallmark histopathologic finding of chronic pulmonary congestion due to heart failure.[1][4]

The following figure demonstrates hemosiderin-laden macrophages in the lung, showing the characteristic golden-brown pigment on H&E (Panel A) and confirmation with iron staining (Panel B):

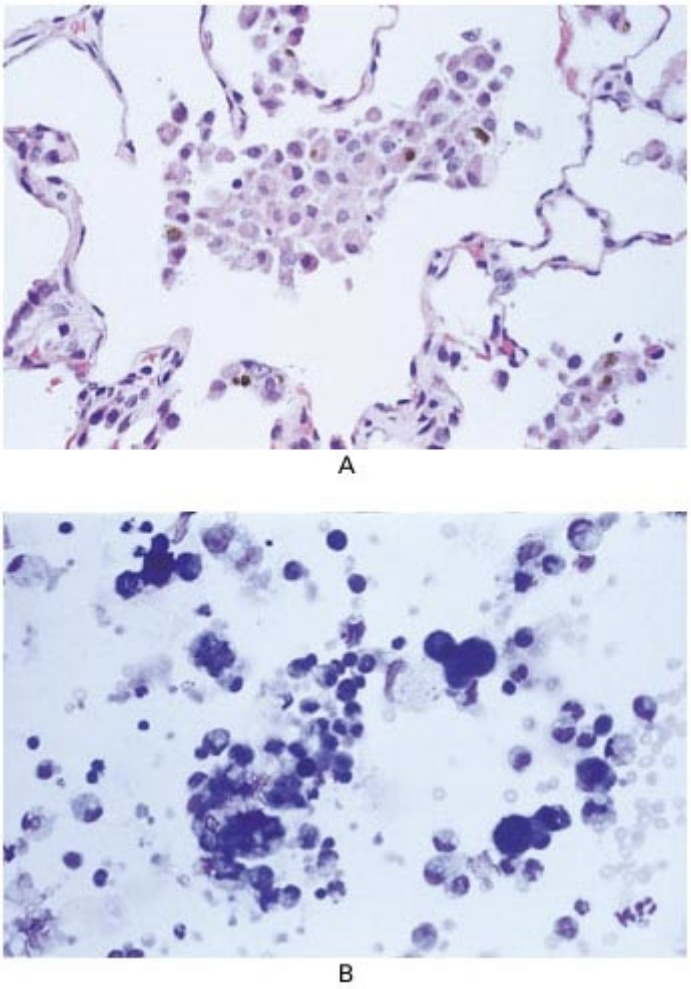


Figure 1.

Used under license from The New England Journal of Medicine.

Why the other options are incorrect:

- **B. Positive Prussian-blue staining of kidney tissue** — Prussian blue stains iron (hemosiderin), but renal hemosiderosis is associated with chronic intravascular hemolysis (e.g., paroxysmal nocturnal hemoglobinuria, mechanical heart valves), not heart failure per se.
- **C. Ground-glass hepatocytes** — This finding is characteristic of hepatitis B virus infection (reflecting accumulation of HBsAg in the endoplasmic reticulum), unrelated to this clinical scenario.
- **D. Positive Congo-red staining of cardiac tissue** — Congo red staining with apple-green birefringence under polarized light indicates amyloid deposition, seen in cardiac amyloidosis. While amyloidosis can cause heart

failure, this patient's history of two prior MIs provides a clear ischemic etiology for his cardiomyopathy.

Would you like to explore the distinction between acute versus chronic pulmonary congestion findings at autopsy and how they correlate with different stages of heart failure?

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Question 1130

A 35-year-old woman comes to the physician because of intermittent episodes of heart palpitations for 3 weeks. The palpitations are accompanied by chest pain that is sharp and localized to the left 3rd intercostal space. The patient does not smoke. She drinks one to two glasses of wine on the weekends. She appears nervous. Her pulse is 110/min and irregularly irregular, and blood pressure is 135/85 mmHg. Examination shows a fine tremor on both hands and digital swelling. There is retraction of the left upper eyelid. A systolic ejection murmur is heard along the right upper sternal border. The extremities are warm, and pulses are 2+ bilaterally. Which of the following is the most appropriate pharmacotherapy?

Answer Choices:

(A) Propranolol
(B) Digoxin
(C) Amiodarone
(D) Warfarin

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/721ce21a-4891-477f-af50-b0be1844ff6c

OpenEvidence Explanation

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The correct answer is **A. Propranolol**.

This patient presents with classic features of **hyperthyroidism** (likely Graves disease) — fine tremor, digital swelling, lid retraction, nervousness, warm extremities, and tachycardia — complicated by **atrial fibrillation** (irregularly irregular pulse at 110/min). The systolic ejection murmur along the right upper sternal border reflects the hyperdynamic circulatory state of thyrotoxicosis.

Beta blockers are the recommended first-line pharmacotherapy for rate control and symptom relief in AF complicating thyrotoxicosis (Class I recommendation, AHA/ACC/HRS guidelines).[1][2] Among beta blockers, **propranolol** is particularly advantageous because, as a nonselective beta blocker, it addresses the hyperadrenergic symptoms more broadly and additionally **reduces peripheral conversion of T4 to T3**.[2][3]

Why not the other options?

- **Digoxin (B):** Not first-line for rate control in thyrotoxicosis. Hyperthyroidism increases digoxin clearance, making it less effective, and it does not address the hyperadrenergic symptoms.
- **Amiodarone (C):** Antiarrhythmic drugs are generally unsuccessful while the thyrotoxic state persists, and amiodarone itself can worsen thyroid dysfunction (both thyrotoxicosis and hypothyroidism).[1][4]
- **Warfarin (D):** Anticoagulation is guided by CHA_2DS_2-VASc score. This 35-year-old woman with a CHA_2DS_2-VASc score of 1 (sex category only) does not meet the threshold for anticoagulation based on current guidelines. Regardless, anticoagulation does not address the acute symptoms of tachycardia and palpitations, making it not the most appropriate initial pharmacotherapy.[5][6]

Restoration of sinus rhythm is unlikely until a euthyroid state is achieved; spontaneous reversion typically occurs within 1–3 weeks after thyroid hormone levels normalize.[2][6]

Would you like to explore the comparative efficacy of different beta blockers (propranolol vs. atenolol vs. metoprolol) in managing thyrotoxicosis-related atrial fibrillation?

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Question 1132

A 68-year-old woman presents with an intermittent throbbing headache with an onset approximately 3 weeks ago. The pain is bilateral, “band-like,” and extends to the neck. The patient rates the 4 points out of 10 on a visual scale. The headache is not accompanied by nausea, vomiting, photophobia, or phonophobia, and is not aggravated by movements, but gets worse when the patient coughs or laughs. The headache has persisted throughout the day and is usually worse in the morning an hour after she has breakfast and taken her medications. The patient was diagnosed with stage 1 arterial hypertension 2 years ago and stable angina pectoris 3 weeks ago. Currently, she takes aspirin (81 mg once daily), rosuvastatin (10 mg once daily), lisinopril (20 mg once daily), and isosorbide mononitrate (60 mg once daily). She has been menopausal for the last 15 years. In addition to her chief complaint, she also notes that she had a runny nose with a temperature elevation approximately 3 weeks ago, and her headache was linked to that acute illness. The vital signs are as follows: blood pressure 135/80 mm Hg, heart rate 76/min, respiratory rate 14/min, and temperature 36.5°C (97.7°F). The physical examination reveals S2 accentuation that is best heard in the second intercostal space at the right sternal border. Palpation of the paranasal sinuses is painless. The neurologic exam shows no focal symptoms, no pain on palpation of the trigeminal points, and no meningeal symptoms. What is the most likely mechanism underlying the patient’s headaches?

Answer Choices:

(A) Meningeal irritation by blood products originating from a chronic subdural hematoma
(B) Dissection of an intracerebral vessel
(C) Meningeal irritation by a growing intracranial neoplasm
(D) Dilation of the intracerebral arterioles

Correct Answer:

(D)

> **OpenEvidence Response:**
>
> **(D)** ✓

OpenEvidence Link: https://openevidence.com/ask/ff603600-4a74-4317-bddc-68515c491525

OpenEvidence Explanation

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The correct answer is **D. Dilation of the intracerebral arterioles**.

This patient's headache is best explained by a side effect of **isosorbide mononitrate**, which she started approximately 3 weeks ago when diagnosed with stable angina pectoris — the same time her headache began. The mechanism is **vasodilation of intracerebral arteries** mediated by nitric oxide (NO) release.

Key clinical clues pointing to nitrate-induced headache:

- **Temporal correlation**: The headache onset coincides with the initiation of isosorbide mononitrate 3 weeks ago for newly diagnosed stable angina.[1]
- **Timing within the day**: The headache is worst in the morning, approximately an hour after she takes her medications (including isosorbide mononitrate), consistent with peak drug effect.[1]
- **Headache characteristics**: Bilateral, throbbing, band-like quality without nausea, vomiting, photophobia, or phonophobia — consistent with the "immediate" type of nitrate-induced headache, which is typically mild-to-moderate and non-migrainous.[2]
- **Dose-related effect**: At 60 mg once daily, headache occurs in approximately 51% of patients in clinical trials, making it the most common adverse effect.[1]

Mechanism: Isosorbide mononitrate is an NO donor that activates the NO-cGMP pathway in vascular smooth muscle, causing **dilation of intracranial arteries and arterioles**. This vasodilation stimulates and sensitizes perivascular meningeal nociceptors innervated by trigeminal afferents, producing headache.[2][3][4] The worsening with coughing and laughing (Valsalva-like maneuvers) is consistent with transient increases in intracranial pressure further stimulating already-sensitized meningeal afferents.[5]

Why the other options are less likely:

- **A (Chronic subdural hematoma)**: While aspirin use is a risk factor, there is no history of trauma, no focal neurological deficits, and the headache pattern correlates with medication timing rather than a progressive mass lesion.
- **B (Intracerebral vessel dissection)**: Typically presents with sudden, severe unilateral headache/neck pain, often with focal neurological signs — none of which are present here.
- **C (Intracranial neoplasm)**: Although the headache worsens with Valsalva maneuvers, the absence of focal neurological deficits, the clear temporal relationship to medication initiation, and the morning post-medication worsening pattern strongly favor a drug-related etiology over neoplasm.[6][7]

The FDA label for isosorbide mononitrate explicitly notes that headaches are "a marker of the activity of the drug" and recommends that patients not alter their dosing schedule to avoid headaches, as loss of headache may indicate loss of antianginal efficacy.[1]

Would you like to explore strategies for managing nitrate-induced headaches while maintaining antianginal efficacy?

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Question 1133

A 31-year-old male comes to your office for his annual exam. He states that he received all of his recommended vaccinations prior to beginning college, but has not had any vaccines in the past 13 years. His medical history is significant for intermittent, exercise-induced asthma. He has been sexually active in the past with multiple female partners. In addition to an influenza vaccine, which vaccine should be administered to this patient during this visit?

> **Answer Choices:**
>
> (A) Pneumococcal vaccine
> (B) Tetanus, diphtheria, and acellular pertussis booster (Tdap) vaccine
> (C) Haemophilus influenza B (HIB) vaccine
> (D) Human papillomavirus (HPV) vaccine

> **Correct Answer:**
>
> **(B)**
>
> **OpenEvidence Response:**
>
> **(B)** ✓

OpenEvidence Link: https://openevidence.com/ask/d1af0144-7cc9-4071-98ec-9048c1d87899

OpenEvidence Explanation

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The correct answer is **B. Tetanus, diphtheria, and acellular pertussis booster (Tdap) vaccine**.

This patient is 31 years old and last received vaccinations 13 years ago (at age 18, prior to college). The key vaccine considerations for each answer choice:

Tdap (Answer B): A **Td or Tdap booster is recommended every 10 years** for all adults.[1][2] Since this patient's last vaccinations were 13 years ago, he is overdue for a tetanus-containing booster. Additionally, per ACIP guidelines, adults aged ≥19 years who have never received Tdap should receive one dose of Tdap; if he received Tdap as an adolescent, he is still due for a decennial booster with either Td or Tdap.[2][3]

Why the other options are incorrect:

- **A. Pneumococcal vaccine:** Pneumococcal vaccination for adults aged 19–64 is only indicated for those with specific chronic medical conditions (e.g., chronic heart, lung, or liver disease, diabetes, immunocompromising conditions, asplenia) or for all adults ≥65 years. Exercise-induced asthma alone is not an indication for pneumococcal vaccination in this age group.[3]
- **C. HIB vaccine:** Haemophilus influenzae type B vaccine is not routinely recommended for immunocompetent adults. It is indicated only for specific high-risk populations such as those with functional or anatomic asplenia, sickle cell disease, or hematopoietic stem cell transplant recipients.
- **D. HPV vaccine:** HPV vaccination is routinely recommended through **age 26** for catch-up vaccination. At age 31, this patient falls into the 27–45 age range where HPV vaccination is only considered through **shared clinical decision-making**, not as a routine recommendation. While his history of multiple sexual partners could factor into a shared decision-making discussion, HPV vaccination would not be the standard recommendation at this visit — unlike the Tdap booster, which is clearly overdue.[4][5]

The Tdap booster is the most clearly indicated vaccine for this patient, as it is a universally recommended, time-based vaccination that is overdue by approximately 3 years.

Would you like to explore the current ACIP recommendations for pneumococcal vaccination indications in patients with asthma, including which severity thresholds qualify?

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Question 1134

A 24-year-old woman presents to the emergency department with a 2-week history of a foot ulcer. She says that she punctured her foot with a rusty nail while she was playing tennis and that the puncture wound has since progressed to a non-healing ulcer. Over the last 2 days, she has also been experiencing a fever and drainage from the wound. On presentation, she is found to have a slightly fruity smelling red ulcer with purulent drainage. Probing the ulcer goes all the way down to bone. Which of the following characteristics is true of the most likely cause of this patient's symptoms?

Answer Choices:

(A) Gram-negative bacilli
(B) Gram-negative diplococci
(C) Gram-positive cocci in chains
(D) Gram-positive cocci in clusters

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/e670a330-d277-4627-996b-8903638dcd83

OpenEvidence Explanation

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The answer is **A. Gram-negative bacilli**.

This clinical scenario describes a young, non-diabetic patient who sustained a **puncture wound through a sneaker (tennis shoe) while playing tennis**, which progressed to a non-healing ulcer with fever, purulent drainage, a fruity odor, and a positive **probe-to-bone test** — all classic for **Pseudomonas aeruginosa osteomyelitis**.

Key clinical clues pointing to Pseudomonas:

- **Puncture wound through a sneaker** — *P. aeruginosa* colonizes the foam insole of athletic shoes, and puncture wounds through sweat-saturated sneakers are classically associated with Pseudomonas osteochondritis/osteomyelitis. The IDSA guidelines specifically note that "*P. aeruginosa* is the most common bacterial cause of calcaneal osteomyelitis in individuals who develop this infection after stepping on nails while wearing sneakers". [1][2]
- **Fruity odor** — Pseudomonas produces a characteristic grape-like or fruity smell due to the production of 2-aminoacetophenone.
- **Positive probe-to-bone test** — indicates osteomyelitis, which is the expected deep complication in this setting.[2]
- **Non-diabetic patient** — In non-diabetic patients with puncture wound infections, Pseudomonas is the most common pathogen causing both soft tissue infections and osteomyelitis.[3][4]

Pseudomonas aeruginosa is a **gram-negative bacillus (rod)**, making option A correct. The other options describe organisms that do not fit this classic presentation: gram-negative diplococci (e.g., *Neisseria*), gram-positive cocci in chains (e.g., *Streptococcus*), and gram-positive cocci in clusters (e.g., *Staphylococcus*).

Would you like to explore the recommended antibiotic regimens and surgical management approach for Pseudomonas osteomyelitis following puncture wounds?

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Question 1135

A 23-year-old man comes to the physician because of a 1-week history of anorexia, nausea, upper abdominal pain, and dark-colored urine. He recently returned from a trip to Belize. His temperature is 38.3°C (100.9°F). Physical examination shows scleral icterus and tender hepatomegaly. Serum studies show markedly elevated transaminases and anti-hepatitis A virus antibodies. In this patient, infected cells express more MHC class I molecules on their surfaces. This cellular event is primarily induced by a molecule that is also responsible for which of the following changes?

Answer Choices:

(A) Upregulated expression of exogenously synthesized antigens
(B) Enhanced macrophage phagocytic function
(C) Activation of eukaryotic initiation factor 2
(D) Increased breakdown of intracellular RNA

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/84d336a4-20e5-48c9-8241-ae3806b9b163

OpenEvidence Explanation

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The correct answer is **D. Increased breakdown of intracellular RNA**.

In this case of acute hepatitis A, the upregulation of **MHC class I molecules** on infected hepatocytes is primarily induced by **interferon-gamma (IFN-γ)**, which is secreted by activated T cells and NK cells during the immune response.[1][2][3] IFN-γ upregulates MHC class I expression through the JAK/STAT1 signaling pathway, inducing transcription factors such as IRF-1 and NLRC5 that drive MHC class I gene expression.[1][3]

Why IFN-γ leads to increased breakdown of intracellular RNA:

IFN-γ (along with other interferons) induces the expression of **2'-5' oligoadenylate synthetase (OAS)**, a key interferon-stimulated gene. When activated by double-stranded RNA (a viral replication intermediate), OAS synthesizes 2'-5' linked oligoadenylates (2-5A), which in turn activate the latent endoribonuclease **RNase L**. Activated RNase L cleaves both viral and cellular single-stranded RNA, leading to **increased degradation of intracellular RNA** and thereby inhibiting viral replication.[4][5][6][7]

Why the other options are incorrect:

- **A. Upregulated expression of exogenously synthesized antigens** — IFN-γ upregulates MHC class I presentation of endogenously synthesized (intracellular) antigens, not exogenous antigens. MHC class II presents exogenous antigens.
- **B. Enhanced macrophage phagocytic function** — While IFN-γ does activate macrophages, this is not the primary mechanism by which the same molecule upregulates MHC class I. The question asks about the molecule that induces MHC class I upregulation — interferons broadly — and their other antiviral effects, which center on the OAS/RNase L pathway.[8]
- **C. Activation of eukaryotic initiation factor 2 (eIF2)** — The interferon-induced PKR kinase actually **phosphorylates and inactivates** eIF2α, inhibiting translation initiation. It does not activate eIF2; rather, it blocks its function to shut down viral protein synthesis.[9][10][11]

The OAS/RNase L pathway represents one of the four major IFN-induced antiviral effector systems, alongside PKR, Mx GTPases, and ISG15.[7]

Would you like to explore the specific mechanisms by which cytotoxic T lymphocytes recognize and eliminate hepatitis A virus-infected hepatocytes through MHC class I-restricted killing?

Relevant images

(CONTENT OMITTED)

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Question 1137

A 32-year-old Caucasian woman is referred to a gastroenterologist by her family physician for 8 months of abdominal pain, foul-smelling diarrhea with floating, bulky stools, weight loss, and macrocytic anemia. Her personal history is relevant for allergic rhinitis. Physical examination shows grouped, erythematous papulovesicular lesions on her arms, torso, and abdomen. Which of the following is the most appropriate approach for the management of this patient?

> **Answer Choices:**
>
> (A) Amitriptyline
> (B) Octreotide
> (C) Gluten-free diet
> (D) Methysergide maleate

> **Correct Answer:**
>
> (C)
>
> **OpenEvidence Response:**
>
> (C) ✓

OpenEvidence Link: https://openevidence.com/ask/0995adb6-8b8f-413c-86b9-f0ed739e8f41

OpenEvidence Explanation

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The correct answer is **C. Gluten-free diet**.

This clinical presentation is classic for **celiac disease** with its cutaneous manifestation, **dermatitis herpetiformis (DH)**. The combination of chronic foul-smelling diarrhea with floating, bulky (steatorrheic) stools, weight loss, and macrocytic anemia reflects gluten-driven small bowel villous atrophy causing malabsorption of folate and/or vitamin B12.[1][2] The grouped erythematous papulovesicular lesions on the arms, torso, and abdomen are characteristic of DH, which is pathognomonic for underlying celiac disease.[3][4]

Why a gluten-free diet is the correct management:

A strict, lifelong gluten-free diet is the cornerstone treatment for both celiac disease and dermatitis herpetiformis. It resolves gastrointestinal symptoms (typically within days to weeks), heals small bowel villous atrophy, corrects malabsorption-related anemia, and clears the skin rash.[3][5][6] Approximately 81–89% of anemic celiac patients normalize hemoglobin within 1–2 years on a gluten-free diet.[1] Dapsone may be added initially for rapid control of the skin lesions, but the gluten-free diet remains the definitive therapy.[3][7]

Why the other options are incorrect:

- **A. Amitriptyline** – Used for functional GI disorders (e.g., irritable bowel syndrome) as a visceral pain modulator; it does not address the underlying autoimmune/malabsorptive process.
- **B. Octreotide** – A somatostatin analog used for secretory diarrhea (e.g., carcinoid syndrome, VIPomas); not indicated for celiac disease.
- **D. Methysergide maleate** – A serotonin antagonist historically used for carcinoid syndrome or migraine prophylaxis; not relevant here.

Would you like to explore the diagnostic workup for celiac disease, including the role of serologic testing (anti-tTG, anti-endomysial antibodies) and small bowel biopsy in confirming the diagnosis?

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Question 1138

A 62-year-old woman with small-cell lung cancer comes to the physician because of a painful, burning red rash on her face and hands that developed 30 minutes after going outside to do garden work. She wore a long-sleeved shirt and was exposed to direct sunlight for about 10 minutes. The patient is light-skinned and has a history of occasional sunburns when she does not apply sunscreen. Current medications include demeclocycline for malignancy-associated hyponatremia and amoxicillin for sinusitis. Physical examination shows prominent erythema and a papular eruption on her forehead, cheeks, neck, and the dorsum of both hands. Which of the following is the most likely cause of this patient's symptoms?

Answer Choices:

(A) Degranulation of presensitized mast cells
(B) Formation of drug-induced autoantibodies
(C) Accumulation of porphobilinogen
(D) Cell injury due to drug metabolites

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/04f7e365-a95d-4bfc-800b-7a6015bd30d2

OpenEvidence Explanation

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The correct answer is **D. Cell injury due to drug metabolites**.

This patient is experiencing a **phototoxic reaction caused by demeclocycline**, a tetracycline antibiotic well known for its photosensitizing properties. The clinical presentation — acute onset of erythema and papular eruption confined to sun-exposed areas (face, neck, dorsal hands) after brief sunlight exposure, with covered areas spared — is classic for drug-induced phototoxicity.

Mechanism of phototoxicity: Demeclocycline (and other tetracyclines) absorb UV-A radiation, which activates the drug or its metabolites to an excited state. This generates **reactive oxygen species (ROS)** and free radicals that cause direct cellular damage to keratinocytes, cell membranes, and DNA.[1][2][3] The FDA label for demeclocycline specifically warns that phototoxic reactions "are characterized by severe burns of exposed surfaces resulting from direct exposure of patients to sunlight".[4] The reaction is dose-dependent and does not require prior sensitization, distinguishing it from immune-mediated mechanisms.[3][5]

Why the other options are incorrect:

- **A. Degranulation of presensitized mast cells** — This describes a type I (IgE-mediated) hypersensitivity reaction such as urticaria or anaphylaxis. Phototoxicity is not mast cell–mediated.
- **B. Formation of drug-induced autoantibodies** — This would describe drug-induced lupus or a photoallergic reaction (type IV hypersensitivity). Photoallergy requires prior sensitization, presents as eczematous dermatitis (not exaggerated sunburn), and typically appears 24–72 hours after exposure. This patient's rapid onset and sunburn-like morphology are inconsistent with photoallergy.[5]
- **C. Accumulation of porphobilinogen** — This would suggest porphyria. While tetracyclines can rarely cause pseudoporphyria, the clinical scenario is most consistent with straightforward phototoxicity from demeclocycline, which is among the most phototoxic tetracyclines.[6][7]

The key risk factors here include the patient's light skin (Fitzpatrick type 1–2), which increases susceptibility to tetracycline phototoxicity, and the use of demeclocycline specifically, which carries a higher phototoxicity risk than other tetracyclines.[1][4][6]

Would you like to explore the management of SIADH in small-cell lung cancer, including alternatives to demeclocycline such as tolvaptan?

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Question 1141

A 35-year-old woman comes to the physician for sleeping problems and the inability to concentrate for 3 months. She says she is worried because she and her husband have been trying to conceive for more than a year with no success. Conception by in vitro fertilization was attempted once 3 months ago but was unsuccessful. Analysis of her husband's semen has shown normal sperm counts and morphology. She has a 6-year-old daughter who was born at term after an uncomplicated pregnancy. She has no history of severe illness and tries to stay healthy by going to the gym an hour per day. Her menses occur at regular 28-day intervals and last 5 to 6 days; her last menstrual period started 2 days ago. Physical examination shows no abnormalities. Which of the following is the most likely cause of this patient's inability to conceive?

Answer Choices:

(A) Pelvic inflammatory disease
(B) Diminished ovarian reserve
(C) Hypogonadotropic hypogonadism
(D) Premature ovarian failure

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/276c30eb-ec81-4abe-9722-7763b56b31b5

OpenEvidence Explanation

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The most likely answer is **B. Diminished ovarian reserve**.

Key reasoning:

This 35-year-old woman presents with secondary infertility (>12 months of failed conception), a failed IVF attempt, normal partner semen analysis, regular 28-day menstrual cycles, and a prior uncomplicated pregnancy. The critical distinction among the answer choices lies in her preserved menstrual regularity:

- **Diminished ovarian reserve (DOR)** is defined as a condition in women of reproductive age who have **regular menses** but whose response to ovarian stimulation is reduced compared to age-matched peers. Women with DOR typically continue to menstruate regularly, rarely exhibiting outward symptoms other than the inability to conceive. A failed IVF cycle is a classic presentation, as these women have an impaired response to ovarian hyperstimulation. Age 35 is the inflection point at which ovarian reserve decline accelerates, and female age is the single most important predictor of fecundity.[1][2][3][4][5]

- **Premature ovarian failure (POF/primary ovarian insufficiency)** is characterized by **amenorrhea or oligomenorrhea** with elevated FSH, representing overt loss of ovarian function before age 40. This patient's regular 28-day cycles argue strongly against POF.[6][7]

- **Hypogonadotropic hypogonadism** (functional hypothalamic amenorrhea) presents with **absent or irregular menses** due to suppressed GnRH/gonadotropin secretion, often from excessive exercise, low body weight, or eating disorders. While this patient exercises daily, her regular cycles and normal physical exam make this unlikely.[5]

- **Pelvic inflammatory disease** causing tubal factor infertility would not explain a failed IVF cycle, since IVF bypasses the fallopian tubes entirely.

The combination of age 35, secondary infertility, regular menses, and failed IVF is the hallmark presentation of diminished ovarian reserve.[1][2][8]

Would you like to explore the recommended ovarian reserve testing strategies (AMH, FSH, antral follicle count) and how they guide IVF treatment planning?

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Question 1142

A 25-year-old female is brought to the emergency department by her family. They found her somnolent next to her computer and scattered pill bottles over two hours ago. The family cannot recall the types of pill bottles that they found and did not bring them to the ED. The patient's past medical history is notable for anxiety, obesity, hypertension, and polycystic ovarian syndrome. She is currently not on any medications other than an exercise program with which she is non-compliant. A physical exam is performed and is within normal limits. The patient begins communicating with the physician and states that she did take acetaminophen but it was only a few pills. Her temperature is 99.5°F (37.5°C), pulse is 82/min, blood pressure is 125/85 mmHg, respirations are 11/min, and oxygen saturation is 97% on room air. Which of the following is the next best step in management?

Answer Choices:

(A) N-acetylcysteine
(B) Charcoal
(C) IV fluids
(D) Syrup of ipecac

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/f24d8d63-484e-47e3-883a-47a4428b5781

OpenEvidence Explanation

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The best answer is **A. N-acetylcysteine (NAC)**.

This scenario presents a suspected intentional overdose with an unreliable history — the patient was found somnolent next to scattered pill bottles over 2 hours ago, the family cannot identify the medications, and the patient minimizes the ingestion by claiming "only a few pills." Several key factors drive the decision:

Why NAC is the best next step:

- The ACG/AGA Acute Liver Failure Guidelines state that NAC should begin **as soon as toxicity is suspected, especially if the time of ingestion is unknown**, because there is proven benefit even with late administration. It is reasonable to proceed with treatment while awaiting diagnostic test results.[1]
- The patient's history is unreliable (found somnolent, scattered pill bottles, minimizing ingestion), and the exact timing and amount of acetaminophen ingested are uncertain. When the treating physician is not confident of the history of ingestion, treatment with NAC should be commenced.[2]
- NAC administered within **8–12 hours** of ingestion virtually assures minimal liver damage, making early empiric treatment critical when timing is uncertain.[2][3]

Why not the other options:

- **Charcoal (B):** Activated charcoal is most effective within **4 hours** of ingestion and ideally within 2 hours. The patient was found over 2 hours ago already somnolent, meaning the actual ingestion likely occurred well before that. Additionally, her altered mental status (somnolence) raises aspiration risk, which is a consideration when administering charcoal. While charcoal may still have some benefit, NAC is the definitive antidote and takes priority.[1][2]
- **IV fluids (C):** Supportive but not the specific intervention needed for acetaminophen toxicity.

- **Syrup of ipecac (D):** No longer recommended for poisoning management due to risk of aspiration and lack of demonstrated benefit.[2]

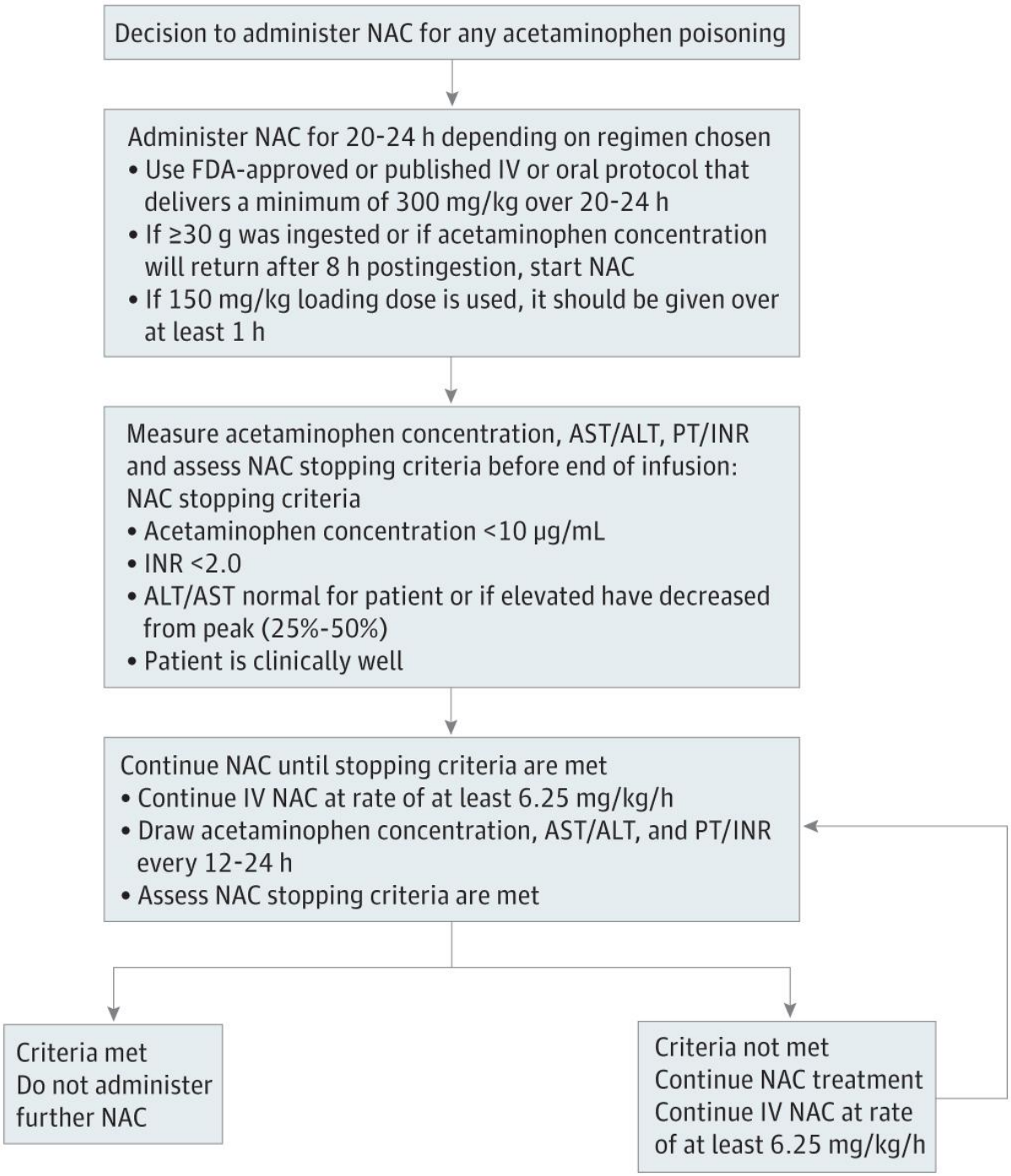


Figure 3. Administration of Acetylcysteine in the Management of Acetaminophen Poisoning

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Would you like to explore the specific NAC dosing protocols (IV vs. oral) and stopping criteria for acetaminophen overdose management?

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Question 1144

A 58-year-old Caucasian female presents to her primary care physician with concerns about several recent health changes. The patient has recently gained weight and can't seem to exercise like she used to. She also notes that her thinking seems slow. Physical examination shows thickened, dry skin. Serum analysis confirms the physician's suspicions. Which of the following findings was most helpful in the diagnosis?

Answer Choices:

(A) High T4 and T3
(B) Low T4 and T3
(C) High TSH
(D) Hypercholesterolemia

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/4d740312-fa30-45a2-8a4e-5c2b145f292a

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OpenEvidence Explanation

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The answer is **C. High TSH**. This patient's presentation — weight gain, exercise intolerance, cognitive slowing ("slow thinking"), and thickened, dry skin — is classic for **hypothyroidism**, and **serum TSH is the single most helpful diagnostic test**.

TSH is recommended as the initial and most reliable diagnostic test for primary hypothyroidism, with a sensitivity of approximately **98%** and specificity of **92%** for identifying overt thyroid dysfunction.[1][2] The American Thyroid Association confirms that serum TSH concentration is the "single best biomarker" to confirm a diagnosis of primary thyroid disease.[3]

Why the other options are less correct:

- **A. High T4 and T3** — This pattern would suggest hyperthyroidism, which is the opposite of this patient's clinical picture.
- **B. Low T4 and T3** — While low T4 is seen in overt hypothyroidism, T3 levels typically remain within the reference range until profound hypothyroidism develops. More importantly, T4/T3 are secondary tests obtained after TSH is found to be elevated; TSH is the first-line and most sensitive diagnostic marker.[1][4][5]
- **D. Hypercholesterolemia** — Dyslipidemia can be associated with hypothyroidism, but it is a nonspecific finding seen in many conditions and is not diagnostic of hypothyroidism.[1]

The key teaching point is that an **elevated TSH** is the cornerstone of hypothyroidism diagnosis. Free T4 is then measured to distinguish overt hypothyroidism (low free T4) from subclinical hypothyroidism (normal free T4), and routine T3 testing has no role in the diagnosis of hypothyroidism.[1][5]

Would you like to explore the management approach for newly diagnosed hypothyroidism, including levothyroxine dosing strategies and monitoring parameters?

Relevant images

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Question 1145

A 33-year-old woman at 17-weeks gestation comes to the physician for evaluation of a painless mass in the right breast for the last 3 weeks that has not increased in size. Physical examination shows dense breasts and a 2.5-cm rubbery, mobile mass that is nontender in the upper outer quadrant of the right breast. A biopsy of the mass shows rounded contour with overgrowth of fibrous and glandular tissue. Which of the following is the most likely diagnosis?

> **Answer Choices:**
>
> (A) Fibroadenoma
> (B) Normal pregnancy-related changes
> (C) Fat necrosis
> (D) Phyllodes tumor

> **Correct Answer:**
>
> **(A)**
>
> **OpenEvidence Response:**
>
> **(A)** ✓

OpenEvidence Link: https://openevidence.com/ask/df0328d2-4b78-46fd-8ae2-fd7b8b350794

OpenEvidence Explanation

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The most likely diagnosis is **A. Fibroadenoma**.

This presentation is classic for fibroadenoma: a **painless, rubbery, mobile, well-circumscribed breast mass** in a young woman of reproductive age, with biopsy showing a **rounded contour with overgrowth of fibrous and glandular tissue** (i.e., a biphasic proliferation of epithelial and stromal elements).[1][2] Several features strongly support this diagnosis:

- **Age and demographics:** Fibroadenomas are the most common cause of breast masses in young women, with a median presentation age of 25 years. They are also the most frequent breast lesion found during pregnancy and lactation.[1][3]
- **Clinical characteristics:** The 2.5-cm, rubbery, mobile, nontender mass is the textbook description — often referred to as a "marble" in the breast.[2]
- **Histology:** The biopsy description of a rounded contour with proliferation of fibrous and glandular tissue is characteristic of fibroadenoma, which is a well-circumscribed, unencapsulated biphasic lesion with admixed epithelial and stromal components.[2]
- **Pregnancy context:** Fibroadenomas are estrogen-sensitive and may become clinically apparent or enlarge during pregnancy due to hormonal stimulation.[3][4]

Why not the other options?

- **Phyllodes tumor (D):** While also a biphasic fibroepithelial lesion, phyllodes tumors typically present 1–2 decades later (median age ~40 years), are larger (often >3 cm), show rapid growth, and histologically demonstrate a characteristic **leaf-like architecture with hypercellular stroma and stromal fronds** rather than a rounded contour. The stable size and rounded histologic contour argue against phyllodes.[4][5]
- **Normal pregnancy-related changes (B):** Pregnancy causes diffuse breast engorgement and increased density, but does not produce a discrete, well-circumscribed mass with a distinct biphasic histologic pattern on biopsy.
- **Fat necrosis (C):** Fat necrosis typically follows trauma or surgery and presents as a firm, irregular, often tender mass with histology showing lipid-laden macrophages and fibrosis — not a biphasic fibroglandular proliferation.

Would you like to explore how fibroadenomas are managed during pregnancy, including indications for excision versus observation?

Relevant images

(CONTENT OMITTED)

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Question 1146

A 27-year-old male presents for emergency surgery to reattach his left arm, severed during a high-speed car accident, and has lost significant amounts of blood. His wife arrives within minutes to the hospital exclaiming that under no circumstance should he receive any blood transfusions during surgery. After reviewing his medical chart, you see also see an annotation indicating no blood transfusions for religious reasons. Knowing that he needs a blood transfusion to save his life, what do you do?

> **Answer Choices:**
>
> (A) Administer a blood transfusion to save the patient's life
> (B) Call the ethics board of the hospital to discuss the issue
> (C) Respect the patient's written instructions and do not adminster a blood transfusion
> (D) Convince the wife to administer a blood transfusion to her husband

> **Correct Answer:**
>
> (C)
>
> **OpenEvidence Response:**
>
> (C) ✓

OpenEvidence Link: https://openevidence.com/ask/f761deff-efad-400c-850a-c06c945e72c2

OpenEvidence Explanation

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The answer is **C. Respect the patient's written instructions and do not administer a blood transfusion**.

This scenario involves a competent adult patient who has documented an advance directive in his medical chart clearly refusing blood transfusions for religious reasons, corroborated by his wife's statement. The principle of **patient autonomy** — the right of a competent adult to refuse treatment, even life-saving treatment — is the governing ethical and legal standard here.

Why the other options are incorrect:

- **A (Administer a blood transfusion):** In almost all instances, a physician is liable for violating the religious belief of a patient with capacity if a blood transfusion is administered without consent or against the patient's documented request. The WSES-AAST guidelines explicitly state that "when a patient has an advance directive clearly refusing allogeneic blood transfusion, **that directive must be followed**". Transfusing against a documented refusal could constitute battery.[1][2]

- **B (Call the ethics board):** While ethics consultation is valuable in ambiguous situations, this case is not ambiguous — there is a clear written directive in the chart and a corroborating surrogate. The emergency nature of the surgery does not allow for the delay an ethics board consultation would entail, and the ethical principle is already well-established.[1][2]

- **D (Convince the wife):** The wife is not the decision-maker here; the patient himself has already made his wishes known through a documented advance directive. Attempting to convince the wife to override the patient's own documented wishes would be ethically inappropriate and would not change the legal standing of the patient's directive.[1]

Key nuances in practice: Even while respecting the refusal of allogeneic blood products, clinicians should pursue **alternative strategies** including crystalloid/colloid volume expanders, cell salvage (if acceptable to the patient), tranexamic acid, recombinant factor VIIa, deliberate hypotensive anesthesia, and other blood conservation modalities.[1][3] Many patients who refuse whole blood and primary components will accept blood fractions such as clotting factor concentrates, albumin, or immunoglobulins.[2] The heterogeneity of individual preferences underscores the importance of clarifying exactly which products and techniques are acceptable.[1][4]

Would you like to explore the specific bloodless surgery techniques and alternative hemostatic strategies available for managing massive hemorrhage in patients who refuse transfusion?

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Question 1147

The parents of a 14-year-old patient are concerned and have questions about the use of insulin for their son's recently diagnosed type 1 diabetes. The patient has developed an upper respiratory infection while at school. He is coughing and has a runny nose. His temperature is 37.8° C (100.2° F) and vital signs are within normal limits. Physical examination is unremarkable. Which of the following modifications to his insulin regimen would you recommend to this patient and his parents?

Answer Choices:

(A) Increase the frequency of blood glucose checks.
(B) Reduce the insulin dose.
(C) Continue same regimen.
(D) Hold insulin until the patient gets better.

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/3f9e1e25-c20b-46da-ba84-4dc954a4cabc

OpenEvidence Explanation

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The correct answer is **A. Increase the frequency of blood glucose checks**.

During intercurrent illness in a child with type 1 diabetes, the most important initial modification is **more frequent blood glucose monitoring**, not a change in insulin dose. Here is the rationale:

Why increase monitoring frequency?

Acute infections — even mild ones like an upper respiratory infection — induce significant **insulin resistance** through stress-related counterregulatory hormones (cortisol, catecholamines) and cytokine release, which can cause hyperglycemia and increase the risk of diabetic ketoacidosis (DKA).[1][2][3] The ADA recommends that individuals with type 1 diabetes and their caregivers be educated on **sick-day management**, which includes frequent monitoring of blood glucose and ketone levels, adequate fluid and carbohydrate intake, and additional short- or rapid-acting insulin as needed.[1][4][5] More frequent glucose checks allow timely detection of hyperglycemia or hypoglycemia and guide appropriate insulin dose adjustments.

Why not the other options?

- **Reducing insulin (B) or holding insulin (D)** would be dangerous. Insulin should **never be withheld** in type 1 diabetes, as this is a major cause of DKA. Illness typically increases — not decreases — insulin requirements. A consensus panel recommended increasing basal and bolus insulin by 10–20% if blood glucose is elevated during illness.[5][6]
- **Continuing the same regimen without modification (C)** is insufficient because illness-related glucose fluctuations require closer surveillance and potential dose adjustments. Simply maintaining the baseline regimen without increased monitoring misses the opportunity to detect and respond to glycemic excursions.

The key teaching point is that sick-day management in pediatric type 1 diabetes centers on **increased glucose and ketone monitoring**, maintaining hydration, never omitting insulin, and adjusting doses based on the monitored values.[1][4][7]

Would you like to explore specific sick-day insulin adjustment protocols, including when and how to administer supplemental correction doses during illness in pediatric type 1 diabetes?

Relevant images

(CONTENT OMITTED)

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Question 1148

A researcher evaluates healthy breast tissue from 100 women, 50 women that were pregnant at the time of the study and 50 age-matched non-pregnant women. The breast tissue in pregnant women contained an increased number of acinar glands with epithelial proliferation compared to the non-pregnant women. Which process caused this change?

Answer Choices:

(A) Hyperplasia
(B) Hypertrophy
(C) Atrophy
(D) Metaplasia

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/b7eb751c-ad2c-4db2-a0f8-de336416dfd2

OpenEvidence Explanation

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The answer is **A. Hyperplasia**.

The key distinction here is between an increase in **cell number** (hyperplasia) versus an increase in **cell size** (hypertrophy). The question describes an **increased number of acinar glands with epithelial proliferation**, which is the

hallmark of hyperplasia — growth through an increase in the number of cells and structural units.[1][2]

During pregnancy, the breast undergoes dramatic remodeling driven by rising estrogen, progesterone, and prolactin levels. This includes **ductal proliferation and elongation**, expansion of the ductal system into adipose tissue, and the formation of thousands of new alveoli (acini) — saccular outpouchings from the ductal system that will eventually produce milk.[3][4] Breast epithelial cell proliferation is markedly increased during pregnancy, with Ki67 indices averaging ~15.4% compared to ~1.8% in normally cycling women.[5] This represents a massive increase in epithelial cell number through cell division, which is the defining feature of hyperplasia.

The other answer choices can be distinguished as follows:

- **Hypertrophy** (B) would involve an increase in cell size without cell division — not consistent with "epithelial proliferation" and increased numbers of glands.
- **Atrophy** (C) refers to a decrease in cell size or number, the opposite of what is described.
- **Metaplasia** (D) involves replacement of one differentiated cell type with another, which is not occurring here.

Would you like to explore the hormonal mechanisms that drive lobuloalveolar development during pregnancy and how they relate to breast cancer risk?

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Question 1149

A 21-month-old boy is brought to the physician for a well-child examination. His mother noticed deformities in both of his legs since he started walking independently. He has been healthy apart from an upper respiratory tract infection 6 months ago. He was delivered at 38 weeks' gestation. His 6-year-old sister was treated for developmental dysplasia of the hip. He can kick a ball and say a 2-word phrase. He plays well with other children at his day care. His immunizations are up-to-date. He is at the 40th percentile for height and 50th percentile for weight. Vital signs are within normal limits. Examination shows closed anterior and posterior fontanelles. The knees do not stay together when both the feet and ankles are placed together. The gait is unremarkable. The mother is concerned that he has a growth disorder. Which of the following is the most appropriate next step in management?

Answer Choices:

(A) Vitamin D supplementation
(B) Reassurance and follow-up
(C) X-ray of the lower extremities
(D) Bracing of the lower extremities

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/53fb1710-2bfb-4918-8a11-e2e20ffcb68c

OpenEvidence Explanation

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The most appropriate next step is **B. Reassurance and follow-up**. This child presents with **physiologic genu varum (bowlegs)**, which is a normal developmental variant in toddlers under 2 years of age that typically resolves spontaneously.

Key features supporting physiologic genu varum in this case:

- Age 21 months — within the expected window for physiologic bowing, which is most common in children under 2 years[1]
- **Bilateral and symmetric** bowing (both legs affected)
- Normal height (40th percentile) and weight (50th percentile) — no evidence of a growth disorder, rickets, or skeletal dysplasia
- **Unremarkable gait** with age-appropriate developmental milestones (kicking a ball, 2-word phrases, social play)
- No signs of pathologic bowing (no asymmetry, no short stature, no radiographic red flags described)

Why the other options are not indicated:

- **Vitamin D supplementation (A):** While some studies have associated genu varum with lower vitamin D levels, there is no clinical evidence of rickets here (normal growth parameters, no radiographic abnormalities, no systemic findings). Empiric supplementation is not the standard next step for physiologic bowing.[2]
- **X-ray of the lower extremities (C):** Radiologic studies are not routinely required for genu varum in this age group and are reserved to exclude pathologic conditions such as Blount disease or rickets when there are concerning features (asymmetry, worsening after age 2, obesity, short stature). This child lacks those red flags.[3]

- **Bracing (D):** Bracing is not indicated for physiologic genu varum. It may be considered in early Blount disease, but there is no evidence of pathologic bowing here.[1][4]

Physiologic genu varum presenting before 18 months typically shows initial correction between 18–24 months and resolves by 30 months; cases presenting between 18–23 months show correction by 24–30 months and resolution by 36 months.[5] Primary care management focuses on monitoring progression or resolution at well-child visits, with orthopedic referral reserved for cases that worsen or fail to correct.[3][5]

Would you like to explore the clinical criteria that distinguish physiologic genu varum from early Blount disease and when radiographic evaluation becomes necessary?

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Question 1151

A 1900-g (4-lb 3-oz) newborn is delivered at term to a 36-year-old primigravid woman. Pregnancy was complicated by polyhydramnios. Apgar scores are 7 and 7 at 1 and 5 minutes, respectively. He is at the 2nd percentile for head circumference and 15th percentile for length. Examination shows a prominent posterior part of the head. The ears are low-set and the jaw is small and retracted. The fists are clenched, with overlapping second and third fingers. The calcaneal bones are prominent and the plantar surface of the foot shows a convex deformity. Abdominal examination shows an omphalocele. Further evaluation of this patient is most likely to show which of the following findings?

Answer Choices:

(A) Ventricular septal defect
(B) Ebstein's anomaly
(C) Pheochromocytoma
(D) Holoprosencephaly

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/f6b9702c-7f31-4e68-8318-623481a6f8bb

OpenEvidence Explanation

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The answer is **A. Ventricular septal defect**.

The clinical presentation described — intrauterine growth restriction, polyhydramnios, prominent occiput, low-set ears, micrognathia, **clenched fists with overlapping fingers**, rocker-bottom feet, and omphalocele — is the classic phenotype of **trisomy 18 (Edwards syndrome)**. According to the American Heart Association, 80–90% of infants with trisomy 18 have congenital heart disease, with **VSD** being the most common cardiac anomaly, along with ASD, PDA, and polyvalvular dysplasia.[1]

Key distinguishing features in this vignette:

- **Clenched fists with overlapping fingers** (characteristically the index finger overlapping the 3rd, and the 5th overlapping the 4th) are a hallmark of trisomy 18, not trisomy 13.
- **Rocker-bottom feet** (prominent calcaneus with convex plantar surface) are another classic trisomy 18 finding.
- **Prominent occiput** is characteristic of trisomy 18.
- Advanced maternal age (36 years) increases risk for all trisomies.

Regarding the other options:

- **Ebstein's anomaly** (B) is associated with maternal lithium use, not chromosomal aneuploidies.
- **Pheochromocytoma** (C) has no association with trisomy 18.
- **Holoprosencephaly** (D) is associated with trisomy 13 (Patau syndrome), which presents with midline defects such as cleft lip/palate, microphthalmia, and polydactyly — features absent in this vignette.[2]

Would you like to explore the full spectrum of cardiac anomalies in trisomy 18 and their impact on management decisions?

Relevant images

(CONTENT OMITTED)

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Question 1153

A 68-year-old man presents to his primary care physician with complaints of increased fatigue and back pain for the past year. His symptoms are progressively getting worse over the past few months despite adequate rest and trial of over the counter analgesics. His back pain is constant and non-radiating in nature. He denies any trauma to his back. His past medical history is insignificant. On examination, there is mild tenderness over the lumbar region in the midline with an absence of paraspinal muscle tenderness. Straight leg raise test is negative. His skin and conjunctiva appear pale. The physician orders basic blood work. His results are provided below.
Complete blood count
RBC 4.9 million cells/μL
Hemoglobin 9.8 g/dL
Hematocrit 41%
Total leukocyte count 6,800 cells/μL
Neutrophils 70%
Lymphocyte 26%
Monocytes 3%
Eosinophil 1%
Basophils 0%
Platelets 230,000 cells/μL
Basic Metabolic Panel
Sodium 136 mEq/L
Potassium 5.1 mEq/L
Chloride 101 mEq/L
Bicarbonate 24 mEq/L
Albumin 3.6 mg/ dL
Urea nitrogen 31 mg/dL
Creatinine 2.7 mg/dL
Uric Acid 6.7 mg/dL
Calcium 12.1 mg/dL
Glucose 105 mg/dL
Urinalysis shows proteinuria without any RBCs or pus cells. The patient's proteinuria best fits in which of the following category?

Answer Choices:

(A) Overflow proteinuria
(B) Transient (functional) proteinuria
(C) Orthostatic proteinuria
(D) Isolated proteinuria

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/25ffb155-5beb-4e97-9fc5-ac8857d5ac35

OpenEvidence Explanation

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The answer is **A. Overflow proteinuria**.

This clinical presentation is classic for **multiple myeloma** — a 68-year-old man with progressive back pain, normocytic anemia (Hb 9.8 g/dL), hypercalcemia (Ca 12.1 mg/dL), renal insufficiency (Cr 2.7 mg/dL), and proteinuria without RBCs or pus cells. These findings correspond to the classic "CRAB" criteria (Calcium elevation, Renal insufficiency, Anemia, Bone disease).[1] In multiple myeloma, the proteinuria is due to **overflow of monoclonal free light chains (Bence Jones proteins)** that are overproduced by neoplastic plasma cells, filtered at the glomerulus, and exceed the tubular reabsorptive capacity.[2][3]

Why the other options are incorrect:

- **B. Transient (functional) proteinuria** occurs temporarily with fever, exercise, stress, or cold exposure and resolves when the inciting factor is

removed. This patient has a chronic, progressive illness — not a transient trigger.[3][4]

- **C. Orthostatic proteinuria** normalizes completely in the recumbent position and is a benign condition most common in adolescents. It does not present with anemia, hypercalcemia, or renal failure.[4]

- **D. Isolated proteinuria** occurs in asymptomatic patients without evidence of any systemic disease or abnormality of the urine sediment. This patient clearly has systemic disease (anemia, hypercalcemia, renal insufficiency, bone pain), making isolated proteinuria an inappropriate classification.[4]

Overflow proteinuria is mechanistically distinct from glomerular or tubular proteinuria — it results from the overproduction of low-molecular-weight proteins (in this case, monoclonal light chains) that overwhelm normal tubular reabsorption.[2][3] Notably, standard urine dipstick testing may not detect Bence Jones proteins, as dipsticks primarily detect albumin; urine protein electrophoresis (UPEP) and immunofixation are needed for definitive identification.[1][5]

Would you like to explore the diagnostic workup and initial management approach for suspected multiple myeloma presenting with renal impairment?

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Question 1154

A 68-year-old postmenopausal woman presents to the clinic for a dual-energy X-ray absorptiometry (DEXA) scan. The patient states that she has mild joint pain, which she attributes to osteoarthritis, but she notes no recent fractures. She says that her mother had osteoporosis and she is concerned that she may develop it as well. She takes calcium and vitamin D supplements daily. After review of her DEXA scan, her physician states that she has osteopenia. Which of the following is this patient's most likely DEXA scan result?

Answer Choices:

(A) T-score of 1.2
(B) T-score of -0.8
(C) Z-score of -2.0
(D) T-score of -1.6

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/b9eabce3-8962-40be-87fd-4c0f08f1e3e0

OpenEvidence Explanation

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The correct answer is **D. T-score of -1.6**.

Osteopenia is defined by the World Health Organization (WHO) as a **T-score between -1.0 and -2.5** on DEXA scan. A T-score of **-1.6** falls squarely within this range.

Here is how the other options are ruled out:

- **A. T-score of 1.2** — A T-score above -1.0 is classified as **normal** bone density. A positive value indicates bone density above the mean for a young healthy reference population.
- **B. T-score of -0.8** — This also falls within the **normal** range (T-score ≥ -1.0).
- **C. Z-score of -2.0** — The **Z-score** compares bone density to an age- and sex-matched population and is used primarily in **premenopausal women, men under 50, and children**. For a 68-year-old postmenopausal woman, the **T-score** (not Z-score) is the appropriate metric for diagnosing osteopenia or osteoporosis per WHO criteria.

WHO Classification Summary:

- **Normal:** T-score ≥ -1.0
- **Osteopenia:** T-score between -1.0 and -2.5
- **Osteoporosis:** T-score ≤ -2.5

This patient's clinical profile — postmenopausal status, family history of osteoporosis, and use of calcium/vitamin D supplementation — is consistent with appropriate screening, and a T-score of -1.6 correctly identifies osteopenia warranting monitoring and potential further risk stratification (e.g., FRAX score).

Would you like to explore when pharmacologic treatment should be initiated in patients with osteopenia based on FRAX fracture risk assessment?

Question 1155

An investigator is studying the growth pattern of a particular bacterial strain that caused a respiratory disease outbreak in children in rural Venezuela. The bacteria are found to be able to grow in a specialized culture that contains sheep blood, cystine, and potassium tellurite; the colonies are black and have a shining surface. The isolated bacteria are most likely which of the following?

Answer Choices:

(A) Legionella pneumophila
(B) Haemophilus influenzae
(C) Bordetella pertussis
(D) Corynebacterium diphtheriae

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/f7d7cbd0-1acb-4e35-b51d-5a0abd875870

OpenEvidence Explanation

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D. Corynebacterium diphtheriae. The described medium is essentially **Tinsdale/tellurite-containing medium**, on which C. diphtheriae characteristically forms **black, shiny colonies** due to tellurite reduction and cystinase activity.[1][2]

Why the other choices are less likely:

- **Legionella pneumophila** grows on **BCYE agar** with iron and cysteine, not tellurite medium.
- **Haemophilus influenzae** requires **chocolate agar** with **factor X (hemin)** and **factor V (NAD)**.
- **Bordetella pertussis** classically grows on **Bordet-Gengou** or **Regan-Lowe** medium, not potassium tellurite medium.[3][4]

This organism is the classic cause of **respiratory diphtheria** in underimmunized children.

Would you like to explore the classic distinguishing culture media and lab identification features for the major respiratory bacterial pathogens tested on exams?

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Question 1157

A 4-year-old boy with acute lymphoblastic leukemia is admitted to the hospital to undergo allogeneic bone marrow transplantation. Two weeks after the conditioning regimen is started, he develops a temperature of 38.5°C (101.3°F). Laboratory studies show:
Hemoglobin 8 g/dL
Leukocyte count 1400/mm3
Segmented neutrophils 20%
Eosinophils 0.5%
Lymphocytes 87%
Monocytes 1%
Platelet count 110,000/mm3
Which of the following is the most appropriate pharmacotherapy for this patient?

Answer Choices:

(A) Transforming growth factor-β
(B) Erythropoietin
(C) Interleukin-5
(D) Granulocyte-macrophage colony-stimulating factor

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/84f3a7b3-ea59-4f5e-b7b7-9bca93bca8db

OpenEvidence Explanation

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Computed value for Absolute Neutrophil Count (ANC): 280.0 cells/µL

Computed value for Interpretation: Severe neutropenia (<500 cells/µL) — high risk for serious infection

Computed value for NCI Risk Category: NCI Risk Category 4: ANC <500 cells/µL

The correct answer is **D. Granulocyte-macrophage colony-stimulating factor (GM-CSF)**.

This patient has **febrile neutropenia** following a conditioning regimen for allogeneic bone marrow transplantation. The ANC is **280 cells/µL** (1,400 × 20% = 280), indicating **severe neutropenia** (<500 cells/µL), and the fever of 38.5°C meets the threshold for febrile neutropenia.[1]

Why GM-CSF is correct:

GM-CSF (sargramostim) is FDA-approved specifically for use after allogeneic and autologous bone marrow transplantation to accelerate neutrophil recovery.[2][3] In a landmark randomized controlled trial, rhGM-CSF accelerated neutrophil recovery to ≥500/µL by 7 days compared to placebo (19 vs. 26 days), reduced infections, shortened antibiotic use, and decreased hospitalization duration after bone marrow transplantation.[4] Similarly, in allogeneic BMT, GM-CSF significantly increased neutrophil and monocyte counts during the second and third weeks post-transplant and decreased the incidence of pneumonia.[5] The NCCN Hematopoietic Growth Factors guidelines also support considering GM-CSF or G-CSF in patients with febrile neutropenia who are clinically worsening.[6][7]

Why the other options are incorrect:

- **A. TGF-β** — An immunosuppressive cytokine that inhibits hematopoiesis; it would worsen neutropenia.

- **B. Erythropoietin** — Stimulates red blood cell production; while the patient has anemia, the acute life-threatening problem is febrile neutropenia, not anemia.
- **C. IL-5** — Stimulates eosinophil production and differentiation; it would not address neutropenia.

Would you like to explore the specific dosing protocols and monitoring parameters for sargramostim (GM-CSF) versus filgrastim (G-CSF) in the post-transplant setting?

Relevant images

(CONTENT OMITTED)

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Question 1160

A 31-year-old female patient presents with significant swelling and redness of her fingers that is causing her significant pain. Her right knee has also been stiff and slightly swollen for the past 6 weeks. She is overall fatigued and has difficulty moving around but has not sought medical attention until now. On physical examination, the distal interphalangeal joints are swollen, warm, and painful; her nails are pitted and cracked. There are also rough, erythematous skin patches seen over her elbows which have been present for the last few months. She reports that herer father has a similar condition. They both use hydrating creams and topical glucocorticoids with moderate benefit. Which of the following is the most likely diagnosis?

Answer Choices:

(A) Gout
(B) Reactive arthritis
(C) Psoriatic arthritis
(D) Dermatomyositis

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/be16194c-3961-4e14-9079-ec761f2ceb9d

OpenEvidence Explanation

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The most likely diagnosis is **C. Psoriatic arthritis**.

This presentation is classic for psoriatic arthritis, with multiple hallmark features converging in a single patient:

- **Distal interphalangeal (DIP) joint involvement** — swollen, warm, and painful DIP joints are characteristic of psoriatic arthritis and help distinguish it from rheumatoid arthritis, which typically spares the DIP joints.[1]
- **Nail changes** — pitting and cracking of the nails occur in **80–90% of patients with psoriatic arthritis** and are a key diagnostic feature included in the CASPAR classification criteria.[2][3]
- **Psoriatic skin lesions** — the rough, erythematous patches over the elbows are consistent with psoriasis plaques. In approximately 85% of patients with psoriatic arthritis, skin disease precedes or occurs concurrently with joint involvement.[2]
- **Large joint involvement** — the right knee stiffness and swelling for 6 weeks reflects inflammatory arthritis, consistent with the oligoarticular pattern commonly seen in psoriatic arthritis.[1]
- **Family history** — a positive family history of psoriasis is a well-recognized risk factor and is one of the CASPAR criteria for classification.[1][4]
- **Age and demographics** — psoriatic arthritis most commonly presents between ages 30 and 50, consistent with this 31-year-old patient.[5]

The following figure illustrates the diverse clinical manifestations of psoriatic arthritis, including DIP joint involvement with nail changes, dactylitis, and enthesitis.



Figure 1. Clinical Features of Psoriatic Arthritis.

Used under license from The New England Journal of Medicine.

Why the other options are incorrect:

- **Gout (A)** — typically presents as acute monoarticular arthritis (classically the first MTP joint), not with DIP joint polyarthritis, nail pitting, or psoriatic skin lesions.[1]
- **Reactive arthritis (B)** — follows a genitourinary or gastrointestinal infection and classically presents with the triad of arthritis, urethritis, and conjunctivitis; it does not cause nail pitting or psoriatic plaques.
- **Dermatomyositis (D)** — presents with proximal muscle weakness and characteristic skin findings (heliotrope rash, Gottron papules), not DIP joint arthritis or nail pitting.

Would you like to explore the current treatment algorithm for psoriatic arthritis, including when to initiate DMARDs versus biologics based on disease severity and domain involvement?

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Question 1161

A 44-year-old woman presents to her primary care physician because she has been having fever, chest pain, and cough for the last several weeks. She presented to the physician because she discovered blood in her sputum after coughing. She recently returned from a year of traveling abroad, but has otherwise been healthy. Based on clinical suspicion, an acid fast stain is performed showing the causative organism, and she is started on appropriate therapy. Two weeks later, she returns with a skin rash, diarrhea, and confusion, and is given a factor to take in addition to the medications previously prescribed. Which of the following is a characteristic of the factor that was most likely provided?

Answer Choices:

(A) Required for collagen hydroxylation
(B) Required for dehydrogenase enzymes
(C) Required for methionine processing
(D) Required for methylmalonyl-CoA processing

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/14f53de8-299e-44c3-ad98-1e47b2df99a0

OpenEvidence Explanation

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The answer is **B. Required for dehydrogenase enzymes**.

This question involves a classic clinical scenario: a patient with tuberculosis (acid-fast bacilli on stain) is started on anti-TB therapy including **isoniazid (INH)**. Two weeks later, she develops the triad of **dermatitis (skin rash), diarrhea, and dementia (confusion)** — the classic "3 Ds" of **pellagra** (niacin/vitamin B3 deficiency). The factor added is **niacin (vitamin B3)**.

Isoniazid depletes pyridoxine (vitamin B6), which is a cofactor for the conversion of tryptophan to niacin. This secondary niacin deficiency produces pellagra.[1][2] The key distinguishing feature here is the symptom triad: peripheral neuropathy (from B6 deficiency alone) would not explain the combination of dermatitis, diarrhea, and confusion — pellagra does.

Niacin (vitamin B3) in its active forms (NAD^+ and $NADP^+$) serves as a coenzyme for **dehydrogenase enzymes** involved in oxidation-reduction reactions throughout metabolism, making option B correct.[3]

The other options correspond to different vitamins:

- **A (collagen hydroxylation)** — Vitamin C (ascorbic acid), a cofactor for prolyl and lysyl hydroxylases
- **C (methionine processing)** — Vitamin B12 (cobalamin), required for methionine synthase
- **D (methylmalonyl-CoA processing)** — Also Vitamin B12, required for methylmalonyl-CoA mutase[3]

Would you like to explore the mechanisms by which isoniazid causes secondary niacin deficiency through its effects on tryptophan metabolism?

Relevant images

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Question 1162

A 51-year-old Asian woman presents to her primary care provider with abdominal pain. On examination, she is found to have rebound tenderness in the lower right quadrant of her abdomen. Further workup suggests ovarian cancer, which is confirmed later in the week to be stage 4 with confirmed distant metastases in the lungs and brain. Which of the following routes describes the most likely lymphatic route for this malignancy to have metastasized to the brain?

Answer Choices:

(A) Sentinel node - left lumbar trunk - cisterna chyli - right bronchomediastinal trunk - right lymphatic duct - right subclavian vein - systemic circulation
(B) Sentinel node - left lumbar trunk - cisterna chyli - thoracic duct - left subclavian vein - systemic circulation
(C) Sentinel node - right lumbar trunk - cisterna chyli - right bronchomediastinal trunk - right lymphatic duct - right subclavian vein - systemic circulation
(D) Sentinel node - right lumbar trunk - cisterna chyli - thoracic duct - left subclavian vein - systemic circulation

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/6da4aa19-5052-4a1c-bcd1-1ade2e4b5f6f

OpenEvidence Explanation

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The correct answer is **D. Sentinel node → right lumbar trunk → cisterna chyli → thoracic duct → left subclavian vein → systemic circulation**.

The key anatomical reasoning involves two critical points:

1. The right ovary drains via the right lumbar trunk. The patient has rebound tenderness in the **right lower quadrant**, indicating a right-sided ovarian mass. Ovarian lymphatic drainage is **ipsilateral** — the right ovary drains primarily to the right lumbar (paracaval/lateral-caval) lymph nodes.[1][2] Cadaveric studies confirm that the right ovary shows preferential lateral-caval (right lumbar) involvement in 60% of cases.[1] This eliminates options A and B, which incorrectly route through the left lumbar trunk.

2. The thoracic duct — not the right bronchomediastinal trunk — is the continuation of the cisterna chyli. The right and left lumbar trunks converge into the **cisterna chyli**, which transitions into the **thoracic duct**.[3][4] The thoracic duct then empties into the venous system at the junction of the **left subclavian vein** and left internal jugular vein.[4][5][6] This eliminates option C, which incorrectly routes lymph from the cisterna chyli through the right bronchomediastinal trunk. The right lymphatic duct and right bronchomediastinal trunk drain only the right upper quadrant of the body (right arm, right thorax, right head/neck) — they do not receive lymph from the cisterna chyli.[3][7]

Once lymph enters the left subclavian vein, it joins the systemic venous circulation, passes through the heart, and reaches the lungs and brain via arterial distribution, accounting for the distant metastases described.

Would you like to explore the patterns and frequency of lymph node metastasis in different stages of epithelial ovarian cancer and how this impacts surgical management?

Relevant images

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Question 1166

A 15-year-old girl is brought to the physician by her mother because of worsening grades over the past year. Since she started high school one year ago, her academic performance has decreased. She also has had difficulty finding friends at the new school. She is afraid that her classmates will make fun of her and think that she is “stupid.” One month ago, when she had to give a presentation, she could not stop wondering how her classmates were going to react if she said something wrong. During the presentation, her heart started racing and she became flushed. Since this event, she avoids saying anything in class. She spends her breaks in the restroom because she is worried that nobody will talk to her. Physical and neurologic examinations show no abnormalities. On mental status examination, the girl avoids eye contact and appears uncomfortable and anxious. Which of the following is the most appropriate pharmacotherapy for this patient's condition?

Answer Choices:

(A) Clomipramine
(B) Phenelzine
(C) Fluoxetine
(D) Propranolol

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/b72cb91e-c2ec-4ea7-a7f6-e0391c813a9d

OpenEvidence Explanation

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The correct answer is **C. Fluoxetine**.

This patient presents with **social anxiety disorder** (social phobia) — characterized by persistent fear of social situations, worry about being judged or embarrassed, avoidance of social interactions, and physiologic symptoms (tachycardia, flushing) during a performance situation. The condition is causing significant functional impairment (declining grades, social isolation, avoidance behaviors).

SSRIs such as fluoxetine are the first-line pharmacotherapy for social anxiety disorder in children and adolescents. The AACAP recommends that SSRIs be offered to patients aged 6–18 with social anxiety disorder.[1] Multiple Cochrane reviews and meta-analyses confirm the efficacy of SSRIs, with response rates of approximately 55% vs. 32% for placebo.[2][3]

Why not the other options?

- **A. Clomipramine** — A tricyclic antidepressant with serotonergic properties that has efficacy in anxiety disorders but is not first-line due to its unfavorable side-effect profile (anticholinergic effects, cardiac conduction abnormalities, risk in overdose). SSRIs are preferred due to their superior risk-benefit ratio, particularly in children and adolescents.[4]
- **B. Phenelzine** — A monoamine oxidase inhibitor (MAOI) that showed early benefits in RCTs for social anxiety disorder, but is associated with risks of hypertensive crisis, dietary tyramine restrictions, and numerous drug interactions. It is not appropriate first-line therapy, especially in an adolescent.[5]
- **D. Propranolol** — A beta-blocker sometimes used as-needed for the **performance-only subtype** of social anxiety disorder (e.g., isolated stage fright). However, this patient has **generalized social anxiety disorder** — her symptoms extend well beyond performance situations to include fear of peer interactions, avoidance of social contact during breaks, and pervasive

worry about being judged. Propranolol lacks clinical trial evidence for generalized social anxiety and is not recommended for this presentation.[5]

Would you like to explore the evidence for combining CBT with SSRI therapy in adolescents with social anxiety disorder, including optimal sequencing of these treatments?

Relevant images

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Question 1168

A 26-year-old woman developed rapidly progressive septic shock associated with nuchal rigidity, petechiae, and purpura. She tested positive for both Kernig and Brudzinski's signs and shows signs of confusion, dyspnea, and hypotension. The blood culture results confirmed the presence of Neisseria meningitidis, and a complete blood count (CBC) revealed leukocytosis. Which one of the cytokines below takes part in the pathogenesis of septic shock?

Answer Choices:

(A) Tumor necrosis factor-α
(B) Interleukin-5
(C) Interleukin-12
(D) Interleukin-4

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/1420f56c-feda-469b-8654-6c8ea2353dac

OpenEvidence Explanation

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The answer is **A. Tumor necrosis factor-α (TNF-α)**.

TNF-α is a pivotal proinflammatory cytokine in the pathogenesis of septic shock. In this case of meningococcal septicemia, *Neisseria meningitidis* releases lipooligosaccharide (endotoxin), which activates macrophages and monocytes to produce TNF-α as one of the earliest cytokines in the inflammatory cascade.[1] Key points supporting this:

- **TNF-α is the prime mediator of septic shock.** Injection of TNF-α into experimental animals produces a syndrome largely indistinguishable from septic shock, including vasodilation, increased vascular permeability, hypotension, and disseminated intravascular coagulation (DIC). TNF-α is released within 30 minutes of the inciting event, making it one of the earliest regulators of the septic response.[1][2]
- In meningococcal disease specifically, serum TNF-α levels correlate with disease severity and mortality. Studies of children with meningococcal purpura fulminans showed TNF-α was elevated in 91% of patients, and levels were significantly higher in those who died. Elevated TNF-α concentrations are associated with increased 28-day sepsis mortality.[3][4]
- TNF-α acts synergistically with IL-1 to induce vascular permeability, pulmonary edema, hemorrhage, and the coagulopathy seen in this patient's petechiae and purpura.[1][5]

Why the other options are incorrect:

- **IL-5 (B)** is involved in eosinophil differentiation and allergic/parasitic responses, not septic shock.
- **IL-12 (C)** promotes Th1 differentiation and NK cell activation but is not a primary mediator of the hemodynamic collapse in septic shock.
- **IL-4 (D)** is a Th2 cytokine involved in allergic responses and IgE class switching. Notably, IL-4 was undetectable in patients with acute meningococcal infections.[6]

Would you like to explore the role of anti-TNF therapies and why clinical trials targeting TNF-α in sepsis have had disappointing results despite strong preclinical evidence?

Relevant images

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Question 1169

A 35-year-old man comes to the physician because of episodes of difficulty swallowing for the past 3 months. He feels solid food getting stuck in his chest behind the sternum when he eats. Drinking does not cause any difficulty swallowing. He has no coughing or nasal regurgitation. He has no hoarseness or weight loss. He has had heartburn for 2 years with no response to high-dose omeprazole. His past medical history is also significant for asthma and eczema. He takes no medications except for omeprazole. His vital signs are within normal limits. Physical examination shows no abnormal findings. Which of the following best explains these findings?

Answer Choices:

(A) Achalasia
(B) Diffuse esophageal spasm
(C) Eosinophilic esophagitis
(D) Esophageal reflux disease

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/284551e8-7d1b-464b-9483-a26da2beccac

OpenEvidence Explanation

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The answer is **C. Eosinophilic esophagitis (EoE)**.

This presentation is classic for EoE, with several key features pointing to the diagnosis:

- **Solid-food dysphagia** is the hallmark symptom of EoE in adults, described as food "getting stuck" retrosternally. Notably, liquids do not cause difficulty, which is characteristic of a mucosal/structural process rather than a motility disorder.[1][2]
- **Heartburn refractory to high-dose PPI therapy** is a well-recognized presentation of EoE. The ACG guidelines note that EoE should be ruled out in patients with PPI-refractory heartburn.[3][4]
- **Concurrent atopic conditions** (asthma and eczema) strongly raise suspicion for EoE. At least 60%–80% of patients with EoE have concomitant allergic conditions, and the more atopic comorbidities present, the more likely EoE becomes.[2]
- **Young adult male** — EoE is most common in adult White men.[1]

Why not the other options?

- **Achalasia** typically causes dysphagia to both solids and liquids (due to impaired lower esophageal sphincter relaxation and absent peristalsis), often with regurgitation of undigested food. This patient has dysphagia only to solids.[5]
- **Diffuse esophageal spasm** presents with intermittent dysphagia to both solids and liquids along with chest pain, and is not associated with atopic disease.[6]
- **Esophageal reflux disease (GERD)** would be expected to respond to high-dose PPI therapy. The lack of PPI response, combined with solid-food dysphagia and the strong atopic history, makes GERD alone an insufficient explanation.[4][7]

Would you like to explore the current evidence-based treatment approach for EoE, including the role of dietary elimination, topical corticosteroids, and dupilumab?

Relevant images

(CONTENT OMITTED)

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Question 1170

A 33-year-old man presents to the emergency department with altered mental status. He was at work as a construction worker when his coworkers found him down at the work site. The patient recently underwent anesthesia for an appendectomy several months ago. He also has a past medical history of schizophrenia well controlled with haloperidol and is currently taking phenytoin for epilepsy. He is also currently taking propranolol for anxiety and hyperthyroidism. His temperature is 106°F (41.1°C), blood pressure is 109/62 mmHg, pulse is 170/min, respirations are 23/min, and oxygen saturation is 95% on room air. Physical exam is notable for an altered man with a Glasgow Coma Scale of 10. He has minimal muscle tone and is incoherent when answering questions. The patient is covered in sweat and dirt. Which of the following is the most likely diagnosis?

Answer Choices:

(A) Exertional heat stroke
(B) Malignant hyperthermia
(C) Neuroleptic malignant syndrome
(D) Thyroid storm

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/ecec7ac1-286a-4bcb-99db-d8c7e038acf8

OpenEvidence Explanation

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The most likely diagnosis is **A. Exertional heat stroke**.

This patient is a **construction worker** (strenuous physical labor in a likely hot outdoor environment) who was found down at the work site with **hyperthermia (106°F/41.1°C), altered mental status (GCS 10), tachycardia, and profuse sweating** — the classic triad of exertional heat stroke: core temperature >40°C, CNS dysfunction, and recent physical exertion.[1][2][3]

Key distinguishing features supporting exertional heat stroke over the other options:

- **Minimal muscle tone** is a critical differentiator. Both neuroleptic malignant syndrome (NMS) and malignant hyperthermia (MH) are characterized by **muscle rigidity** — "lead-pipe" rigidity is a cardinal feature of NMS, and generalized muscle rigidity is nearly pathognomonic for MH. This patient has the opposite finding: minimal/decreased muscle tone, which is consistent with heat stroke.[4][5][6]
- **Sweating is present**, which is typical of exertional heat stroke. While diaphoresis can occur in NMS, the overall clinical picture here fits heat stroke far better.[1]
- **Malignant hyperthermia** occurs during or shortly after exposure to volatile anesthetic agents or succinylcholine. This patient's anesthesia was **months ago**, far outside the temporal window for MH, which manifests within minutes to hours of anesthetic exposure.[6][7]
- **Neuroleptic malignant syndrome** typically develops within 72 hours of dopamine antagonist exposure or dose change. While the patient takes haloperidol, there is no mention of a recent dose change or initiation, and the **absence of rigidity** argues strongly against NMS.[4][8]
- **Thyroid storm** is possible given the history of hyperthyroidism, but the clinical context (outdoor construction worker found down at work site, covered in sweat and dirt) and the absence of other thyroid storm features

(GI symptoms, heart failure, atrial fibrillation) make this less likely. Additionally, propranolol use would provide some protection against thyroid storm by blocking adrenergic effects and peripheral T4-to-T3 conversion.[9][10]

Notably, antiepileptic medications like phenytoin have been associated with impaired thermoregulation and may increase heat stroke risk, and antipsychotics like haloperidol can also impair central heat dissipation mechanisms — both of which may have contributed to this patient's susceptibility.[11][12]

Would you like to explore the evidence-based acute management of exertional heat stroke, including optimal cooling methods and target timelines?

Relevant images

(CONTENT OMITTED)

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Question 1175

A 27-year-old woman with no past medical history presents to the emergency department with recurrent wrist and neck pain for the last 2 months. She reports that her fingers feel stiff in the morning and the symptoms tend to improve as the day progresses. She denies any recent trauma or other inciting events. Family history is significant for a grandmother who suffered from fibromyalgia. Her temperature is 37°C (98.6°F), blood pressure is 120/70 mm Hg, respiratory rate is 16/min, and heart rate is 70/min. On physical examination, her metacarpophalangeal joints are erythematous and tender. Which of the following would be most helpful for diagnosing this patient's condition?

Answer Choices:

(A) Synovial fluid analysis
(B) Anti-cyclic citrullinated peptide (anti-CCP) antibody
(C) Rheumatoid factor
(D) X-ray of cervical spine

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/2f544636-d73e-494e-9be1-13a43a915499

OpenEvidence Explanation

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The answer is **B. Anti-cyclic citrullinated peptide (anti-CCP) antibody**.

This patient's presentation — a young woman with symmetric MCP joint erythema and tenderness, morning stiffness that improves with activity, and symptoms lasting 2 months — is classic for **rheumatoid arthritis (RA)**. Among the options listed, anti-CCP antibody is the most helpful diagnostic test due to its **superior specificity** compared to the other choices.

Why anti-CCP over the other options:

- **Anti-CCP antibody** has a specificity of **95–96%** for RA, compared to only ~85–90% for rheumatoid factor (RF). A meta-analysis of 37 studies found anti-CCP had a positive likelihood ratio of 12.46 versus 4.86 for IgM RF. Anti-CCP is also detectable early in the disease course and predicts erosive disease progression.[1][2][3]
- **Rheumatoid factor (option C)** is less specific — it can be positive in many other conditions (hepatitis C, Sjögren syndrome, endocarditis, healthy elderly individuals), making it less useful as a standalone diagnostic test.[1]
- **Synovial fluid analysis (option A)** is primarily used to evaluate for crystal arthropathy or septic arthritis, not to diagnose RA specifically.
- **X-ray of cervical spine (option D)** may show cervical spine involvement in advanced/established RA (e.g., atlantoaxial subluxation) but would not be expected to show diagnostic findings in early disease of 2 months' duration.

Both anti-CCP and RF are included in the 2010 ACR/EULAR classification criteria for RA, where high-positive serology contributes up to 3 points toward the ≥6-point threshold for classification.[4]

Would you like to explore the initial treatment approach for early RA, including the evidence for early DMARD initiation within the window of opportunity?

Relevant images

(CONTENT OMITTED)

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Question 1176

A 66-year-old man comes to the physician because of fatigue and swelling of his legs and feet for 6 weeks. During this time he has felt like his eyes have been unusually puffy in the mornings and his urine has been frothy. He has hypertension and rheumatoid factor-positive rheumatoid arthritis. Current medications include amlodipine, methotrexate, and ibuprofen. He does not smoke. He has a history of chronic alcohol abuse. His temperature is 36.7°C (98°F), pulse is 80/min, and blood pressure is 148/86 mm Hg. Physical examination shows pallor, periorbital edema, 2+ pedal edema, and ascites. He has swan-neck deformities and nodules of multiple fingers and swelling and restricted range of motion of bilateral knee joints. Laboratory studies show:
Hemoglobin 8.2 mg/dl
Prothrombin time 12 seconds
Serum
Albumin 2.8 g/dl
Total bilirubin 1.0 mg/dl
Alkaline phosphatase 120 U/L
AST 20 U/L
ALT 19 U/L
Urea 18 mg/dl
Creatinine 1.2 mg/dl
Urine
Protein 3+
WBCs 5–10/hpf
RBCs negative
Bacteria negative
Ultrasound of the liver and kidneys shows no abnormalities. Which of the following is the most likely cause of this patient's findings?

Answer Choices:

(A) Adverse effect of ibuprofen
(B) Decreased cardiac ejection fraction

(C) Renal deposition of AL amyloid
(D) Increased serum amyloid A production

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/0e364703-9c47-4f7f-8b41-b2a006c1b8df

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OpenEvidence Explanation

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The answer is **D. Increased serum amyloid A production**.

This patient presents with **nephrotic syndrome** (frothy urine, 3+ proteinuria, hypoalbuminemia, periorbital edema, pedal edema, ascites) in the setting of long-standing **rheumatoid arthritis (RA)** — the classic clinical picture of **AA (secondary) amyloidosis** with renal involvement.

Why AA amyloidosis (Answer D)?

Rheumatoid arthritis is the most common disease complicated by AA amyloidosis in developed countries, occurring in approximately 5–20% of RA patients.[1][2] The pathogenesis centers on chronic systemic inflammation driving sustained overproduction of **serum amyloid A (SAA)**, an acute-phase reactant synthesized by hepatocytes under proinflammatory cytokine regulation.[3][4] SAA-derived fragments misfold into insoluble amyloid fibrils that deposit in the kidneys (predominantly glomeruli), causing progressive proteinuria and nephrotic syndrome.[5][6] The kidney is the most commonly affected organ, and proteinuria or renal dysfunction is the presenting feature in over 90% of cases.

[7] This patient's advanced RA (swan-neck deformities, nodules, bilateral knee involvement) indicates long-standing, poorly controlled disease — exactly the clinical substrate for AA amyloidosis.

Why not the other options?

- **A. Adverse effect of ibuprofen** — NSAIDs can cause interstitial nephritis (presenting with WBCs in urine, eosinophiluria, and mild proteinuria) or minimal change disease. However, NSAID-induced nephropathy typically does not produce this degree of nephrotic syndrome with the full constellation of findings in a patient with long-standing RA. The clinical picture is more consistent with AA amyloidosis.

- **B. Decreased cardiac ejection fraction** — Heart failure can cause edema and ascites, but would not explain the heavy proteinuria, frothy urine, and hypoalbuminemia. Additionally, cardiac involvement is very rare in AA amyloidosis.[8]

- **C. Renal deposition of AL amyloid** — AL (primary) amyloidosis is associated with plasma cell dyscrasias, not chronic inflammatory conditions. In the context of RA, the amyloid type is AA, not AL. The distinction is critical: AA fibrils derive from serum amyloid A protein (the acute-phase reactant), while AL fibrils derive from immunoglobulin light chains.[8][9]

Would you like to explore the role of biologic DMARDs in preventing or treating AA amyloidosis in rheumatoid arthritis?

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Question 1178

A 6-year-old Russian boy who recently immigrated to the United States presents to your office with fever and dyspnea. On examination of the oropharynx, you note a grayish-white pseudomembrane and uneven elevation of the soft palate. The patient displays marked enlargement of the cervical lymph nodes. Which of the following describes the organism responsible for this patient's disease?

> **Answer Choices:**
>
> (A) Yeast with pseudohyphae
> (B) Gram-positive bacteria producing exotoxin that acts via ADP ribosylation
> (C) Gram-positive cocci with hyaluronic acid capsule
> (D) Gram-negative encapsulated bacteria producing IgA protease

> **Correct Answer:**
>
> **(B)**
>
> **OpenEvidence Response:**
>
> **(B)** ✓

OpenEvidence Link: https://openevidence.com/ask/1157b263-04d8-45b9-b5a3-1e173435af2c

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OpenEvidence Explanation

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The answer is **B. Gram-positive bacteria producing exotoxin that acts via ADP ribosylation**.

This clinical presentation — a febrile child from a region with suboptimal vaccination coverage presenting with a **grayish-white pharyngeal pseudomembrane**, uneven soft palate elevation, and prominent cervical lymphadenopathy ("bull neck") — is classic for **diphtheria**, caused by *Corynebacterium diphtheriae*.[1][2]

C. diphtheriae is a **Gram-positive, nonmotile, nonencapsulated, club-shaped bacillus** that produces diphtheria toxin, a potent exotoxin encoded by a lysogenic bacteriophage.[2][3] The toxin's mechanism of action involves **ADP-ribosylation of elongation factor 2 (EF-2)**, which inactivates EF-2 and blocks protein synthesis, leading to cell death.[4][5][6] Specifically, the toxin's A fragment catalyzes the transfer of ADP-ribose from NAD^+ to a unique diphthamide residue on EF-2.[7] This toxin-mediated damage is responsible for the systemic complications of diphtheria, including myocarditis and polyneuropathy.[8]

The epidemiologic context is also important: diphtheria remains endemic in parts of the former Soviet Union, and the disease has historically re-emerged in Russia and Eastern Europe when vaccination programs were disrupted.[9] Unvaccinated or poorly immunized children are particularly susceptible.[2][10]

Why the other options are incorrect:

- **A (Yeast with pseudohyphae)** — Describes *Candida* species, which can cause oral thrush but produces white plaques rather than a firmly adherent pseudomembrane with bull-neck lymphadenopathy.
- **C (Gram-positive cocci with hyaluronic acid capsule)** — Describes *Streptococcus pyogenes* (Group A Strep), which causes pharyngitis with tonsillar exudates but not a true pseudomembrane.
- **D (Gram-negative encapsulated bacteria producing IgA protease)** — Describes organisms like *Haemophilus influenzae* or *Neisseria meningitidis*, neither of which produces pharyngeal pseudomembranes.

Would you like to explore the current recommendations for diphtheria antitoxin administration and antibiotic treatment in suspected cases?

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Question 1180

A 62-year-old woman with a history of hypertension and type 2 diabetes mellitus comes to the physician for a routine health maintenance examination. She has smoked 1 pack of cigarettes daily for the last 15 years. Current medications include glyburide and amlodipine. The physician prescribes a medication that decreases the production of mevalonate. Which of the following changes to the serum is most likely to develop as an adverse effect of the prescribed drug?

Answer Choices:

(A) Increased creatine kinase concentration
(B) Decreased glucose concentration
(C) Increased triglyceride concentration
(D) Increased bradykinin concentration

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/67db981c-d1a9-48f7-be40-ef4d58719ef9

OpenEvidence Explanation

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The answer is **A. Increased creatine kinase concentration**.

The medication that decreases the production of **mevalonate** is an **HMG-CoA reductase inhibitor (statin)**. Mevalonate is the product of HMG-CoA reductase, the rate-limiting enzyme in cholesterol biosynthesis. Statins are indicated here given this patient's cardiovascular risk factors (hypertension, diabetes, smoking history).

A well-recognized adverse effect of statins is **myopathy**, which manifests as muscle pain, tenderness, or weakness accompanied by an **elevated serum creatine kinase (CK) concentration**. This ranges from mild myalgias to rare but serious rhabdomyolysis. The mechanism involves impaired muscle cell membrane integrity and mitochondrial dysfunction related to reduced downstream products of the mevalonate pathway (e.g., coenzyme Q10, isoprenoids).

Why the other options are incorrect:

- **B. Decreased glucose concentration** — Statins are actually associated with a modest *increase* in blood glucose and a slightly elevated risk of new-onset type 2 diabetes, not hypoglycemia.
- **C. Increased triglyceride concentration** — Statins generally *decrease* triglycerides, not increase them. Increased triglycerides are a side effect of bile acid sequestrants.
- **D. Increased bradykinin concentration** — This is associated with **ACE inhibitors**, which prevent the degradation of bradykinin, leading to side effects such as dry cough and angioedema.

Would you like to explore the risk factors and management strategies for statin-induced myopathy?

Question 1181

A 21-year-old woman comes to the physician for evaluation of excess hair growth on her face. Menses occur irregularly at 45 to 65-day intervals. She is 159 cm (5 ft 3 in) tall and weighs 59 kg (130 lb); BMI is 23 kg/m2. Physical examination shows facial acne and growth of coarse dark hair on the face, chest, and lower back. Pelvic examination shows no abnormalities. Serum studies show:
Sodium 141 mEq/L
Potassium 4.2 mEq/L
Glucose 109 mg/dL
Cortisol (1600 h) 4 µg/dL
Prolactin 14 ng/mL
17-hydroxyprogesterone 390 ng/dL (N=20–300 ng/dL)
Testosterone 91 ng/dL (N=8–60 ng/dL)
A urine pregnancy test is negative. This patient's condition is most likely associated with which of the following?

Answer Choices:

(A) Hyperproliferation of theca interna cells
(B) Exogenous anabolic steroid use
(C) Ovarian fibrosis and multiple cystic follicles
(D) Hyperplasia of the adrenal cortex

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/096598d3-3b4e-479a-b06f-243ecbf6d9f3

OpenEvidence Explanation

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The answer is **D. Hyperplasia of the adrenal cortex**.

This patient's presentation — hirsutism, acne, oligomenorrhea, elevated testosterone (91 ng/dL), and an **elevated 17-hydroxyprogesterone (390 ng/dL)** above the normal range of 20–300 ng/dL — is consistent with **non-classic congenital adrenal hyperplasia (NCCAH)** due to 21-hydroxylase deficiency. In this condition, a partial deficiency of the enzyme 21-hydroxylase impairs cortisol synthesis, leading to compensatory increased ACTH secretion and subsequent **hyperplasia of the adrenal cortex**. Steroidogenic precursors proximal to the enzymatic block (particularly 17-OHP) accumulate and are shunted toward androgen synthesis, producing the hyperandrogenic phenotype.[1][2]

Why the other options are incorrect:

- **A. Hyperproliferation of theca interna cells** — This describes the ovarian pathology in PCOS, which is the most common cause of hyperandrogenism. However, PCOS does not cause elevated 17-OHP above the normal range. The elevated 17-OHP is the key distinguishing feature pointing to an adrenal rather than ovarian source.[1][3]
- **B. Exogenous anabolic steroid use** — There is no history suggesting exogenous steroid use, and exogenous androgens would not elevate 17-OHP.[4]
- **C. Ovarian fibrosis and multiple cystic follicles** — This describes the morphologic changes seen in PCOS. While non-classic CAH can mimic PCOS clinically and even show polycystic ovarian morphology on ultrasound in 30–40% of cases, the elevated 17-OHP specifically implicates an adrenal enzymatic defect rather than a primary ovarian process.[1][5]

The normal electrolytes and only mildly low afternoon cortisol (4 µg/dL at 1600h) are consistent with the non-classic form, which preserves 25–50% residual enzyme activity and maintains adequate cortisol and aldosterone production.[1][2]

Would you like to explore the diagnostic workup for confirming non-classic CAH, including the role of ACTH stimulation testing and CYP21A2 genotyping?

Relevant images

(CONTENT OMITTED)

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Question 1182

A 64-year-old man with coronary artery disease and hypertension comes to the physician for a follow-up examination. His blood pressure ranged from 160/100 mm Hg to 150/94 mm Hg on his previous 3 visits over the past 4 months. Current medications include aspirin, atorvastatin, hydrochlorothiazide, and metoprolol. Three weeks ago, he was also started on amlodipine. His blood pressure today is 158/98 mm Hg. Physical examination shows no other abnormalities. Renal duplex ultrasonography shows 90% occlusion of the right renal artery. Decreased renal blood flow is most likely to cause which of the following?

Answer Choices:

(A) Hyperplasia of juxtaglomerular cells
(B) Dilation of efferent arteriole
(C) Decreased prostaglandin synthesis by macula densa
(D) Decreased reabsorption of bicarbonate at proximal tubule

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/8087dc3a-2f0e-4889-ab41-6914612e1928

OpenEvidence Explanation

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The answer is **A. Hyperplasia of juxtaglomerular cells**.

This patient has **renal artery stenosis** (90% occlusion of the right renal artery), which is the classic cause of renovascular hypertension. The decreased renal blood flow distal to the stenosis reduces perfusion pressure to the juxtaglomerular apparatus, which directly stimulates **renin release** and, over time, causes **hyperplasia of the juxtaglomerular (JG) cells**.[1][2]

The pathophysiology follows the classic Goldblatt two-kidney, one-clip model: hypoperfusion of the JG apparatus activates the renin-angiotensin-aldosterone system (RAAS), increasing angiotensin II and aldosterone production. This leads to systemic vasoconstriction, sodium/water retention, and sustained hypertension.[3] Striking hyperplasia of the juxtaglomerular apparatus has been documented in cases of renovascular hypertension, with reversal of hypertension achievable by partial nephrectomy or ACE inhibitor use.[1]

Why the other options are incorrect:

- **B. Dilation of efferent arteriole** — Angiotensin II preferentially *constricts* the efferent arteriole (not dilates it), which helps maintain GFR in the setting of reduced renal perfusion.[4]
- **C. Decreased prostaglandin synthesis by macula densa** — Prostaglandin E2 synthesis by the macula densa is actually *increased* in response to reduced luminal NaCl delivery and low perfusion states. PGE2 is a key paracrine mediator that stimulates renin release from JG cells.[5][6]
- **D. Decreased reabsorption of bicarbonate at proximal tubule** — Angiotensin II stimulates proximal tubular sodium and bicarbonate reabsorption, so reabsorption would be *increased*, not decreased.[7]

Would you like to explore the clinical management of renovascular hypertension, including the role of ACE inhibitors/ARBs and indications for revascularization?

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Question 1187

A 15-year-old boy is brought to the emergency department because of severe abdominal pain and vomiting for 8 hours. He has had around 3–4 episodes of greenish colored vomit during this period. He has major depressive disorder with psychosis. His mother has Graves' disease. Current medications include sertraline and haloperidol. He appears uncomfortable. His temperature is 37.3°C (99.1°F), pulse is 87/min, and blood pressure is 118/72 mm Hg. He is diagnosed with acute appendicitis and is taken to the operating room for an emergency laparoscopic appendectomy. The appendix is gangrenous and perforated with purulent fluid in the pelvis. Just after the appendiceal base is ligated, the patient shows muscle rigidity and profuse diaphoresis. His temperature is 39.1°C (102.4°F), pulse is 130/min, and blood pressure is 146/70 mm Hg. The pupils are equal and reactive to light. The end-tidal CO2 is 85 mm Hg. Which of the following is the most appropriate treatment for this patient's condition?

Answer Choices:

(A) Dantrolene
(B) Bromocriptine
(C) Cyproheptadine
(D) Surgical embolectomy

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/19016906-e8c9-47a1-845b-ae502cb5258d

OpenEvidence Explanation

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The answer is **A. Dantrolene**. This clinical scenario — acute onset of **muscle rigidity, profuse diaphoresis, hyperthermia (39.1°C), tachycardia, and markedly elevated end-tidal CO_2 (85 mmHg)** occurring intraoperatively during general anesthesia — is classic for **malignant hyperthermia (MH)**, not neuroleptic malignant syndrome or serotonin syndrome.

Key distinguishing features pointing to malignant hyperthermia:

- **Timing**: Symptoms developed acutely during surgery under general anesthesia (exposure to inhalational anesthetic agents), which is the hallmark trigger for MH.[1]
- **Markedly elevated end-tidal CO_2 (85 mmHg)**: This is one of the earliest and most characteristic signs of MH, reflecting the hypermetabolic state with massive CO_2 production. A rising $ETCO_2$ is often the first indicator noticed by the anesthesiologist.[1]
- **Muscle rigidity + diaphoresis + rapid-onset hyperthermia** in the operative setting further support MH.

Why not the other options?

- **Bromocriptine (B)** is used for neuroleptic malignant syndrome (NMS). While this patient takes haloperidol (a dopamine antagonist that can cause NMS), NMS typically develops over **days**, not acutely intraoperatively, and does not cause a dramatically elevated $ETCO_2$.[1][2]
- **Cyproheptadine (C)** is the recommended antidote for serotonin syndrome. Although the patient takes sertraline, serotonin syndrome is characterized by **clonus, hyperreflexia, and myoclonus** rather than the lead-pipe rigidity and massively elevated $ETCO_2$ seen here.[1][3]
- **Surgical embolectomy (D)** would be indicated for a pulmonary embolism, which would not explain the muscle rigidity, diaphoresis, or hyperthermia.

Dantrolene is the definitive treatment for malignant hyperthermia. It is a direct-acting skeletal muscle relaxant that inhibits calcium release from the sarcoplasmic reticulum, thereby reducing the hypermetabolic crisis.[2] In MH, dantrolene should be administered immediately at a dose of 2.5 mg/kg IV, repeated as needed, along with discontinuation of all triggering anesthetic agents, active cooling, and correction of metabolic derangements.

Would you like to explore the specific perioperative risk factors and screening strategies for malignant hyperthermia susceptibility?

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Question 1188

After a T cell progenitor leaves the bone marrow, most of its development takes place in the thymus. It passes through several stages during its maturation. Positive selection is an important process during maturation of T lymphocytes, and it ensures the preservation of self-major histocompatibility complex (MHC)-restricted T cells. During which of the following developmental stages does a T cell undergo this process?

Answer Choices:

(A) Pre-T cell
(B) Double-positive T cell
(C) Single-positive CD4+ T cell
(D) Single-positive CD8+ T cell

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/62d030e6-8c26-473e-885a-970464f064c2

OpenEvidence Explanation

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The correct answer is **B. Double-positive T cell**.

Positive selection occurs at the **double-positive ($CD4^+$ $CD8^+$) stage** of T cell development in the thymic cortex. At this stage, thymocytes express both CD4

and CD8 co-receptors along with a newly rearranged αβ TCR. They interact with cortical thymic epithelial cells (cTECs) presenting self-peptide–MHC complexes: [1][2][3]

- DP thymocytes whose TCRs bind self-peptide–MHC with **moderate affinity** receive survival signals and are positively selected, subsequently differentiating into single-positive $CD4^+$ or $CD8^+$ T cells depending on whether the selecting MHC is class II or class I, respectively.[1][4]
- DP thymocytes that **fail to interact** with self-peptide–MHC undergo apoptosis ("death by neglect"), which accounts for approximately 90% of DP thymocytes.[2]
- DP thymocytes that bind with **excessively high affinity** can undergo negative selection.[1]

The following figure illustrates the spatial organization of positive selection in the cortex at the DP stage, followed by migration to the medulla as single-positive cells for further maturation and negative selection.

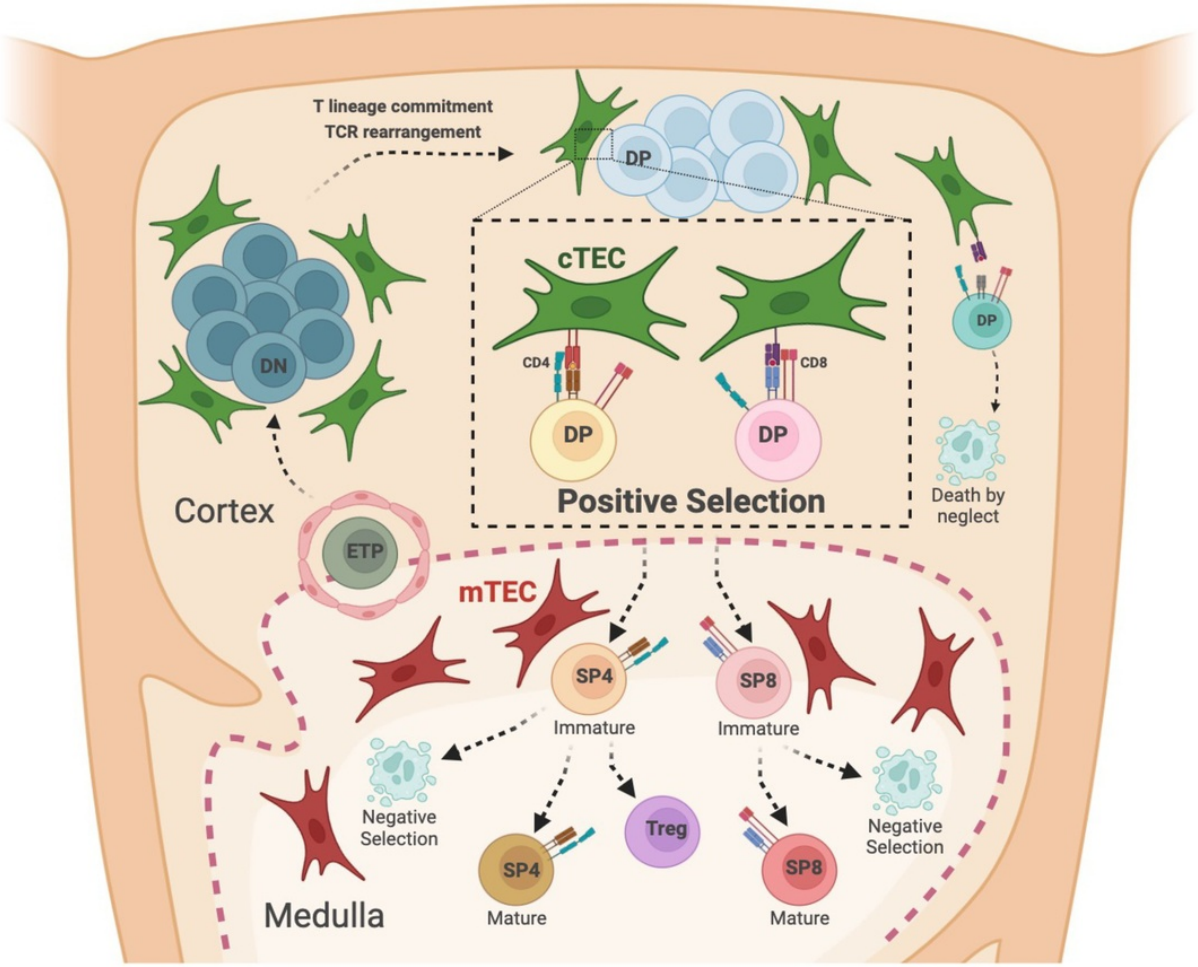


Figure 1. A general overview of the role of cTECs and mTECs in the development and selection of αβ T cells.

The other options are incorrect because:

- **Pre-T cells (A)** have not yet completed TCR rearrangement or expressed both co-receptors, so they cannot undergo MHC-restricted selection.
- **Single-positive $CD4^+$ (C) and $CD8^+$ (D) T cells** are the products of positive selection — they have already been selected and committed to a lineage.[3][5]

Would you like to explore how the thymoproteasome and other unique antigen-processing machinery in cortical thymic epithelial cells generate the specialized peptide repertoire that drives positive selection?

References

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Question 1189

A 28-year-old male presents with a recent onset of upsetting dreams, anxiety, and disturbing flashbacks. The patient reports that he returned from active duty in Iraq 3 months ago and was adjusting to life back at home until about 7 weeks ago when he began having intense fear of loud noises and seeing sudden flashbacks to bombing attacks he endured during his time in Iraq. He had to take a leave from his army instructor duties as he was not able to handle the familiar settings of practice shooting ranges and sudden loud explosions during battalion training. After refusing to leave his house, he was finally persuaded by his wife to visit your clinic. What is the most likely diagnosis?

Answer Choices:

(A) Acute stress disorder
(B) Performance anxiety
(C) Posttraumatic stress disorder
(D) Panic attack

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/8c16e76a-8fbd-4a8f-bdcd-62bea9416f58

OpenEvidence Explanation

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The most likely diagnosis is **C. Posttraumatic stress disorder (PTSD)**.

The critical distinguishing factor in this case is the **duration of symptoms**. This patient's symptoms — intrusive flashbacks, hyperarousal (fear of loud noises), avoidance behavior (refusing to leave the house, inability to tolerate shooting ranges), and distressing dreams — have been present for approximately **7 weeks**, which exceeds the 1-month threshold required for a PTSD diagnosis.[1][2]

Why the other options are incorrect:

- **A. Acute stress disorder (ASD):** ASD presents with similar symptoms to PTSD but is restricted to a duration of **3 days to 1 month** following traumatic exposure. Since this patient's symptoms have persisted for 7 weeks, ASD is excluded. Patients with ASD symptoms lasting longer than one month should be evaluated for PTSD.[1][2]

- **B. Performance anxiety:** Performance anxiety is situational anxiety related to task execution and is not associated with re-experiencing a traumatic event through flashbacks, nightmares, or hyperarousal triggered by trauma-related cues.[1]

- **D. Panic attack:** Panic attacks involve discrete episodes of intense fear with somatic symptoms (palpitations, shortness of breath, chest pain) that are not necessarily tied to a specific traumatic event. This patient's symptoms are clearly linked to combat trauma and include avoidance and re-experiencing, which are hallmarks of PTSD rather than isolated panic attacks.[1]

This presentation is classic for combat-related PTSD: a military veteran with exposure to life-threatening events (bombing attacks) who develops intrusive re-experiencing, avoidance of trauma-related stimuli, hyperarousal, and significant functional impairment (inability to work, social withdrawal) persisting beyond one month.[2][3] Delayed expression of PTSD is particularly common among deployed military personnel, accounting for approximately 25% of chronic PTSD cases.[3][4]

Would you like to explore the evidence-based first-line treatment options for combat-related PTSD, including the VA/DoD guideline recommendations for psychotherapy and pharmacotherapy?

Relevant images

(CONTENT OMITTED)

References

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Question 1190

A patient with a1-antitrypsin deficiency is warned by his physician that his increasing dyspnea may be worsened by his continued cigarette smoking. Which of the following factors, released by both neutrophils and alveolar macrophages, is responsible for the patient's condition?

Answer Choices:

(A) Major Basic Protein
(B) Mucus
(C) Surfactant
(D) Elastase

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/b3a50290-28e1-4ccd-95bf-862a7392c108

OpenEvidence Explanation

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The correct answer is **D. Elastase**.

Neutrophil elastase, released by both neutrophils and alveolar macrophages, is the key protease responsible for the lung destruction seen in alpha-1 antitrypsin (AAT) deficiency. AAT normally functions as a serine protease inhibitor that neutralizes neutrophil elastase in the lung. When AAT is deficient, unopposed

elastase activity cleaves structural proteins of the lung — particularly elastin — leading to alveolar wall destruction and **panacinar emphysema**.[1][2]

Cigarette smoking compounds this problem through two mechanisms: (1) oxidants in cigarette smoke directly inactivate residual AAT by oxidizing its active-site methionines, further reducing its ability to inhibit neutrophil elastase; and (2) smoking increases neutrophil recruitment and activation in the lungs, amplifying the protease burden.[1][3] This is the classic **protease–antiprotease imbalance** hypothesis of emphysema pathogenesis.[3][4]

Why the other options are incorrect:

- **A. Major Basic Protein** — released by eosinophils, not neutrophils/macrophages; involved in parasitic infections and allergic disease, not emphysema.
- **B. Mucus** — while mucus hypersecretion occurs in COPD (partly stimulated by neutrophil elastase itself), mucus is not the destructive factor causing emphysema.[5]
- **C. Surfactant** — produced by type II pneumocytes to reduce alveolar surface tension; not a destructive protease.

Would you like to explore the role of AAT augmentation therapy in slowing emphysema progression in patients with alpha-1 antitrypsin deficiency?

Relevant images

(CONTENT OMITTED)

References

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Question 1194

A 32-year-old male presents to the emergency department because of fever and diarrhea. He was in his normal state of health until 2 weeks ago when he went abroad on a vacation. During his trip he went kayaking, visited spas, interacted with local animals, and ate local foods. Since returning he has had 3-day history of fever, cough, headache, and diarrhea. He drinks socially and has a 15-pack-year history of smoking. On presentation his temperature is 102.3°F (39.1°C), blood pressure is 105/62 mmHg, pulse is 91/min, respirations are 18/min, and O2 saturation is 91% on room air. Chest exam reveals fine crackles on auscultation. Chest radiograph reveals patchy infiltrates in both lungs and labs reveal mild hyponatremia and mild elevation of AST/ALT levels. The organism that is most likely responsible for this patient's symptoms is associated with which of the following characteristics?

Answer Choices:

(A) Can form an endospore
(B) Has no cell wall
(C) Is more common in parrot owners
(D) Is transmitted by air conditioning

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/74732a59-3fa4-471d-b783-9e4330d30d72

OpenEvidence Explanation

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The answer is **D. Is transmitted by air conditioning**.

This clinical presentation — pneumonia with fever, cough, headache, **diarrhea**, **hyponatremia**, **elevated transaminases**, and bilateral patchy infiltrates in a traveler with exposure to spas and water activities — is classic for **Legionnaires' disease** caused by *Legionella pneumophila*.

Why air conditioning is the correct association:

Legionella pneumophila thrives in warm freshwater environments and is most commonly transmitted via inhalation of contaminated aerosols from man-made water systems. The most important epidemiological reservoirs include **cooling towers associated with large air conditioning systems**, hot tubs, whirlpool spas, plumbing systems, and fountains.[1][2][3] This patient's exposure to spas during travel is a well-recognized risk factor. Large outbreaks have been repeatedly linked to contaminated cooling towers and evaporative air conditioning units.[2][4]

Why the other options are incorrect:

- **A (Endospore formation):** *Legionella* is a gram-negative rod that does not form endospores. Endospore-forming organisms include *Bacillus* and *Clostridium* species.
- **B (No cell wall):** This describes *Mycoplasma pneumoniae*, which causes atypical pneumonia but typically presents in younger patients with a more indolent course and lacks the prominent GI symptoms, hyponatremia, and liver enzyme elevations seen here.
- **C (More common in parrot owners):** This describes *Chlamydia psittaci* (psittacosis), which causes atypical pneumonia associated with bird exposure. While it can cause hepatitis and pneumonia, the constellation of diarrhea, hyponatremia, and spa/water exposure points away from psittacosis.

The classic diagnostic triad to remember for Legionella is pneumonia with prominent **GI symptoms** (especially diarrhea), **hyponatremia**, and **elevated liver enzymes**, particularly in the setting of exposure to contaminated water systems. [3][5][6]

Would you like to explore the diagnostic approach and optimal antibiotic management for suspected Legionnaires' disease?

References

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Question 1195

A 14-year-old boy presents to the emergency department with hand pain after falling from his skateboard one day ago. He reports that he lost his balance while attempting a new trick and fell on his outstretched hands. He has been icing his hand and taking several tablets of ibuprofen every few hours, but the pain and swelling have not improved. The patient reports that he has not been able to use the hand to take notes in school. His past medical history is significant for infectious mononucleosis last year and type 1 diabetes mellitus for which he has an insulin pump. On physical exam, there is mild swelling over the dorsal aspect of the hand and wrist. He has tenderness in the region between the extensor pollicus longus and the extensor pollicus brevis of the right hand.

Which of the following is the best next step in management?

Answer Choices:

(A) Radiograph of the wrist
(B) MRI of the wrist
(C) Thumb spica cast
(D) Radial gutter cast

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/b10ec4b7-6425-4427-87a6-9654fd3dedeb

OpenEvidence Explanation

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The best next step in management is **A. Radiograph of the wrist**.

This patient presents with a classic mechanism for a **scaphoid fracture** — a fall on an outstretched hand (FOOSH) — and has tenderness in the **anatomical snuffbox** (the region between the extensor pollicis longus and extensor pollicis brevis), which is the hallmark physical examination finding for suspected scaphoid injury.[1][2] The scaphoid is the most commonly fractured carpal bone, and in adolescents, fracture patterns are similar to those in adults, with the majority occurring at the scaphoid waist.[3]

Why radiograph first? Plain radiographs are the **initial imaging modality of choice** for suspected scaphoid fractures.[1][4] The standard workup begins with wrist radiographs (typically four views: posteroanterior, lateral, semipronated oblique, and PA in ulnar deviation).[1][5] Most scaphoid fractures are identified on initial radiographs, though up to 16–30% may be missed.[1][5]

Why not the other options?

- **MRI (B)** — MRI is a second-line imaging modality reserved for cases where radiographs are negative but clinical suspicion remains high (occult fracture). It should not be ordered before obtaining plain radiographs.[4][6][7]
- **Thumb spica cast (C)** — While empiric immobilization with a thumb spica cast is sometimes used when radiographs are negative but suspicion persists, applying a cast without any imaging is not the appropriate first step. A diagnosis should be established or at least initial imaging obtained before immobilization.[1][7]
- **Radial gutter cast (D)** — A radial gutter cast is used for metacarpal fractures (e.g., 2nd or 3rd metacarpal), not for scaphoid fractures. Scaphoid fractures, when immobilized, are treated with a thumb spica cast.[7]

Would you like to explore the management algorithm for when initial scaphoid radiographs are negative but clinical suspicion remains high?

References

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Question 1196

A 22-year-old woman comes to the physician for the evaluation of irregular menstrual bleeding. Menses have occurred at 45- to 90-day intervals since menarche at the age of 15 years. Her last menstrual period was 5 weeks ago. The patient reports that she was too embarrassed to discuss this issue with anyone until now. Over the past two years, she was unable to become pregnant despite having unprotected sexual intercourse with her husband on a regular basis. There is no personal or family history of serious illness. She is 170 cm (5 ft 7 in) tall and weighs 85 kg (187 lb); BMI is 29.4 kg/m2. Her vital signs are within normal limits. Examination shows oily skin and severe facial acne. There is abnormal pigmented hair on the upper lip and around both nipples. The patient wishes to have children. In addition to recommending lifestyle modifications, which of the following is the most appropriate step in management?

Answer Choices:

(A) In vitro fertilization with patient's egg
(B) Progesterone therapy
(C) Clomiphene therapy
(D) Leuprolide therapy

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/ab69cc32-fc18-4a0c-8338-9d0d81a1174b

OpenEvidence Explanation

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The correct answer is **C. Clomiphene therapy**.

This patient presents with classic features of **polycystic ovary syndrome (PCOS)**: oligomenorrhea (cycles at 45–90 day intervals since menarche), anovulatory infertility, overweight/obesity (BMI 29.4), and clinical hyperandrogenism (oily skin, severe acne, hirsutism). She desires fertility, making ovulation induction the appropriate first-line pharmacological intervention alongside lifestyle modifications.

Why clomiphene (or letrozole) is correct: For anovulatory infertility in PCOS with no other infertility factors, ovulation induction is the standard first-line approach. Clomiphene citrate is a selective estrogen receptor modulator that blocks negative feedback of estradiol, increasing GnRH pulse frequency and pituitary FSH/LH production to promote follicular growth and ovulation.[1] It is the correct answer among the choices listed.

It is worth noting that current guidelines now recommend **letrozole** over clomiphene as the preferred first-line agent, based on superior live birth rates (27.5% vs 19.1% in the PPCOS II trial) and higher ovulation and clinical pregnancy rates.[1][2][3] However, letrozole is not among the answer choices, making clomiphene the best available option.

Why the other options are incorrect:

- **A. In vitro fertilization** — IVF is reserved as third-line therapy after failure of ovulation induction and gonadotropins; it is premature and unnecessarily invasive at this stage.[4]
- **B. Progesterone therapy** — Progesterone can regulate menstrual cycles and protect the endometrium but does not induce ovulation or treat infertility.[5]
- **D. Leuprolide therapy** — A GnRH agonist that suppresses gonadotropin secretion and would worsen anovulation; it is not used for ovulation induction in PCOS.

The following figure illustrates the management algorithm for PCOS based on whether the patient desires pregnancy:

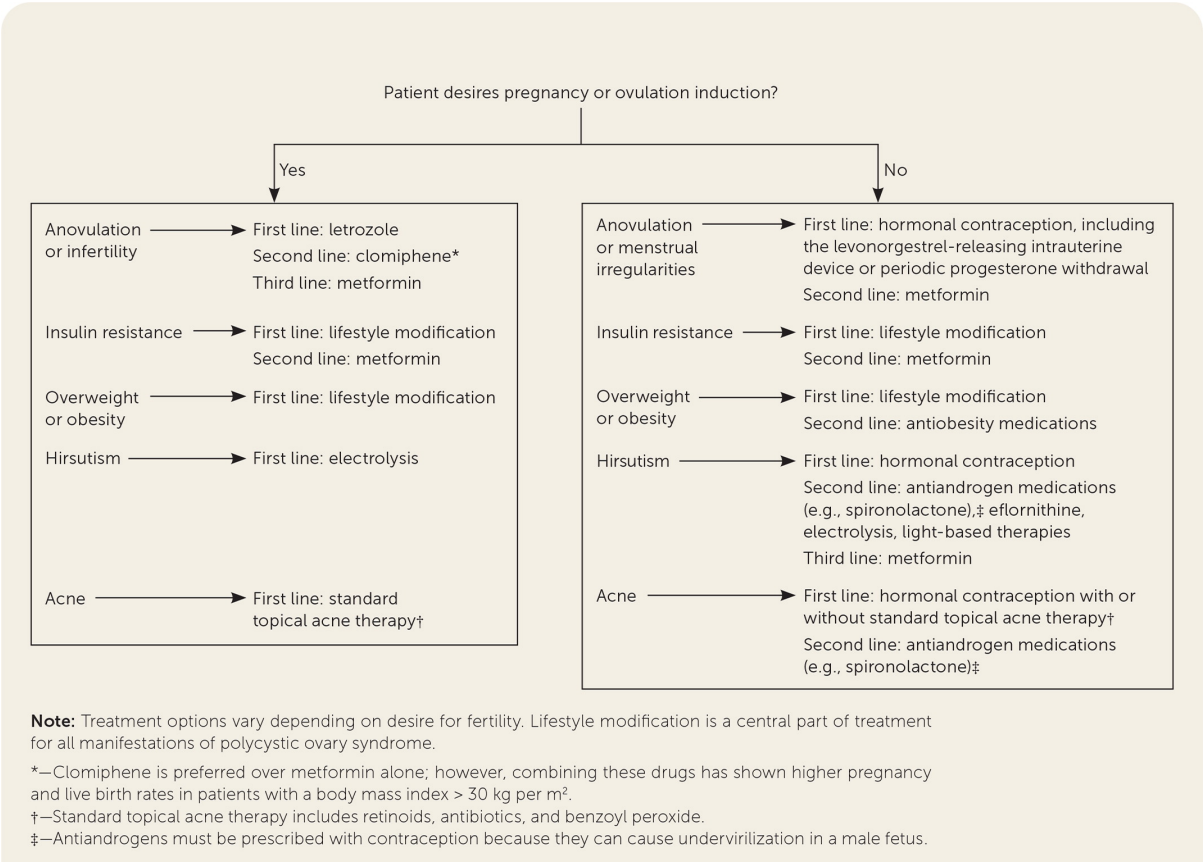


Figure 2. Management of polycystic ovary syndrome. Adapted with permission from Williams T, Mortada R, Porter S. Diagnosis and treatment of polycystic ovary syndrome. Am Fam Physician. 2016;94(2):109, with additional information from references 4 and 5.

Would you like to explore the stepwise approach to ovulation induction in PCOS, including when to escalate from first-line agents to gonadotropins or IVF?

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Question 1198

A 27-year-old man with a history of cocaine abuse comes to the physician 2 weeks after undergoing successful arthroscopic repair of a torn medial collateral ligament in his left knee. There were no complications. He was discharged with prescriptions for oxycodone and acetaminophen. He complains of severe pain that prevents him from participating in physical therapy and wakes him from sleep. Physical examination of the left knee shows a healing incision; there is no joint effusion, erythema, or evidence of wound dehiscence, and his gait is normal. When the physician recommends switching to ibuprofen for pain, he becomes visibly angry and demands a refill of oxycodone. Which of the following is the most appropriate response to this patient's request?

Answer Choices:

(A) Prescribe a long-acting opioid for better pain relief if he is willing to sign a pain contract
(B) Request further information about which drugs he has taken recently and in the past
(C) Request consent for urine test to assess current drug use
(D) Refer to a substance use counselor for addiction counseling

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/e31d2540-330e-46bd-96ce-d038872b159a

OpenEvidence Explanation

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The most appropriate response is **B. Request further information about which drugs he has taken recently and in the past**.

Before making any prescribing decision in a patient with a known history of cocaine abuse who is displaying concerning behaviors (pain out of proportion to exam findings, anger when a non-opioid alternative is suggested), the critical first step is to **gather a thorough substance use history**. This includes asking about current and past drug use — both illicit and prescription — to properly assess risk and guide management.

The CDC Clinical Practice Guideline for Prescribing Opioids (2022) explicitly recommends that clinicians **ask patients about their drug and alcohol use** when considering opioid prescriptions, particularly in patients with substance use disorders.[1] Validated single screening questions (e.g., "How many times in the past year have you used an illegal drug or used a prescription medication for nonmedical reasons?") have been shown to be 100% sensitive and 73.5% specific for detecting drug use disorders.[1] This information is essential to determine whether the patient has active polysubstance use, whether opioids have been misused, and whether the clinical picture is consistent with drug-seeking behavior versus undertreated pain.

Why the other options are less appropriate:

- **A (Long-acting opioid with pain contract):** Escalating to a long-acting opioid in a patient with a substance use history and a benign postoperative exam 2 weeks after arthroscopic surgery is inappropriate and increases risk for opioid use disorder and overdose.[1]
- **C (Urine drug test):** While urine toxicology screening is a useful adjunct, it should supplement — not replace — a direct conversation with the patient about substance use. Jumping to a urine test without first taking a history can feel punitive and damage the therapeutic relationship.
- **D (Substance use counselor referral):** Referral may ultimately be appropriate, but it is premature before gathering the necessary history to

determine whether the patient meets criteria for a substance use disorder or is at risk for one.[1][2]

The clinical picture here — normal gait, healing incision, no effusion or erythema at 2 weeks post-arthroscopy, with disproportionate pain complaints and anger at opioid discontinuation — raises concern for opioid misuse. However, the appropriate next step is a nonjudgmental, thorough substance use assessment before determining the management plan.[2]

Would you like to explore evidence-based strategies for managing acute postoperative pain in patients with active or historical substance use disorders?

References

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Question 1200

A 28-year-old man is brought to the emergency department because of a 3-day history of fever, chills, and generalized weakness. He has no cough. He was treated for a neck abscess 6 months ago. He takes no medications. He has smoked one pack of cigarettes daily for 10 years and drinks two to three beers daily. He has been using intravenous cocaine and heroin for 6 years. He appears ill. His temperature is 38.6°C (101.5°F), pulse is 112/min, respirations are 20/min, and blood pressure is 110/70 mm Hg. Examination shows track marks on both cubital fossae. There are retinal hemorrhages with pale centers. The lungs are clear to auscultation. A grade 3/6 holosystolic murmur is heard best at the lower left sternal border.
Laboratory studies show:
Hemoglobin 13.3 g/dL
Leukocyte count 14,300/mm3
Platelet count 278,000/mm3
Serum
Glucose 96 mg/dL
Creatinine 1.0 mg/dL
Total bilirubin 0.4 mg/dL
AST 18 U/L
ALT 22 U/L
Transthoracic echocardiography shows multiple vegetations on the tricuspid valve and moderate tricuspid regurgitation. Two sets of blood cultures are collected. Which of the following is the most appropriate next step in management?

Answer Choices:

(A) Transesophageal echocardiography
(B) Intravenous vancomycin therapy
(C) X-ray of the chest
(D) CT pulmonary angiogram

Correct Answer:

(B)

> **OpenEvidence Response:**
>
> **(B)** ✓

OpenEvidence Link: https://openevidence.com/ask/9a7f3263-2ec3-4b64-b7f2-865f213dd26c

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OpenEvidence Explanation

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The most appropriate next step is **B. Intravenous vancomycin therapy**.

This patient presents with classic infective endocarditis (IE) in the setting of intravenous drug use: fever, Roth spots (retinal hemorrhages with pale centers), a new holosystolic murmur at the lower left sternal border (tricuspid regurgitation), and TTE confirming tricuspid valve vegetations. The diagnosis is essentially established, and the priority is initiating **empiric antimicrobial therapy** while awaiting blood culture results.

Why vancomycin? In people who inject drugs, **Staphylococcus aureus** — particularly MRSA — is the most common causative organism of right-sided IE. AHA/IDSA guidelines recommend empiric coverage with anti-MRSA antibiotics such as vancomycin when gram-positive organisms are suspected, with tailoring once culture and susceptibility data are available.[1] The standard vancomycin dose is 30 mg/kg per 24 hours divided into 2–3 doses intravenously.[1]

Why not the other options?

- **Transesophageal echocardiography (A):** TEE is recommended when TTE is nondiagnostic, when complications are suspected (abscess, fistula), or in prosthetic valve IE. Here, TTE has already identified vegetations and characterized the valve lesion. For uncomplicated right-sided native valve IE, TTE alone may be sufficient given the anterior location of the tricuspid valve. TEE is not the immediate priority over starting antibiotics.[1][2][3][4]

- **Chest X-ray (C):** While a chest radiograph is reasonable to evaluate for septic pulmonary emboli (common with tricuspid valve IE), it does not take precedence over initiating antimicrobial therapy in a febrile, tachycardic patient with confirmed endocarditis.
- **CT pulmonary angiogram (D):** This would evaluate for pulmonary embolism, but the patient has no respiratory symptoms, and the clinical picture is explained by IE. This is not the most appropriate next step.

The critical action is to **start empiric antibiotics promptly** once blood cultures have been drawn, as delays in antimicrobial therapy increase morbidity and mortality in IE.[2]

Would you like to explore the specific antibiotic regimens and duration of therapy for right-sided native valve endocarditis in people who inject drugs, including the evidence for shortened courses?

References

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Question 1203

A 36-year-old man presents to his physician for a regular checkup, and he expresses an intent to quit smoking. He is a financial director with a 15-pack-year history of smoking who tried quitting several times. He tried different nicotine replacement products, none of which helped him. The patient has gastrointestinal reflux disease and takes omeprazole. The medical history is significant for a head trauma after which he had two seizure episodes. He does not have a history of any other disorders. Currently, he is not on any antiepileptic medication. He heard from his friend about an antidepressant that efficiently helps with smoking cessation. He would like to try this medication, and asks his physician for an advice. Which of the following statements regarding the use of the mentioned medication is correct?

Answer Choices:

(A) Omeprazole interferes with bupropion metabolism and should be taken one hour prior to omeprazole consumption.
(B) Bupropion is only effective when used together with nicotine replacement products.
(C) Bupropion lowers the seizure threshold and it should not be taken by patients with a history of seizure disorder.
(D) The physician may prescribe bupropion for this patient only after a full cardiac workup is performed.

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/3230056b-5713-4c12-b473-8a4076cdca9c

OpenEvidence Explanation

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The correct answer is **C. Bupropion lowers the seizure threshold and it should not be taken by patients with a history of seizure disorder.**

The medication described — an antidepressant that helps with smoking cessation — is **bupropion** (sustained-release), which is FDA-approved for both major depressive disorder and smoking cessation.[1][2] This patient's history of head trauma followed by two seizure episodes represents a key contraindication.

Why C is correct:

The FDA label explicitly states that bupropion **is contraindicated in patients with a seizure disorder** and in conditions that increase seizure risk, including **severe head injury**.[3][4][5] Bupropion has the highest disproportionality signal for seizures among all antidepressants (ROR 8.57).[6] The ACC Expert Consensus and NCCN guidelines both state that bupropion reduces the seizure threshold and should not be used in patients at increased risk for seizures.[2][7]

Why the other options are incorrect:

- **A** is incorrect because omeprazole does not have a clinically significant interaction with bupropion metabolism. Bupropion is primarily metabolized by **CYP2B6**, whereas omeprazole inhibits CYP2C19 and CYP3A4. There is no recommendation to separate their administration.[8][9]
- **B** is incorrect because bupropion is **effective as monotherapy** for smoking cessation. A Cochrane meta-analysis demonstrated that bupropion alone significantly increases quit rates compared to placebo (RR 1.64; 95% CI, 1.52–1.77). While combination with NRT may enhance efficacy, bupropion does not require co-administration with NRT.[1][2][10]
- **D** is incorrect because there is no requirement for a cardiac workup before prescribing bupropion. Clinical trials in patients with cardiovascular disease have found no evidence of increased cardiovascular events compared with placebo.[2][11]

Would you like to explore alternative pharmacotherapy options (such as varenicline) for smoking cessation in patients with a seizure history?

Relevant images

(CONTENT OMITTED)

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Question 1204

A 32-year-old woman, gravida 2, para 0, at 22 weeks' gestation comes to the emergency department for abdominal pain and heavy vaginal bleeding for 2 hours. She has had no prenatal care. Her temperature is 37.2°C (99.0°F), pulse is 102/min, respirations are 16/min, and blood pressure is 138/82 mm Hg. The abdomen is nontender, and regular contractions are felt every 2 minutes. The uterus is consistent in size with a 20-week gestation. There is blood on the vulva, introitus, and medial aspect of the thighs. Ultrasound shows complete detachment of the placenta from the uterus. Fetal heart tones are absent. An emergent cesarean delivery is performed. Following the procedure, the patient becomes tearful and distraught. Which of the following is the most appropriate initial response by the physician?

Answer Choices:

(A) “I'm sorry for your loss. This must be a difficult situation for you.”
(B) “Losing a baby is difficult, but I'm sure next time it'll work out.”
(C) “Losing a baby is difficult; but I see this every day, and I know you'll get through it.”
(D) “I'm sorry for your loss. I can write you a prescription to help with your anxiety and grief.”

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/ca4867be-891f-4bd1-837a-00dccf574d43

OpenEvidence Explanation

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The most appropriate initial response is **A. "I'm sorry for your loss. This must be a difficult situation for you."**

This response demonstrates **empathetic acknowledgment** — it validates the patient's grief, expresses compassion, and opens space for the patient to share her feelings without minimizing the loss or prematurely offering solutions.

Why the other options are inappropriate:

- **B** ("I'm sure next time it'll work out") minimizes the current loss by redirecting to a hypothetical future pregnancy. This is a form of **false reassurance** that dismisses the patient's present grief and is particularly insensitive given her history of two pregnancies with no living children (G2P0).
- **C** ("I see this every day") normalizes the loss in a way that centers the physician's experience rather than the patient's. Telling a grieving mother that fetal demise is routine is dismissive and undermines the therapeutic relationship.
- **D** (offering a prescription) bypasses the emotional moment entirely and **medicalizes a normal grief response**. Acute grief following pregnancy loss is expected, not pathological. Pharmacologic intervention is not appropriate as an initial response; the patient first needs emotional support and acknowledgment.

The cornerstone of effective physician communication in acute grief is **empathic presence** — acknowledging the loss, validating the emotional response, and allowing the patient to process before moving to any next steps.

Would you like to explore evidence-based frameworks for breaking bad news in obstetric settings, such as the SPIKES protocol?

Question 1207

A 23-year-old man presents with swelling of the left knee. He noticed the swelling a day ago while preparing for the college basketball game. He has had approximately 10 different sexual partners in the past 3 months. Synovial fluid tap shows a WBC count of 90,000 cells/mm3. What is the mechanism of action of the drug which is indicated for the treatment of this patient's most likely condition?

> **Answer Choices:**
>
> (A) Metabolic inhibitor
> (B) Cell wall inhibitor
> (C) Neutrophil migration inhibitor
> (D) Prostaglandin inhibitor

> **Correct Answer:**
>
> **(B)**
>
> **OpenEvidence Response:**
>
> **(B)** ✓

OpenEvidence Link: https://openevidence.com/ask/b0bfd71d-1c51-492c-b3ec-6133fd61c4de

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OpenEvidence Explanation

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The answer is **B. Cell wall inhibitor**.

This clinical scenario describes a young, sexually active male with acute monoarticular knee swelling and a **synovial fluid WBC count of 90,000 cells/**

mm³, which is consistent with **septic arthritis**. Given his high-risk sexual behavior (10 partners in 3 months), the most likely causative organism is **Neisseria gonorrhoeae** — the leading cause of septic arthritis in sexually active adolescents and young adults.[1]

The treatment of choice for gonococcal septic arthritis is **ceftriaxone**, a third-generation cephalosporin.[1][2][3] Ceftriaxone is a bactericidal agent that acts by **inhibition of bacterial cell wall synthesis** — it binds to penicillin-binding proteins (PBPs), blocking the transpeptidase-mediated cross-linking of peptidoglycan in the bacterial cell wall, which leads to cell lysis.[4][5]

The other answer choices correspond to different drug classes:

- **A (Metabolic inhibitor)** — e.g., trimethoprim or sulfonamides (folate synthesis inhibitors)
- **C (Neutrophil migration inhibitor)** — e.g., colchicine (used for gout/crystal arthropathy)
- **D (Prostaglandin inhibitor)** — e.g., NSAIDs (anti-inflammatory, not antimicrobial)

Would you like to explore how to distinguish gonococcal from non-gonococcal septic arthritis based on synovial fluid analysis and clinical features?

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Question 1208

Which of the following patient presentations seen in a pediatric immunology clinic is most consistent with a diagnosis of Bruton's agammaglobulinemia?

Answer Choices:

(A) A 15-month-old girl who has had repeated otitis media, pneumonia, and progressive clumsiness since beginning to walk in the past three months
(B) A 10-month-old boy who has had recurrent viral infections as well as hypocalcemia during neonatal period
(C) A 4-year-old girl who has had repeated oral candidasis in the past nine months
(D) A 9-month-old boy who has had recurrent otitis media and pneumococcal pneumonia in the past three months

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/34b76bc5-63bd-4642-9da4-83714ff10235

OpenEvidence Explanation

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The answer is **D. A 9-month-old boy who has had recurrent otitis media and pneumococcal pneumonia in the past three months**.

Bruton's agammaglobulinemia (X-linked agammaglobulinemia, XLA) is caused by mutations in the *BTK* gene and has several cardinal features that align perfectly with this presentation:

- **X-linked inheritance** — affects **males** almost exclusively, immediately making the two girls in options A and C far less likely.[1][2]
- **Onset after maternal antibody waning** — affected boys are typically well for the first 6–12 months of life due to transplacentally acquired maternal IgG, then develop recurrent infections as these antibodies decline.[2][3][4]
- **Recurrent bacterial sinopulmonary infections** — the hallmark infections are **otitis media, sinusitis, and pneumonia**, caused predominantly by encapsulated organisms such as *Streptococcus pneumoniae* and *Haemophilus influenzae*. Chronic fungal infections and most viral infections are handled normally (T-cell function is intact).[2][3][5][6]

Why the other options are less consistent:

- **A (15-month-old girl, otitis/pneumonia + progressive clumsiness):** The female sex argues against XLA. The progressive ataxia raises concern for **ataxia-telangiectasia**, which presents with combined immunodeficiency and cerebellar degeneration.
- **B (10-month-old boy, recurrent viral infections + neonatal hypocalcemia):** Recurrent viral infections and neonatal hypocalcemia are classic for **DiGeorge syndrome** (22q11.2 deletion), a T-cell deficiency associated with thymic hypoplasia and parathyroid dysfunction.[6]
- **C (4-year-old girl, recurrent oral candidiasis):** Chronic mucocutaneous candidiasis points toward a **T-cell or combined immunodeficiency**, not a pure B-cell/antibody deficiency. XLA patients rarely develop chronic fungal infections.[6]

Option D presents the classic triad: a **male infant**, presenting after **6 months of age** with **recurrent bacterial infections** (otitis media and pneumococcal pneumonia) — the prototypical presentation of Bruton's agammaglobulinemia.[2][3][5]

Would you like to explore the diagnostic workup for suspected XLA, including the role of flow cytometry for B-cell enumeration and BTK protein analysis?

Relevant images

(CONTENT OMITTED)

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Question 1209

A 29-year-old man is brought to the emergency department by a concerned neighbor. The patient appears disheveled, has a flat affect, and appears to be having auditory hallucinations. He is alert and oriented to time, person, and place and has an intact long-term and short-term memory. His neighbor says that he never really knew the patient that well and that he mostly kept to himself. They have been neighbors for the past 3 years at an apartment close to the hospital. What worried the neighbor was a sudden change in the patient's behavior which started last week. He suddenly seemed interested in attending all the local council meetings and social gatherings. He is very talkative at these events and boasts highly of himself and starts suggesting changes that the committee could make with his help. He gets very agitated when they deny accepting his suggestions. Which of the following is a predictor of good prognosis for this patient's condition?

Answer Choices:

(A) Affective symptoms
(B) Being single
(C) Male sex
(D) Negative symptoms

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/49ec2f00-427a-4974-b5bf-f158641fbd8f

OpenEvidence Explanation

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The answer is **A. Affective symptoms**.

This clinical vignette describes a patient with features consistent with **schizophrenia** — auditory hallucinations, flat affect, social withdrawal (keeping to himself for years), and now a sudden change with grandiosity, talkativeness, and agitation — and the question asks about predictors of good prognosis.

Among the options, **affective symptoms** (such as depressive or mood-related features) are a well-established predictor of favorable prognosis in schizophrenia. The presence of prominent affective symptoms has traditionally been associated with better outcomes, as it may indicate a schizoaffective component or a more treatment-responsive illness phenotype.[1] Women with schizophrenia, who more commonly present with affective symptoms, tend to have a more favorable prognosis, later onset, and better treatment response.[1][2]

The other options are associated with **worse** prognosis:

- **Being single (B):** Social isolation and lack of a partner are associated with poorer functional outcomes.[3]
- **Male sex (C):** Male gender is consistently linked to earlier onset, more severe negative symptoms, worse cognitive impairment, and poorer overall functional outcomes compared to females.[1][2][4][5]
- **Negative symptoms (D):** Higher baseline negative symptom scores (e.g., flat affect, avolition, social withdrawal) are among the strongest predictors of poor long-term outcome, including lower rates of remission and worse functional recovery.[5][6][7]

Would you like to explore the specific factors that differentiate schizoaffective disorder from schizophrenia and how this distinction affects treatment approach?

Relevant images

(CONTENT OMITTED)

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Question 1213

A 62-year-old man comes to the physician because of worsening involuntary movements of both arms for the past 7 months. He reports that certain daily activities have become more difficult to perform. His father had a similar condition that was treated with medications. The patient appears anxious. Vital signs are within normal limits. Examination shows a low-amplitude tremor bilaterally when the arms are outstretched that worsens when reaching out to grab a pen. Muscle strength and tone is normal bilaterally. Deep tendon reflexes are 2+ bilaterally. On mental status examination, his mood is good. His speech is normal in rate and rhythm. Which of the following is the most appropriate next step in management?

Answer Choices:

(A) Deep brain stimulation
(B) Thalamotomy
(C) Levodopa and carbidopa therapy
(D) Propranolol therapy

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/d1eb3b68-979c-485b-b2bd-4654451a2676

OpenEvidence Explanation

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The correct answer is **D. Propranolol therapy**.

This patient presents with classic **essential tremor (ET)** — a bilateral postural and kinetic tremor (present when arms are outstretched and worsening with intentional movement), positive family history, normal muscle tone and strength, and normal deep tendon reflexes. The absence of resting tremor, rigidity, or bradykinesia effectively rules out Parkinson disease, making levodopa/carbidopa (option C) inappropriate.

Propranolol is the first-line pharmacological treatment for essential tremor and the only FDA-approved medication for this indication.[1][2] The American Academy of Neurology classifies both propranolol and primidone as **Level A (established as effective)** for ET.[2] Across randomized controlled trials, propranolol at doses of 120–240 mg/day reduced tremor amplitudes by approximately **55%** as measured by accelerometry.[1] The International Parkinson and Movement Disorder Society similarly classifies propranolol and primidone as "clinically useful".[3]

> "Because the patient has not yet received any therapy for essential tremor and reports that tremor interferes with daily life tasks, we would recommend treatment initiation with either propranolol or primidone, with a gradual dose adjustment to target doses."
>
> —Dietrich Haubenberger, M.H.Sc., M.D. et al., National Institute of Neurological Disorders and Stroke and other institutions. Essential Tremor. N Engl J Med. May 10, 2018.
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Deep brain stimulation (option A) and **thalamotomy** (option B) are reserved for patients with severe, medication-refractory essential tremor and are not appropriate as initial management.[4][5] These interventional approaches carry procedural risks and are only considered after pharmacotherapy has failed to provide adequate relief.

Would you like to explore the approach to essential tremor that is refractory to first-line pharmacotherapy, including the role of focused ultrasound thalamotomy versus deep brain stimulation?

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Question 1214

Ten days after undergoing a cadaveric renal transplant, a 21-year-old man has pain in the right lower abdomen and generalized fatigue. During the past 2 days, he has had decreasing urinary output. He passed 5 liters of urine on the second postoperative day and serum studies showed a creatinine concentration of 2.1 mg/dL. He has adult polycystic kidney disease and was on maintenance hemodialysis for 2 months prior to transplantation. Current medications include azathioprine, cyclosporine, prednisone, and enalapril. He appears lethargic. His temperature is 37.8°C (100°F), pulse is 101/min, and blood pressure is 164/94 mm Hg. Examination shows a healing surgical incision in the right lower abdomen. The graft site shows tenderness to palpation. His blood urea nitrogen concentration is 52 mg/dL, creatinine concentration is 4.1 mg/dL. A biopsy of the transplanted kidney shows tubulitis. C4d staining is negative. Which of the following is the most likely responsible for this patient's findings?

Answer Choices:

(A) Recipient T-cells in the graft
(B) Drug-induced nephrotoxicity
(C) Fibrosis of the glomerular vessels
(D) Newly formed anti-HLA antibodies

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/592bb961-ac9e-4253-a285-6247ca9a0e02

OpenEvidence Explanation

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The answer is **A. Recipient T-cells in the graft**, consistent with **acute T-cell–mediated rejection (TCMR)**.

The key findings that point to this diagnosis are:

- **Tubulitis on biopsy** — infiltration of mononuclear cells (lymphocytes) into the tubular epithelium is the hallmark histologic feature of acute TCMR per the Banff classification. Mononuclear cell tubulitis is significantly more common in C4d-negative rejection (100%) compared to C4d-positive/antibody-mediated rejection (70%).[1][2][3]
- **Negative C4d staining** — C4d deposition in peritubular capillaries is a specific marker of antibody-mediated rejection (AMR), reflecting complement activation via the classical pathway triggered by donor-specific antibodies. A negative C4d stain effectively rules against AMR and supports a cell-mediated (T-cell) process.[4][5]
- **Timing (day 10 post-transplant)** — Acute rejection in the first year is primarily T-cell–mediated, with fewer cases of antibody-mediated rejection. Acute cellular rejection typically presents within the first weeks to months after transplantation.[1]
- **Clinical presentation** — Rising creatinine (2.1 → 4.1 mg/dL), decreasing urine output, graft tenderness, low-grade fever, and lethargy are classic features of acute allograft rejection.[2]

Why not the other options:

- **B (Drug-induced nephrotoxicity)** — Cyclosporine nephrotoxicity can cause rising creatinine, but biopsy would show arteriolar hyalinosis and tubular vacuolization, not tubulitis with inflammatory infiltrates.
- **C (Fibrosis of glomerular vessels)** — This describes chronic rejection/transplant glomerulopathy, which occurs months to years post-transplant, not at 10 days.

- **D (Newly formed anti-HLA antibodies)** — This would cause antibody-mediated rejection, which is characterized by positive C4d staining, capillaritis, and circulating donor-specific antibodies — none of which are present here.[4][5]

Would you like to explore the current treatment protocols for acute T-cell–mediated rejection, including the role of pulse corticosteroids versus T-cell–depleting agents for steroid-resistant cases?

Relevant images

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Question 1215

A 58-year-old woman presents to the office for routine follow-up. She recently underwent routine screening for bone density due to a history of hypothyroidism. She also has a history of gastroesophageal reflux disease (GERD) that is being treated with a proton-pump inhibitor (PPI) and more recently with a histamine2 receptor antagonist (H2RA), hypertension being treated with a thiazide diuretic, depression being treated with lithium, and hormone replacement therapy. Her results meet the criteria for osteopenia, with a T-score of -1.6. She is concerned about progressive bone loss and the risk of fractures. Which of the following medication classes should be discontinued?

Answer Choices:

(A) Proton-pump inhibitors
(B) Thiazide diuretics
(C) Lithium
(D) Estrogen

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/8034e7ae-e719-429b-812a-0a469c0f5466

OpenEvidence Explanation

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The answer is **A. Proton-pump inhibitors**.

PPIs are the medication class that should be discontinued in this patient with osteopenia and concern for progressive bone loss. PPI use has been associated with a **moderately increased risk of fractures** at multiple sites, including hip (HR 1.22), spine (HR 1.49), and any-site fractures (HR 1.30) in meta-analyses.[1][2] The proposed mechanisms include hypochlorhydria-associated malabsorption of calcium, gastrin-induced parathyroid hyperplasia, and PPI-induced hypomagnesemia, which can secondarily cause hypocalcemia.[3][4] Importantly, this patient already has an alternative acid-suppression therapy in place (H2RA), making discontinuation of the PPI both feasible and clinically appropriate.

The other medications listed are either bone-protective or should not be discontinued:

- **Thiazide diuretics (B)** have a well-established **bone-protective effect**, associated with a 14% reduction in all fractures and 18% reduction in hip fractures in meta-analyses, likely through reduced renal calcium excretion and increased bone mineral density.[5][6]
- **Lithium (C)** is associated with a **decreased risk of osteoporosis** (HRR 0.62; 95% CI 0.53–0.72), likely mediated by activation of β-catenin via inhibition of glycogen synthase kinase-3β, which stimulates bone formation.[7]
- **Estrogen/HRT (D)** is **protective against bone loss**, reducing vertebral fracture risk by 34%, hip fracture risk by 29%, and nonvertebral fracture risk by 21% in postmenopausal women.[8][9]

Would you like to explore the evidence on when to transition from a PPI to an H2RA and the comparative efficacy of H2RAs for GERD management?

Relevant images

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Question 1219

A 46-year-old woman presents with a 5-month history of worsening dry cough, occasional shortness of breath, and fatigue. She says she is now having trouble walking a full block. For the past week, she also has noticed bilateral swelling of the lower legs. She denies chest pain, fever, chills, syncope, or bloody sputum. Current vitals include: temperature 37.0°C (98.6°F), pulse 63/min, blood pressure 128/91 mm Hg and respiratory rate 15/min. On physical examination, there is elevated jugular venous pressure, decreased breath sounds bilaterally at the lung bases, and 1+ non-pitting edema bilaterally in the lower extremities. A chest X-ray demonstrates a slightly enlarged cardiac silhouette. Which of the following is the most appropriate next step in the diagnosis of this patient?

Answer Choices:

(A) Bronchoalveolar wash
(B) Pulmonary function studies
(C) Echocardiography
(D) Chest CT

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/bb194e69-8405-4bb5-bd90-229160edd3dd

OpenEvidence Explanation

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The answer is **C. Echocardiography**.

This patient presents with progressive dyspnea, dry cough, fatigue, elevated jugular venous pressure, decreased breath sounds at the lung bases (suggesting pleural effusions), bilateral lower extremity edema, and an enlarged cardiac silhouette on chest X-ray — a constellation highly suggestive of **heart failure** or a pericardial process. **Echocardiography is the preferred initial imaging modality** for evaluating suspected heart failure, as recommended by the 2022 AHA/ACC/HFSA Heart Failure Guidelines (Class 1 recommendation).[1]

Transthoracic echocardiography (TTE) provides critical information including left ventricular ejection fraction (LVEF), diastolic function, chamber dimensions, wall thickness, valvular abnormalities, and pericardial disease — all of which are essential for determining the etiology of this patient's symptoms.[1][2] It can also distinguish between cardiomegaly and pericardial effusion as causes of the enlarged cardiac silhouette, and estimate right-sided filling pressures via IVC assessment.[3]

Why the other options are less appropriate:

- **A. Bronchoalveolar wash** — Useful for evaluating infectious or inflammatory pulmonary conditions, but the clinical picture here points to a cardiac rather than primary pulmonary etiology.
- **B. Pulmonary function studies** — Would evaluate for obstructive or restrictive lung disease, but the elevated JVP, enlarged cardiac silhouette, and bilateral edema strongly suggest a cardiac cause.
- **D. Chest CT** — While CT can provide additional cardiac and pulmonary information, it is considered a **second-line** investigation after echocardiography and exposes the patient to ionizing radiation. Echocardiography is more informative for initial cardiac assessment and is the standard first step.[4][5]

The bradycardia (pulse 63/min) is also notable, as it may suggest an infiltrative cardiomyopathy or conduction system disease, which echocardiography can help evaluate.

Would you like to explore the diagnostic workup for specific etiologies of heart failure in a middle-aged woman, such as infiltrative cardiomyopathies or peripartum cardiomyopathy?

Relevant images

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Question 1222

A 53-year-old man comes to the physician for a follow-up appointment three days after being prescribed a selective alpha-1 agonist. He reports improvement in his symptoms and has not experienced any adverse effects. This drug was most likely prescribed for which of the following conditions?

Answer Choices:

(A) Bronchospasm due to bronchial asthma
(B) Urinary hesitancy due to benign prostatic hyperplasia
(C) Nasal congestion due to a viral infection
(D) Blood pressure management prior to pheochromocytoma excision

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/ac7db3c7-f85f-4ae7-8a3c-67f029f2f79c

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OpenEvidence Explanation

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The correct answer is **C. Nasal congestion due to a viral infection**.

Phenylephrine, the prototypical selective alpha-1 adrenergic receptor agonist, is widely used as a nasal decongestant for the symptomatic relief of nasal congestion caused by viral upper respiratory infections, allergic rhinitis, and

sinusitis.[1] It works by activating alpha-1 adrenergic receptors on vascular smooth muscle in the nasal mucosa, causing vasoconstriction that reduces mucosal swelling and relieves congestion.[2] Phenylephrine is available over-the-counter in both topical (nasal spray) and oral formulations, making it a common outpatient prescription or recommendation consistent with the clinical scenario of a follow-up visit three days later with symptom improvement.[1][3]

Why the other options are incorrect:

- **A. Bronchospasm due to bronchial asthma** — Bronchospasm is treated with beta-2 agonists (e.g., albuterol), not alpha-1 agonists. Alpha-1 stimulation does not relax bronchial smooth muscle.
- **B. Urinary hesitancy due to BPH** — BPH-related lower urinary tract symptoms are treated with alpha-1 *antagonists* (blockers) such as tamsulosin, doxazosin, and terazosin, which relax prostatic smooth muscle. An alpha-1 *agonist* would worsen urinary obstruction by increasing smooth muscle tone at the bladder neck and prostate.[4][5]
- **D. Blood pressure management prior to pheochromocytoma excision** — Preoperative preparation for pheochromocytoma requires alpha-adrenergic *blockade* (antagonists such as phenoxybenzamine or doxazosin) to prevent catecholamine-induced hypertensive crises. An alpha-1 agonist would dangerously exacerbate hypertension in this setting.[6][7][8]

Would you like to explore the recent FDA advisory panel findings regarding the efficacy of oral phenylephrine as a nasal decongestant?

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Question 1223

A 31-year-old woman is brought to the emergency department with fever, right upper quadrant pain, and myalgia. Her boyfriend says she recently returned from a trip to Southeast Asia. She appears ill and is lethargic. Her temperature is 39°C (102.2°F). Physical examination shows jaundice and tender hepatomegaly. Laboratory studies show the presence of anti-hepatitis A IgM antibodies. A liver biopsy performed at this time would most likely show which of the following histopathological findings?

> **Answer Choices:**
>
> (A) Hepatocytes with shrunken, eosinophilic cytoplasm and pyknotic nuclei
> (B) Cystic spaces with scattered areas of cellular debris
> (C) Basophilic adipocyte remnants, filled with calcifications
> (D) Engorged hepatocytes with red blood cell infiltration

> **Correct Answer:**
>
> **(A)**
>
> **OpenEvidence Response:**
>
> **(A)** ✓

OpenEvidence Link: https://openevidence.com/ask/d43f7417-db44-4500-aa90-fbe2de2b0bb0

OpenEvidence Explanation

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The answer is **A. Hepatocytes with shrunken, eosinophilic cytoplasm and pyknotic nuclei**.

This description corresponds to **acidophil bodies** (also known as Councilman bodies or apoptotic bodies), which are a hallmark histopathological finding in acute viral hepatitis, including hepatitis A. These represent individual hepatocyte apoptosis — the cell shrinks, the cytoplasm becomes densely eosinophilic, and the nucleus undergoes pyknosis.

Why this is correct: Acute hepatitis A on liver biopsy characteristically shows acute lobular hepatitis consisting of a predominantly lymphocytic inflammatory infiltrate, **spotty necrosis with acidophilic body formation**, hepatocyte swelling (ballooning degeneration), and Kupffer cell hyperplasia.[1] Portal tract inflammation is particularly prominent in hepatitis A, often with plasma cells and disruption of the limiting plate.[2][3] The acidophil bodies — shrunken, eosinophilic hepatocytes with pyknotic nuclei — are the classic finding of individual hepatocyte death in acute viral hepatitis.[1][4]

Why the other options are incorrect:

- **B (Cystic spaces with cellular debris)** — describes liquefactive necrosis, seen in abscess formation (e.g., pyogenic or amebic liver abscess), not viral hepatitis.
- **C (Basophilic adipocyte remnants with calcifications)** — describes fat necrosis with dystrophic calcification (saponification), characteristic of enzymatic fat necrosis as seen in pancreatitis, not hepatitis.
- **D (Engorged hepatocytes with red blood cell infiltration)** — describes hepatic congestion, as seen in right-sided heart failure or Budd-Chiari syndrome, not viral hepatitis.

Would you like to explore the clinical course and complications of hepatitis A, including the rare cholestatic and relapsing variants?

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Question 1225

A 9-month-old boy is brought to his pediatrician by his mother for a routine health checkup. The boy was born at 39 weeks gestation via spontaneous vaginal delivery. He is up to date on all vaccines and is meeting all developmental milestones. He was breastfed for the first 3 months and then switched to cow's milk and about two months ago she started giving him fruits and vegetables. Family history is noncontributory. Today, his heart rate is 120/min, respiratory rate is 40/min, blood pressure is 90/50 mm Hg, and temperature of 37.0°C (98.6°F). On examination, he has a heartbeat with a regular rate and rhythm and his lungs are clear to auscultation bilaterally. Generally, the boy looks pale. His weight and height fall within the expected range. A complete blood count (CBC) shows the following:
Hemoglobin (Hb): 9.1 g/dL
Mean corpuscular volume (MCV): 65 fL
Total iron binding capacity (TIBC): 550 µg/dL
Serum iron: 45 µg/dL
Serum lead: < 5 µg/dL
What is the best treatment for this patient?

Answer Choices:

(A) Iron supplementation only
(B) Proper diet and iron supplementation
(C) Multivitamins
(D) Proper diet only

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/089bdcc4-5e80-4ee0-8ce8-64ce4c06d751

OpenEvidence Explanation

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The best treatment is **B. Proper diet and iron supplementation**.

This 9-month-old presents with **iron deficiency anemia (IDA)**, evidenced by low hemoglobin (9.1 g/dL), microcytosis (MCV 65 fL), elevated TIBC (550 µg/dL), low serum iron (45 µg/dL), and a normal lead level. The underlying cause is nutritional: the infant was switched from breastmilk to **cow's milk at 3 months of age**, which is a well-established risk factor for IDA. Unmodified cow's milk is low in bioavailable iron, can cause occult intestinal blood loss, and inhibits iron absorption. Guidelines recommend that cow's milk not be introduced as the main milk drink before 12 months of age.[1]

Why both diet correction and iron supplementation are needed:

- **Iron supplementation** is the standard treatment for confirmed IDA in infants, with a recommended dose of **2–6 mg/kg/day of elemental iron** (preferably ferrous sulfate) for 3–6 months. Supplementation alone will correct the anemia but does not address the underlying dietary cause.[2][3]
- **Dietary correction** — discontinuing cow's milk as the primary milk source and introducing iron-rich complementary foods (meats, iron-fortified cereals) — is essential to address the root cause and prevent recurrence. A 2025 Lancet Haematology consensus recommendation emphasizes that for infants with IDA, clinicians should identify and address the underlying cause in addition to providing iron supplementation.[1][2][4]

Iron supplementation alone (option A) would treat the anemia but not correct the inappropriate diet. Proper diet alone (option D) is recommended for iron deficiency without anemia but is insufficient when anemia is present.[2] Multivitamins (option C) do not provide adequate therapeutic iron dosing.

Would you like to explore the specific recommended timeline for transitioning this infant off cow's milk and the optimal complementary feeding strategy to prevent recurrence?

Relevant images

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Question 1230

A 63-year-old man comes to the emergency department because of a 4-day history of lower abdominal pain, fever, and nausea. He has a history of constipation. His temperature is 39.1°C (102.4°C). Abdominal examination shows left lower quadrant tenderness with no guarding or rebound. Laboratory studies show a leukocyte count of 19,000/mm3. A CT scan of the abdomen shows segmental wall thickening of the descending colon with multiple diverticula and a 5.0-cm, low-attenuation pelvic lesion with air-fluid levels. CT-guided drainage of the fluid collection yields 250 mL of yellow-greenish fluid. Release of which of the following substances is most likely responsible for the formation of the drained lesion?

Answer Choices:

(A) Staphylococcal coagulase
(B) Lipoteichoic acid
(C) Interleukin-3
(D) Lysosomal enzymes

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/0c72c87e-7cd7-42c7-b74c-dbe15ef7e301

OpenEvidence Explanation

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The answer is **D. Lysosomal enzymes**.

This clinical scenario describes **complicated acute diverticulitis** with a diverticular abscess — a 5-cm pelvic fluid collection with air-fluid levels from which purulent (yellow-greenish) fluid was drained. The question asks about the substance responsible for abscess formation at the cellular level.

The drained fluid represents **pus**, which is composed of dead neutrophils, tissue debris, and bacteria. The formation of this abscess cavity results from **tissue necrosis caused by lysosomal enzymes** released from neutrophils recruited to the site of infection. When neutrophils phagocytose bacteria and undergo degranulation or cell death, they release lysosomal contents — including proteases, elastase, collagenase, and myeloperoxidase — that digest surrounding tissue, creating the liquefied, necrotic center characteristic of an abscess.[1][2]

Why the other options are incorrect:

- **A. Staphylococcal coagulase** — Coagulase is produced by *Staphylococcus aureus* and promotes fibrin clot formation around the organism. Diverticular abscesses are caused by enteric gram-negative bacteria (e.g., Enterobacteriaceae) and anaerobes, not staphylococci.[3]
- **B. Lipoteichoic acid** — This is a cell wall component of gram-positive bacteria that activates innate immunity but is not the primary mediator of abscess cavity formation.
- **C. Interleukin-3** — IL-3 is a hematopoietic growth factor involved in bone marrow stimulation and is not directly responsible for the tissue destruction that creates an abscess cavity.

The key concept is that while bacterial infection initiates the inflammatory cascade, it is the **host neutrophil response** — specifically the release of destructive lysosomal enzymes — that causes the tissue liquefaction and necrosis forming the abscess.

Would you like to explore the management algorithm for complicated diverticulitis, including indications for percutaneous drainage versus surgical intervention based on abscess size and clinical response?

Relevant images

(CONTENT OMITTED)

References

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Question 1232

Background:
Some patients with severe asthma have frequent exacerbations associated with persistent eosinophilic inflammation despite continuous treatment with high-dose inhaled glucocorticoids with or without oral glucocorticoids.
Methods:
In this randomized, double-blind clinical trial we assigned 576 patients with recurrent asthma exacerbations and evidence of eosinophilic inflammation despite high doses of inhaled glucocorticoids to one of three study groups. Patients were assigned to receive mepolizumab, a humanized monoclonal antibody against interleukin-5, which was administered as either a 75-mg intravenous dose or a 100-mg subcutaneous dose or placebo every 4 weeks for 32 weeks. The primary outcome was the rate of exacerbations. Other outcomes included the forced expiratory volume in 1 second (FEV1) and scores on the St. George's Respiratory Questionnaire (SGRQ) and the 5-item Asthma Control Questionnaire (ACQ-5).
Results:
The rate of exacerbations was reduced by 47% (95% confidence interval [CI], 29 to 61) among patients receiving intravenous mepolizumab and by 53% (95% CI, 37 to 65) among those receiving subcutaneous mepolizumab, as compared with those receiving placebo ($p<0.001$ for both comparisons). Exacerbations necessitating an emergency department visit or hospitalization were reduced by 32% in the group receiving intravenous mepolizumab and by 61% in the group receiving subcutaneous mepolizumab. At week 32, the mean increase from baseline in FEV1 was 100 ml greater in patients receiving intravenous mepolizumab than in those receiving placebo ($p=0.02$) and 98 ml greater in patients receiving subcutaneous mepolizumab than in those receiving placebo ($p=0.03$). The improvement from baseline in the SGRQ score was 6.4 points and 7.0 points greater in the intravenous and subcutaneous mepolizumab groups, respectively than in the placebo group, and the improvement in the ACQ-5 score was 0.42 points and 0.44 points greater in the two mepolizumab groups, respectively than in the placebo group ($p<0.001$ for all comparisons).

Conclusions:
Mepolizumab administered either intravenously or subcutaneously significantly reduced asthma exacerbations and was associated with improvements in markers of asthma control.
Given the original research abstract above, which of the following would be true if the authors had inadvertently encountered a type 1 error?

> **Answer Choices:**
>
> (A) A type 1 error occurs when the null hypothesis is true but is rejected in error.
> (B) A type 1 error occurs when the null hypothesis is false, yet is accepted in error.
> (C) A type 1 error is a beta (β) error and is usually 0.1 or 0.2.
> (D) A type 1 error is dependent on the confidence interval of a study.

> **Correct Answer:**
>
> **(A)**
>
> **OpenEvidence Response:**
>
> **(A)** ✓

OpenEvidence Link: https://openevidence.com/ask/76bcbe20-b486-4a00-8898-239709a9409e

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OpenEvidence Explanation

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The correct answer is **A. A type 1 error occurs when the null hypothesis is true but is rejected in error.**

A **Type I error (α error)** is the incorrect rejection of a true null hypothesis — essentially a "false positive." In the context of this MENSA trial, a Type I error

would mean that mepolizumab actually has no effect on asthma exacerbations (the null hypothesis is true), but the study's statistical tests incorrectly concluded that it does (the null hypothesis was rejected). The probability of committing a Type I error is set by the significance level (α), conventionally **0.05** (i.e., a 5% chance of a false positive).

Why the other options are incorrect:

- **B** describes a **Type II error (β error)** — failing to reject a false null hypothesis (a "false negative"), not a Type I error.
- **C** incorrectly labels a Type I error as a β error. The values 0.1 or 0.2 are typical thresholds for **β (Type II error)**, not α.
- **D** is misleading. While the confidence interval level is mathematically related to α (a 95% CI corresponds to $\alpha = 0.05$), a Type I error is defined by the significance level (α), not "dependent on" the confidence interval. The CI is a consequence of the chosen α, not the other way around. More importantly, the definition in option A is the most directly and unambiguously correct statement.

Would you like to explore how sample size calculations balance Type I and Type II error rates in clinical trial design?

Question 1233

A 30-year-old Japanese woman is brought to the emergency department after fainting at work. She says she was only unconscious for a moment and recovered quickly. She reports increasing fatigue and joint pain for the past 4 months. Her blood pressure is 90/60 mm Hg, and her temperature is 36.6°C (98.0°F). On physical examination, the patient is fully conscious. Her radial pulse is absent at her right wrist and 1+ at her left wrist. Laboratory findings are significant for the following:
Hemoglobin: 10.9 g/dL
Hematocrit: 34.7%
Leukocyte count: 5,500/mm3
Neutrophils: 65%
Lymphocytes: 30%
Monocytes: 5%
Mean corpuscular volume: 78.2 µm3
Platelet count: 190,000/mm3
Erythrocyte sedimentation rate: 56 mm/h
What complications is this patient at risk for?

Answer Choices:

(A) Myocardial infarction
(B) Tongue infarction
(C) Palpable purpura
(D) Polyneuropathy

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/a1a96166-8707-4943-bf72-a304485f0c99

OpenEvidence Explanation

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The answer is **A. Myocardial infarction**.

This clinical presentation is classic for **Takayasu arteritis** — a young Asian woman with constitutional symptoms (fatigue, arthralgias), syncope, hypotension, absent/diminished radial pulses, microcytic anemia, and elevated ESR. Takayasu arteritis is a chronic granulomatous large-vessel vasculitis affecting the aorta and its major branches, predominantly seen in women under 40, with highest prevalence in East Asian populations.[1][2]

Why myocardial infarction is the correct complication:

Takayasu arteritis can involve the coronary arteries (either through ostial stenosis from aortic root inflammation or direct coronary arteritis), leading to angina, heart failure, and **myocardial infarction**. A meta-analysis of 3,262 Takayasu arteritis patients found a pooled MI prevalence of **3.4%** and stroke prevalence of **8.9%** at any time during the disease course.[3] The JACC Focus Seminar on Takayasu arteritis explicitly lists coronary artery involvement causing angina, heart failure, and myocardial infarction among the recognized clinical manifestations.[1] Other major cardiovascular complications include stroke/TIA (up to 20%), aortic aneurysm, aortic regurgitation, and renovascular hypertension.[2][4]

Why the other options are incorrect:

- **B. Tongue infarction** — This is associated with giant cell arteritis (temporal arteritis), which typically affects patients over 50 and involves the external carotid branches (including the lingual artery), not Takayasu arteritis.

- **C. Palpable purpura** — This is characteristic of small-vessel vasculitides (e.g., IgA vasculitis, ANCA-associated vasculitis, cryoglobulinemic vasculitis), not large-vessel vasculitis.

- **D. Polyneuropathy** — This is seen in small- and medium-vessel vasculitides (e.g., polyarteritis nodosa, ANCA-associated vasculitis) due to vasa nervorum involvement, not in large-vessel vasculitis like Takayasu arteritis.

Would you like to explore the diagnostic workup and imaging modalities recommended for confirming Takayasu arteritis?

References

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Question 1236

A 45-year-old woman presents to the physician with a history of headache, palpitations, and episodic diaphoresis. She was diagnosed with hypertension in the past and is now regularly taking antihypertensive medication (amlodipine 10 mg once daily). She has had a diffuse thyroid swelling for the past 4 months. She complains of pain in the long bones of her arms and legs for the past 3 months. She is slightly built, appears thin, and is anxious and apprehensive. Her skin is moist and warm. Her weight is 45 kg (99.2 lb) and height is 146 cm (4 ft 7 in); BMI is 21.12 kg/m2. Her pulse is 116/min, the blood pressure is 196/102 mm Hg, the respiratory rate is 29/min, and the temperature is 37.2°C (99.0°F). Diffuse and firm thyromegaly is present. Her upper extremities exhibit fine tremors during an anxiety attack. The laboratory test results reveal elevated 24-hour urinary VMA and metanephrines. Serum epinephrine, calcitonin, and parathormone levels are also elevated. Hypercalcemia and hyperglycemia are also noted. Which of the following is the most likely diagnosis?

Answer Choices:

(A) Von Hippel-Lindau syndrome
(B) Multiple endocrine neoplasia (MEN) 2A
(C) Multiple endocrine neoplasia (MEN) 2B
(D) Neurofibromatosis

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/9f2ebed5-097c-40cf-a64e-0f2a2aeab6f5

OpenEvidence Explanation

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The correct answer is **B. Multiple endocrine neoplasia (MEN) 2A**.

This patient presents with the classic triad of **MEN 2A**: **medullary thyroid carcinoma** (diffuse thyromegaly, elevated calcitonin), **pheochromocytoma** (hypertension, headache, palpitations, episodic diaphoresis, elevated urinary VMA and metanephrines, elevated serum epinephrine), and **primary hyperparathyroidism** (elevated parathormone, hypercalcemia, bone pain in long bones).[1][2]

Why MEN 2A and not MEN 2B?

The key distinguishing feature is the presence of **hyperparathyroidism**, which occurs in up to **25% of MEN 2A** cases but is rare in MEN 2B.[3][4] MEN 2B is characterized by nonendocrine features not present in this patient, including mucosal neuromas of the lips and tongue, distinctive facies with enlarged lips, ganglioneuromatosis of the gastrointestinal tract, and a marfanoid habitus.[2] While this patient is slightly built, she lacks the characteristic mucosal neuromas and other MEN 2B stigmata. Additionally, MEN 2B typically presents much earlier in life (childhood), whereas MEN 2A classically presents in the third or fourth decade, consistent with this patient's age of 45.[5]

Why not the other options?

- **Von Hippel-Lindau syndrome (A)** is characterized by hemangioblastomas (CNS, retina), renal cell carcinoma, and pheochromocytoma — not medullary thyroid carcinoma or hyperparathyroidism.
- **Neurofibromatosis (D)** can be associated with pheochromocytoma but does not include medullary thyroid carcinoma or hyperparathyroidism as part of its syndrome.

Both MEN 2A and MEN 2B are caused by germline gain-of-function mutations in the **RET proto-oncogene**, but they involve different mutations with distinct genotype-phenotype correlations.[1][6]

Would you like to explore the recommended screening protocols and timing of prophylactic thyroidectomy for family members of patients with MEN 2A based on specific RET mutation risk categories?

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Question 1238

A 45-year-old woman presents with sudden-onset dyspnea. Her past medical history is significant for varicose veins in her lower extremities, well-controlled diabetes mellitus type 2, and a 25 pack-year smoking history. The patient currently takes metformin and pioglitazone. Family history is significant for her sister who died at the age of 35 because of a pulmonary embolism. Her temperature is 37.8°C (100.0°F), the pulse is 111/min, the respirations are 18/min, and the blood pressure is 130/60 mm Hg. On physical examination, the patient is pale and diaphoretic. Cardiac exam is significant for an S3 gallop. There is erythema and swelling over multiple varicose veins in her left leg. Ultrasound of her left leg is positive for a deep vein thrombosis. The patient is admitted, and anticoagulation is started with a vitamin K inhibitor. However, despite these interventions, she dies shortly after admission. Which of the following was the most likely etiology of this patient's condition?

Answer Choices:

(A) Distal peripheral microembolism
(B) Necrotizing fasciitis
(C) Protein S deficiency
(D) Waldenström macroglobulinemia

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/0aeca00e-4776-4dbf-8347-92ae4a932cea

OpenEvidence Explanation

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The answer is **C. Protein S deficiency**.

This patient's presentation — a 45-year-old woman with sudden-onset dyspnea, confirmed DVT, tachycardia, S3 gallop (indicating right heart strain), and rapid hemodynamic deterioration leading to death — is consistent with a **massive pulmonary embolism** arising from DVT. The key to identifying the underlying etiology is the strong **family history**: her sister died at age 35 from PE, suggesting an inherited thrombophilia.

Protein S deficiency is an autosomal dominant inherited thrombophilia that predisposes to venous thromboembolism (VTE), including DVT and PE.[1][2] In family-based studies, 55% of heterozygous protein S-deficient individuals develop venous thrombotic events, with the most common manifestations being DVT (74%), superficial thrombophlebitis (72%), and PE (38%). The mean age at first thrombotic event is 28 years, and by age 35, only 32% remain free of thrombosis.[3] This aligns with the sister's fatal PE at age 35 and this patient's presentation at age 45.

Several additional features support this diagnosis:

- **Superficial thrombophlebitis** (erythema and swelling over varicose veins) occurring alongside DVT is a classic pattern in protein S deficiency, where patients often present with various combinations of DVT, superficial thrombophlebitis, and PE simultaneously.[3]
- **Varicose veins** are independently associated with a 5-fold increased risk of DVT, and when combined with an inherited thrombophilia, the risk is compounded.[4]
- Recent population-scale data confirm that true genetic protein S deficiency (type I) carries an OR of **14.01** for VTE, comparable to antithrombin deficiency — the most clinically severe inherited thrombophilia.[2]

The other options are less likely: distal peripheral microembolism (A) would not cause the acute hemodynamic collapse seen here; necrotizing fasciitis (B) would

present with rapidly progressive soft tissue destruction rather than PE; and Waldenström macroglobulinemia (D) causes hyperviscosity syndrome rather than the classic DVT-to-PE pathway seen in this case.

Would you like to explore the specific management considerations for patients with protein S deficiency, including the risk of warfarin-induced skin necrosis when initiating vitamin K antagonist therapy?

Relevant images

(CONTENT OMITTED)

References

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Question 1240

A 3-year-old male was brought to the pediatrician with severe lip lacerations, with a portion of his tongue appearing to be bitten off, as well as missing portions of the fingers on his right hand. A family history is notable for two similar cases in male cousins on the mother's side. A urinalysis revealed a high level of uric acid. Which of the following is the mode of inheritance for this disorder?

> **Answer Choices:**
>
> (A) X-linked recessive
> (B) X-linked dominant
> (C) Autosomal dominant
> (D) Maternally inherited mitochondrial defect

> **Correct Answer:**
>
> **(A)**
>
> **OpenEvidence Response:**
>
> **(A)** ✓

OpenEvidence Link: https://openevidence.com/ask/4b9d6a4e-1029-4bd2-9ea6-7d668674aac2

OpenEvidence Explanation

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The answer is **A. X-linked recessive**.

This clinical presentation is classic for **Lesch-Nyhan syndrome** **(LNS)**, caused by deficiency of the enzyme hypoxanthine-guanine phosphoribosyltransferase

(HPRT), encoded by the HPRT1 gene on the long arm of the X chromosome (Xq26).[1][2] The key features in this vignette — self-mutilating behavior (lip biting, tongue biting, finger mutilation), elevated uric acid, male sex, and affected male maternal cousins — all point to this diagnosis and its inheritance pattern.

Why X-linked recessive:

- The HPRT1 gene is located on the X chromosome. Males, having only one X chromosome, are affected when they inherit a single mutant allele. Females with one mutant copy are typically asymptomatic carriers due to random X-inactivation of the affected allele.[1][3]
- The family history of affected male cousins on the **mother's side** is the hallmark pedigree pattern of X-linked recessive inheritance — carrier females pass the mutation to affected sons, and the trait appears to skip generations through unaffected female carriers.[1][2]

Clinical features supporting Lesch-Nyhan syndrome:

- Self-injurious behavior (biting of fingers, lips, and cheeks) typically develops between ages 2 and 4 years and is the most distinctive behavioral feature.[1][4]
- Hyperuricemia and hyperuricosuria result from uric acid overproduction due to the purine metabolism defect.[2][5]
- Nearly all reported cases occur in males, consistent with X-linked recessive inheritance.[1][2]

Would you like to explore the management strategies for Lesch-Nyhan syndrome, including the role of allopurinol for hyperuricemia and behavioral interventions for self-injury?

References

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Question 1241

An asymptomatic 65-year-old woman is found to have T-score of -2.6 SD on routine bone mineral density screening. She has a 10-year history of hypertension and an esophageal stricture due to severe gastroesophageal reflux disease. She was diagnosed with endometrial hyperplasia 20 years ago and treated with medroxyprogesterone. Menarche started at 11 years of age and her last menstrual period was 8 years ago. Her last mammography and PAP smear 6 months ago showed no abnormalities. Her mother died of breast cancer at the age of 45 years. The patient does not have any children. Current medications include lansoprazole and hydrochlorothiazide. Her blood pressure is 135/85 mm Hg. Physical examination shows no abnormalities. Treatment is begun with a drug that prevents further bone resorption and reduces her risk of developing breast cancer. This drug puts her at an increased risk of which of the following adverse effects?

Answer Choices:

(A) Skin infections
(B) Osteosarcoma
(C) Hypercholesterolemia
(D) Deep vein thrombosis

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/10cdee88-0bba-40c9-ba48-6354ce1e6cb7

OpenEvidence Explanation

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The correct answer is **D. Deep vein thrombosis**.

The drug described in this question is **raloxifene**, a selective estrogen receptor modulator (SERM) that both prevents bone resorption and reduces the risk of invasive breast cancer — making it uniquely suited for this postmenopausal woman with osteoporosis (T-score −2.6) and a strong family history of breast cancer (mother died of breast cancer at age 45). Notably, bisphosphonates — the other major antiresorptive class — are relatively contraindicated here due to her esophageal stricture, and tamoxifen would be less ideal given her history of endometrial hyperplasia (tamoxifen increases endometrial cancer risk, whereas raloxifene does not).[1][2]

Venous thromboembolism (VTE), including deep vein thrombosis and pulmonary embolism, is the most serious adverse effect of raloxifene. The FDA label for raloxifene (Evista) carries a **boxed warning** for increased risk of VTE and death from stroke.[1] In clinical trials, raloxifene was associated with an approximately **2- to 3-fold increased risk of thromboembolism** compared with placebo, with the greatest risk occurring during the first 4 months of treatment.[1][3] In the RUTH trial, the hazard ratio for VTE was 1.44 (95% CI, 1.06–1.95).[4]

Why the other options are incorrect:

- **A. Skin infections** — This is associated with denosumab (a RANKL inhibitor), not raloxifene.
- **B. Osteosarcoma** — This is a concern with teriparatide (parathyroid hormone analog), based on preclinical animal data, not with raloxifene.
- **C. Hypercholesterolemia** — Raloxifene actually has favorable effects on lipid metabolism (estrogen-agonist effect), tending to lower LDL cholesterol rather than raise it.[1]

Would you like to explore the comparative efficacy and safety profiles of different osteoporosis treatments in patients with esophageal disease or other contraindications to oral bisphosphonates?

References

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Question 1243

A 26-year-old man presents to the office complaining of persistent epigastric pain for the past 2 months. He states that his pain is worse a few hours after he eats. His father had similar symptoms. Past medical history is insignificant. He is a non-smoker and does not drink alcohol. The vital signs include blood pressure 120/90 mm Hg, heart rate 83/min, and temperature 37.0°C (98.6°F). Physical examination is insignificant except for mild epigastric tenderness. A metabolic panel reveals the following:
Serum sodium 136 mEq/L
Serum potassium 4.2 mEq/L
Calcium 13.2 mg/dL
Bicarbonate 26 mEq/L
Upper gastrointestinal endoscopy reveals multiple duodenal ulcers. Which of the following is the most likely diagnosis?

Answer Choices:

(A) Gastroesophageal reflux disease
(B) Gastric adenocarcinoma, intestinal type
(C) VIPoma
(D) MEN1

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/fa3570a6-5f40-48ea-b8fd-ae88b231b8dc

OpenEvidence Explanation

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The correct answer is **D. MEN1** (Multiple Endocrine Neoplasia Type 1).

This clinical presentation — a young man with **multiple duodenal ulcers**, **hypercalcemia** (calcium 13.2 mg/dL), postprandial epigastric pain, and a **family history** of similar symptoms — is classic for **MEN1 syndrome**. The key features that point to this diagnosis:

Multiple duodenal ulcers + hypercalcemia: MEN1 is an autosomal dominant syndrome characterized by the triad of parathyroid tumors (causing hypercalcemia), duodenopancreatic neuroendocrine tumors, and pituitary adenomas.[1] Gastrinomas occur in approximately 40% of MEN1 patients and manifest as Zollinger-Ellison syndrome (ZES), with excessive gastric acid secretion leading to multiple peptic ulcers.[1] The epigastric pain occurring two or more hours after meals is characteristic of ZES-associated ulcers.[1]

Hypercalcemia: Parathyroid tumors are the most common and typically earliest manifestation of MEN1, present in >95% of patients, with onset often between ages 20–25 years.[2][3] The calcium of 13.2 mg/dL in this patient is consistent with primary hyperparathyroidism from a parathyroid adenoma.

Family history: MEN1 is inherited in an autosomal dominant pattern, caused by germline mutations in the MEN1 gene on chromosome 11q13.[4] The father's similar symptoms strongly suggest familial transmission.

Why not the other options:

- **A. GERD** — Does not explain hypercalcemia or multiple duodenal ulcers.
- **B. Gastric adenocarcinoma** — Extremely rare at age 26, does not explain hypercalcemia, and would not typically present with multiple duodenal ulcers.
- **C. VIPoma** — Presents with watery diarrhea, hypokalemia, and achlorhydria (WDHA syndrome), not epigastric pain with duodenal ulcers. VIPomas are also exceedingly rare in MEN1 (<2%).[1][3]

Would you like to explore the recommended screening and surveillance protocols for patients with suspected MEN1 syndrome?

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Question 1244

The parents of a 16-year-old boy with type 1 diabetes mellitus present requesting information about the drug, exenatide, an injectable drug that only needs to be administered once a week. The patient's blood glucose levels have been difficult to control on his current insulin regimen due to poor adherence to recommended therapy, and he has had difficulty putting on weight despite eating copiously. The patient is afebrile and his vital signs are within normal limits. His body mass index (BMI) is 19 kg/m2. Which of the following best describes why the patient should not be switched to exenatide?

Answer Choices:

(A) Insulin production by the pancreas is insufficient for exenatide to be effective.
(B) Exenatide suppresses glucagon secretion, which increases the risk of hypoglycemia.
(C) Suppression of appetite makes it even harder for him to gain weight.
(D) Exenatide is contraindicated in children below 18 years.

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/f02e5f81-1d54-4c04-b4b3-335d607d3591

OpenEvidence Explanation

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The correct answer is **A. Insulin production by the pancreas is insufficient for exenatide to be effective.**

Exenatide is a **GLP-1 receptor agonist** that works primarily by enhancing **glucose-dependent insulin secretion** from pancreatic beta cells, suppressing glucagon secretion, slowing gastric emptying, and promoting satiety.[1][2] Critically, its mechanism of action requires **functioning beta cells** to augment endogenous insulin production. In **type 1 diabetes**, autoimmune destruction of beta cells results in absolute insulin deficiency, meaning there is insufficient (or no) endogenous insulin production for exenatide to potentiate. Without residual beta-cell function, exenatide cannot meaningfully improve glycemic control.[1][2]

Why the other options are incorrect:

- **B (Glucagon suppression causing hypoglycemia):** While exenatide does suppress glucagon secretion, its insulin-stimulating effect is glucose-dependent, meaning the risk of hypoglycemia is inherently low when used as monotherapy. This is not the primary reason to avoid it in type 1 diabetes.[2]
- **C (Appetite suppression and weight gain difficulty):** Exenatide does suppress appetite and promote weight loss, which could theoretically be a concern in this underweight patient. However, this is a secondary consideration — the fundamental issue is that the drug simply will not work in the absence of beta-cell function.[3][4][5]
- **D (Contraindicated under age 18):** Exenatide is actually FDA-approved for use in children aged **10 to 17 years** with type 2 diabetes. It is not contraindicated in this age group.[6]

The key clinical teaching point is that all GLP-1 receptor agonists, including exenatide, are indicated for **type 2 diabetes** (where residual beta-cell function exists) and are not appropriate as primary therapy for type 1 diabetes, where the fundamental pathology is autoimmune beta-cell destruction.[1][7]

Would you like to explore the emerging evidence on adjunctive GLP-1 receptor agonist use in type 1 diabetes for weight management or insulin dose reduction?

Relevant images

(CONTENT OMITTED)

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Question 1248

A 44-year-old woman comes to the physician because of a 6-month history of fatigue, intermittent fever, a 4.0-kg (8.8-lb) weight loss, and a progressive, non-productive cough. She does not smoke. Physical examination shows mild wheezing over bilateral lung fields and enlarged supraclavicular and cervical lymph nodes. A CT scan of the chest is shown. A biopsy specimen of a cervical lymph node shows organized epithelioid histiocytes and multinucleated giant cells without focal necrosis. The initial treatment of this patient's condition should include which of the following drugs?

Answer Choices:

(A) Cisplatin
(B) Lamivudine
(C) Isoniazid
(D) Prednisone

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/f873da30-2e5b-44e7-863d-77f082e05d98

OpenEvidence Explanation

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The answer is **D. Prednisone**.

This clinical presentation — fatigue, intermittent fever, weight loss, non-productive cough, bilateral hilar/mediastinal lymphadenopathy on CT, and cervical lymph node biopsy showing **non-caseating granulomas** (organized epithelioid histiocytes and multinucleated giant cells without focal necrosis) — is classic for **sarcoidosis**.

Oral glucocorticoids (prednisone) are the established first-line treatment for symptomatic pulmonary sarcoidosis.[1][2][3] A typical initial dose is prednisone 20–40 mg/day for 2–6 weeks, followed by a gradual taper over 6–18 months.[1][3] Treatment is indicated for patients who are symptomatic with significant cough, dyspnea, or constitutional symptoms, or who have progressive disease on imaging or pulmonary function testing.[1]

Why the other options are incorrect:

- **A. Cisplatin** — a platinum-based chemotherapy agent used for malignancies (e.g., lung cancer, lymphoma). The biopsy findings here are granulomatous, not neoplastic.
- **B. Lamivudine** — a nucleoside reverse transcriptase inhibitor used for HIV and hepatitis B. There is no indication of viral infection in this presentation.
- **C. Isoniazid** — first-line treatment for tuberculosis. While TB can cause granulomatous lymphadenopathy, TB granulomas characteristically show **caseating (central) necrosis**, which is explicitly absent here. The non-caseating pattern strongly favors sarcoidosis over TB.[1][4]

Would you like to explore the evidence comparing methotrexate versus prednisone as first-line therapy for pulmonary sarcoidosis, based on the recent PREDMETH trial?

Relevant images

(CONTENT OMITTED)

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Question 1250

A 37-year-old woman with an HIV infection comes to the physician for a follow-up examination. Six months ago, combined antiretroviral therapy consisting of dolutegravir, tenofovir, and emtricitabine was initiated. Laboratory studies show a decrease in the CD4 count and an increase in the viral load despite ongoing treatment. The patient is switched to a new treatment regimen, including a drug that acts by preventing viral DNA synthesis without undergoing intracellular phosphorylation. Which of the following is the most likely drug?

Answer Choices:

(A) Efavirenz
(B) Ritonavir
(C) Raltegravir
(D) Lamivudine

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/cc3998c9-44cc-42c0-9127-612337b8a540

OpenEvidence Explanation

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The answer is **A. Efavirenz**.

The key to this question is identifying the drug that **prevents viral DNA synthesis without requiring intracellular phosphorylation**. This description matches the mechanism of **non-nucleoside reverse transcriptase inhibitors (NNRTIs)**, of which efavirenz is the only example among the answer choices.

Why efavirenz fits: Efavirenz is an NNRTI that acts by **noncompetitive inhibition of HIV-1 reverse transcriptase**, binding to a hydrophobic allosteric pocket away from the enzyme's active site.[1][2] This conformational change blocks viral DNA polymerization. Critically, NNRTIs do not require any intracellular phosphorylation to become active — they bind directly to reverse transcriptase in their parent form.[2]

Why the other options are incorrect:

- **D. Lamivudine** — An NRTI (nucleoside reverse transcriptase inhibitor) that is a prodrug requiring **triple intracellular phosphorylation** to its active triphosphate form (3TC-TP) before it can inhibit reverse transcriptase via DNA chain termination.[2][3]
- **C. Raltegravir** — An integrase strand transfer inhibitor (INSTI) that blocks integration of viral DNA into the host genome, not viral DNA synthesis.[4]
- **B. Ritonavir** — A protease inhibitor (PI) that prevents cleavage of Gag-Pol polyproteins, resulting in immature, non-infectious virions — an entirely different mechanism unrelated to DNA synthesis.[4]

The distinction between NRTIs (require phosphorylation, act as chain terminators) and NNRTIs (no phosphorylation needed, act as allosteric inhibitors) is the central pharmacologic concept being tested here.

Would you like to explore the clinical considerations for switching antiretroviral regimens in the setting of virologic failure, including resistance testing and preferred second-line regimens?

Relevant images

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Question 1251

A 14-year-old girl presents with sudden drooping of the right side of her face with drooling and excessive tearing. The patient's mother says that the patient was recently in northern Maine and spent most of her time during the trip outdoors. Physical examination reveals a slight asymmetry of the facial muscles with an inability to whistle or close the right eye. A circular red rash with central clearing is present on the trunk. There is also decreased taste sensation. Which of the following most likely transmitted the organism responsible for this patient's illness?

> **Answer Choices:**
>
> (A) Ixodes scapularis
> (B) Tsetse fly
> (C) Culicidae
> (D) Anopheles

> **Correct Answer:**
>
> **(A)**
>
> **OpenEvidence Response:**
>
> **(A)** ✓

OpenEvidence Link: https://openevidence.com/ask/027df4f6-5fae-4091-bee4-60f39abbf2aa

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OpenEvidence Explanation

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The answer is **A. Ixodes scapularis**.

This patient presents with classic **Lyme disease** caused by *Borrelia burgdorferi*, which is transmitted by the **Ixodes scapularis** (blacklegged/deer tick). The key clinical features pointing to this diagnosis include:

- **Erythema migrans** — the circular red rash with central clearing ("bull's-eye" appearance) on the trunk, present in 70–80% of Lyme disease cases[1][2]
- **Facial nerve palsy (Bell's palsy)** — right-sided facial droop with inability to whistle, close the eye, drooling, excessive tearing, and decreased taste sensation, which is the most common neurologic manifestation of disseminated Lyme disease[1][3]
- **Epidemiologic exposure** — recent outdoor activity in northern Maine, a highly endemic area for Lyme disease[4]

Facial nerve palsy occurs in approximately 5% of patients with acute Lyme disease and is the most common manifestation of Lyme neuroborreliosis in the United States.[5] In children specifically, facial nerve palsy and subacute meningitis are the predominant neurologic presentations.[6]

The other answer choices represent different vectors:

- **Tsetse fly** (B) transmits *Trypanosoma brucei* (African sleeping sickness)
- **Culicidae** (C) is the mosquito family, which transmits various arboviruses, malaria, and filarial diseases
- **Anopheles** (D) is a genus of mosquito that specifically transmits *Plasmodium* species (malaria)

None of these vectors are associated with erythema migrans or the clinical syndrome described.

Would you like to explore the recommended antibiotic treatment regimens for Lyme neuroborreliosis with facial nerve palsy in pediatric patients?

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Question 1252

A 66-year-old man with high blood pressure, high cholesterol, and diabetes presents to the clinic with elevated liver function tests from baseline. He has a blood pressure of 136/92 mm Hg and a heart rate of 69/min. On physical examination, his heart sounds are regular and lung sounds are clear. Current medications include simvastatin, metformin, fenofibrate, hydrochlorothiazide, aspirin, glyburide, and lisinopril. Of these medications, which could contribute to the patient's transaminitis?

> **Answer Choices:**
>
> (A) Metformin
> (B) Simvastatin
> (C) Glyburide
> (D) Lisinopril

> **Correct Answer:**
>
> **(B)**
>
> **OpenEvidence Response:**
>
> **(B)** ✓

OpenEvidence Link: https://openevidence.com/ask/28b2c20a-9d18-4c12-986d-be2ac161ddfc

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OpenEvidence Explanation

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The answer is **B. Simvastatin**. Among the listed medications, **simvastatin** (an HMG-CoA reductase inhibitor/statin) is the most well-recognized cause of transaminase elevations and is the best answer for this question.

Simvastatin and transaminitis: Statins cause dose-related, asymptomatic elevations in hepatic transaminases (ALT > AST) in up to **1% of patients** at levels >3× the upper limit of normal.[1][2] The FDA simvastatin label specifically warns that increases in serum transaminases have been reported, typically appearing soon after initiation and usually transient.[2] Serious hepatotoxicity is rare (~1 in 100,000), but transaminase elevation is a well-established class effect.[1][3] Notably, the FDA removed the requirement for routine on-treatment liver enzyme monitoring in 2012, given that clinically significant hepatotoxicity is very uncommon.[3][4]

Why not the other options?

- **Metformin (A):** Not metabolized hepatically and is generally not considered hepatotoxic. Liver injury with metformin is exceedingly rare and based only on isolated case reports.[5][6]
- **Glyburide (C):** While the FDA label does mention rare cholestatic jaundice, hepatitis, and isolated transaminase elevations, this is far less commonly tested and less clinically prominent than statin-associated transaminitis.[7][8]
- **Lisinopril (D):** ACE inhibitor-associated hepatotoxicity has been reported but is rare and idiosyncratic. It is listed among cardiovascular drugs that can cause drug-induced liver injury, but it is not the classic board-style answer for this question.[9][10][11]

It is worth noting that **fenofibrate**, also on this patient's medication list, is another well-known cause of transaminase elevations, though it was not offered as an answer choice.[11]

Would you like to explore the recommended approach to evaluating and managing statin-associated transaminase elevations, including when to discontinue therapy?

Relevant images

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Question 1253

A 7 -day-old newborn boy presents to the emergency department with a history of fever, irritability, and generalized erythema. During the first 2 days of clinical manifestations, the parents of the child tried to control the symptoms using acetaminophen; however, the newborn continued to be ill, and blisters were noticeable around the buttocks, hands, and feet. During the physical examination, the vital signs include body temperature 39.0°C (102.3°F), heart rate 130/min, and respiratory rate 45/min. Ears, nose, and oral mucosa preserved their integrity, while the skin presents with diffuse blanching erythema and flaccid blisters with a positive Nikolsky's sign. What is the most likely diagnosis in this patient?

Answer Choices:

(A) Scarlet fever
(B) Scalded skin syndrome
(C) Impetigo
(D) Pyoderma

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/c3c4391d-30e9-4c8e-aa5e-6815dd3033f5

OpenEvidence Explanation

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The correct answer is **B. Scalded skin syndrome**.

Staphylococcal scalded skin syndrome (SSSS) is a toxin-mediated desquamating skin disease caused by exfoliative toxins (ETA and ETB) produced by *Staphylococcus aureus*. This presentation is classic for SSSS, with every key feature aligning:

- **Age**: SSSS predominantly affects **neonates and children under 5 years**, with neonates being particularly susceptible due to immunological immaturity (low anti-exfoliative toxin antibody titers) and inefficient renal clearance of the toxin.[1][2]
- **Prodrome**: Fever, irritability, and malaise are the typical prodromal symptoms.[1][3]
- **Skin findings**: Diffuse blanching erythema progressing to **flaccid blisters** with a **positive Nikolsky sign** (lateral pressure causes the upper epidermis to shear off) is the hallmark presentation. Blisters commonly affect the buttocks, hands, and flexural areas.[3][4]
- **Mucosal sparing**: A critical distinguishing feature — SSSS **spares the oral and other mucous membranes**, unlike toxic epidermal necrolysis (TEN), which involves mucosal surfaces.[5][6]

Why the other options are incorrect:

- **A. Scarlet fever** — Caused by group A Streptococcus exotoxins; presents with a "sandpaper-like" rash, strawberry tongue, and pharyngitis, but does not produce flaccid blisters or a positive Nikolsky sign.
- **C. Impetigo** — Bullous impetigo (caused by the same exfoliative toxins) produces localized blisters, not the diffuse erythroderma and widespread desquamation seen here. SSSS represents the systemic, hematogenously disseminated form of the same toxin-mediated process.[5][7]
- **D. Pyoderma** — A localized purulent skin infection that does not cause diffuse erythema, flaccid bullae, or Nikolsky sign.

Would you like to explore the recommended antibiotic regimens and supportive care strategies for neonatal SSSS?

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Question 1254

A 60-year-old woman presents to the outpatient clinic complaining of severe vulvar itching that has been gradually worsening for the past year. She mentions that she has tried over-the-counter lubricants, but lubricants do not seem to provide substantial relief. Her medical history is remarkable for diet-controlled type 2 diabetes mellitus and hypertension treated with hydrochlorothiazide. Menopause occurred at 52 years of age. She has been sexually active with her husband until recently and reports severe pain during vaginal intercourse. The physical examination reveals dry, thin, white plaque-like lesions in the vulvar area with atrophy of the labia minora. The clitoris appears retracted. The perianal skin appears pale and wrinkled. Which of the following is the most likely diagnosis?

Answer Choices:

(A) Squamous cell hyperplasia
(B) Lichen sclerosus
(C) Squamous cell carcinoma of the vulva
(D) Lichen planus

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/053fa7e2-c333-4ebf-aaeb-ef6ade02159a

OpenEvidence Explanation

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The most likely diagnosis is **B. Lichen sclerosus**.

This presentation is classic for **lichen sclerosus**, a chronic inflammatory dermatosis with a strong predilection for the vulvar and perianal regions in postmenopausal women.[1][2] Every feature described in this case aligns with the diagnosis:

- **Severe vulvar pruritus** is the hallmark symptom and the most common presenting complaint[1][2]
- **Dyspareunia** results from epithelial thinning, introital narrowing, and fissuring[3][4]
- **White, plaque-like lesions** with a thin, dry appearance correspond to the characteristic porcelain-white papules and plaques described as having a "cigarette paper" or "cellophane" texture[1][2]
- **Atrophy of the labia minora** and a **retracted (buried) clitoris** represent loss of vulvar architecture from progressive scarring, with clitoral phimosis being one of the most common structural abnormalities[2][5]
- **Pale, wrinkled perianal skin** reflects the classic extension of disease from the vulva to the perianal region in a "figure-of-eight" or hourglass pattern[1][6]

Why not the other options?

- **Squamous cell hyperplasia** presents with thickened, raised, often reddish lesions rather than thin, white, atrophic plaques with architectural loss.[1]
- **Squamous cell carcinoma of the vulva** typically presents as a discrete mass, ulcer, or nodule rather than diffuse bilateral white plaques with symmetric architectural changes. While lichen sclerosus carries a 2–5% risk of malignant transformation, the diffuse pattern described here is more consistent with lichen sclerosus itself.[1][5]
- **Lichen planus** can sometimes mimic lichen sclerosus, but erosive lichen planus characteristically involves mucosal surfaces with painful erythematous erosions and Wickham striae (white, lacy, reticulate pattern),

and commonly involves the vagina and oral cavity — features not described here.[1][7]

The following figure illustrates the characteristic appearance of vulvar lichen sclerosus with epithelial thinning and the classic "cigarette paper" texture.



Figure 2. Epithelial thinning in lichen sclerosus leads to a “cigarette paper” appearance of the vulva. Reprinted with permission from O'Connell TX, Nathan LS, Satmary WA, et al. Non-neoplastic epithelial disorders of the vulva. Am Fam Physician. 2008;77(3):322.

A vulvar biopsy is recommended to confirm the diagnosis and exclude vulvar intraepithelial neoplasia or malignancy, given the 2–5% lifetime risk of squamous

cell carcinoma in patients with lichen sclerosus.[1][2] First-line treatment is **clobetasol propionate 0.05% ointment**, applied twice daily until active lesions regress (typically 1–2 months), then tapered to maintenance therapy.[2][5]

Would you like to explore the long-term management and surveillance protocols for vulvar lichen sclerosus, including monitoring for malignant transformation?

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Question 1255

A 50-year-old woman with Systemic Lupus Erythematosus (SLE) presents to your clinic with complaints of left eye pain and reduced vision. She notes that she was in her usual state of health until 3 days prior to presentation when she noticed some mild tenderness around her left eye, unrelieved by any pain relievers. This morning when she woke up she was unable to see out of her left eye and made an appointment to come see you. Other than SLE, her medical history is unremarkable. She has had no additional symptoms other than pain and vision loss. Her vital signs are all within normal limits. On exam, she has no vision in her left eye, but 20/30 visual acuity in her right eye. When you shine a light in her left eye there is no response. What response would you expect when you shine a light in her right eye?

Answer Choices:

(A) Bilateral miosis
(B) Miosis of the right eye only
(C) Miosis of the left eye only
(D) Mydriasis of the left eye

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/14a6b2e4-e863-4bb0-8165-3704e5ad0985

OpenEvidence Explanation

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The answer is **A. Bilateral miosis**.

This patient with SLE presents with acute unilateral painful vision loss consistent with **optic neuritis**, which causes a **relative afferent pupillary defect (RAPD)** in the affected (left) eye.[1][2][3] The key to this question is understanding the distinction between the afferent and efferent limbs of the pupillary light reflex.

Why bilateral miosis occurs when light is shone in the right eye:

In optic neuritis, the lesion is in the **afferent limb** (optic nerve) of the affected eye. The efferent limb (parasympathetic fibers via CN III to both pupils) remains intact bilaterally. When light is shone in the left (affected) eye, the damaged optic nerve cannot transmit the signal adequately, so neither pupil constricts — this is the afferent defect described in the question stem.[2]

However, when light is shone in the **right (unaffected) eye**, the intact right optic nerve transmits the signal normally to the pretectal nucleus, which then sends efferent signals via both Edinger-Westphal nuclei to both pupils. This produces:

- A normal **direct response** (right pupil constricts)
- A normal **consensual response** (left pupil constricts)

The result is **bilateral miosis** — both pupils constrict normally because the afferent input from the right eye is intact and the efferent pathways to both pupils are intact.[4]

This is the hallmark of a relative afferent pupillary defect: the asymmetry is in the afferent input, not the efferent output. An RAPD is almost always present in unilateral optic neuritis and was a required finding for diagnosis in the Optic Neuritis Treatment Trial (ONTT).[1][2][5] Optic neuritis affects approximately 1% of SLE patients and can present with painful monocular vision loss, as in this case.[6]

Would you like to explore the workup and management of SLE-associated optic neuritis, including the role of antiphospholipid antibodies and immunosuppressive therapy?

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Question 1256

A 25-year-old woman presents to the emergency department with abdominal pain. She states that she was walking up the stairs at work when she felt sudden and severe abdominal pain followed by nausea and vomiting. Her past medical history is non-contributory and she is not currently taking any medications. Her temperature is 99.7°F (37.6°C), blood pressure is 122/78 mmHg, pulse is 120/min, respirations are 17/min, and oxygen saturation is 98% on room air. Physical exam is notable for an absence of abdominal tenderness, a left adnexal mass, and left adnexal tenderness. A transvaginal ultrasound demonstrates free fluid surrounding the ovary with edema and the presence of doppler flow. A urinary pregnancy test is negative. The patient's symptoms persisted after ibuprofen and acetaminophen. Which of the following is the best next step in management?

Answer Choices:

(A) Laparoscopy
(B) Laparotomy
(C) MRI of the pelvis
(D) Observation and serial abdominal exams

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/8712c9a0-6dcd-4001-809b-85d0693ad248

OpenEvidence Explanation

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The best next step in management is **A. Laparoscopy**.

This presentation is highly suspicious for **ovarian torsion**: sudden-onset severe abdominal pain with nausea/vomiting, a left adnexal mass with tenderness, and ultrasound findings of free fluid and ovarian edema. Critically, the presence of Doppler flow does **not** rule out torsion — normal Doppler arterial flow has been reported in up to **60%** of surgically confirmed cases of adnexal torsion, which can be explained by intermittent torsion, collateral blood supply, or partial torsion.[1]

Key points supporting laparoscopy:

- **Adnexal torsion is a surgical diagnosis.** Per ACOG Committee Opinion No. 783, there are no clinical or imaging criteria sufficient to confirm the preoperative diagnosis, and **Doppler flow alone should not guide clinical decision making**.[1]
- When ovarian torsion is suspected, **timely intervention with diagnostic laparoscopy** is indicated to preserve ovarian function and future fertility. The risk of ovarian damage or loss outweighs the risk of a diagnostic laparoscopy in patients of reproductive age.[1][2]
- A **minimally invasive surgical approach** (laparoscopy, not laparotomy) is recommended, with detorsion and preservation of the adnexal structures regardless of the ovary's appearance. This makes laparoscopy (A) preferred over laparotomy (B).[1]
- **Observation (D)** is inappropriate given persistent symptoms unresponsive to analgesics and high clinical suspicion, as delay risks ovarian necrosis and loss of fertility.
- **MRI (C)** would only delay definitive management without changing the surgical indication.

Would you like to explore the evidence on ovarian salvage rates and long-term fertility outcomes after detorsion for ovarian torsion?

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Question 1258

A 24-year-old woman comes to the emergency department with her boyfriend 2 hours after an episode of loss of consciousness. She was seated and was being tattooed on her right upper flank when she became diaphoretic, pale, and passed out. According to her boyfriend, the patient slipped to the floor and her arms and legs moved in a jerky fashion for a few seconds. She regained consciousness within half a minute and was alert and fully oriented immediately. She has no history of serious illness. She works as an event manager and has had more stress than usual due to a recent concert tour. She appears well. Her temperature is 37°C (98.4°F), pulse is 68/min, respirations are 16/min, and blood pressure is 120/72 mm Hg. Her cardiopulmonary examination shows no abnormalities. Neurologic examination shows no focal findings. An ECG shows an incomplete right bundle branch block. Which of the following is the most likely diagnosis?

Answer Choices:

(A) Vasovagal syncope
(B) Orthostatic syncope
(C) Cardiac arrhythmia
(D) Cardiac structural abnormality

Correct Answer:

(A)

OpenEvidence Response:

(A) ✓

OpenEvidence Link: https://openevidence.com/ask/48bd531c-4eb5-4b55-bba3-a688695cb44b

OpenEvidence Explanation

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Vasovagal Syncope

The most likely diagnosis is **A. Vasovagal syncope**.

This presentation is classic for a vasovagal (neurocardiogenic) syncopal episode, supported by several key features:

- **Clear trigger**: Pain and emotional stress from the tattooing procedure are well-recognized precipitants of vasovagal syncope.
- **Prodromal symptoms**: Diaphoresis and pallor preceding the loss of consciousness are hallmark features of the vasovagal prodrome, reflecting a surge in vagal tone with resultant hypotension and bradycardia.
- **Brief convulsive movements**: Short-duration myoclonic jerks ("convulsive syncope") can occur during vasovagal episodes due to transient cerebral hypoperfusion and do not indicate epilepsy. These typically last only a few seconds, as described here.
- **Rapid, complete recovery**: Immediate return to full alertness and orientation after the event is characteristic of vasovagal syncope, in contrast to the prolonged postictal confusion seen with seizures.
- **Young, otherwise healthy patient** with situational stress (concert tour workload) further increases susceptibility.

Why not the other options?

- **B. Orthostatic syncope** — She was seated, not standing, at the time of the event, making orthostatic hypotension unlikely. Vital signs are also normal.
- **C. Cardiac arrhythmia** — The incomplete right bundle branch block (iRBBB) is a **normal variant** commonly found in young, healthy individuals and does not indicate arrhythmic risk. There are no features suggesting arrhythmia (no palpitations, exertional syncope, or family history of sudden death).

- **D. Cardiac structural abnormality** — No murmur, no exertional symptoms, and a normal cardiopulmonary exam make structural heart disease very unlikely in this age group.

Would you like to explore the diagnostic criteria and risk stratification tools (such as the San Francisco Syncope Rule or Canadian Syncope Risk Score) used to evaluate syncope in the emergency department?

Question 1260

A 51-year-old man is brought to the physician by his wife because of a 3-week history of abnormal behavior. His wife reports he has been preoccupied with gambling at the local casino. He becomes restless and irritable when his wife attempts to restrict his gambling. Four months ago, he was diagnosed with Parkinson disease and treatment was initiated. Which of the following best describes the mechanism of action of the drug that was most likely prescribed for this patient?

Answer Choices:

(A) Peripheral inhibition of DOPA decarboxylase
(B) Direct activation of dopamine receptors
(C) Selective inhibition of monoamine oxidase B
(D) Inhibition of catechol-O-methyl transferase

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/e83af0aa-6787-492e-b94a-acd225338cec

OpenEvidence Explanation

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The answer is **B. Direct activation of dopamine receptors**.

The clinical scenario describes a patient with newly diagnosed Parkinson disease who develops **pathological gambling** — a classic **impulse control disorder (ICD)** strongly associated with **dopamine agonist** therapy (e.g., pramipexole, ropinirole). Dopamine agonists work by **directly stimulating dopamine receptors** (particularly D2/D3 subtypes) in the striatum, bypassing the need for metabolic conversion.[1][2]

Why dopamine agonists are the most likely culprit:

- Dopamine agonists are commonly used as initial monotherapy in younger Parkinson disease patients (this patient is 51) to delay levodopa-associated motor complications such as dyskinesias.[3][4]
- The DOMINION study (n = 3,090) found ICDs in **17.1% of patients on dopamine agonists** versus 6.9% on other medications (OR 2.72; 95% CI 2.08–3.5), with pathological gambling occurring in ~5%.[5]
- D3 receptor agonism has been particularly implicated in ICD risk, as D3 receptors are concentrated in the mesolimbic reward pathway.[6]

Why not the other options:

- **A (Peripheral DOPA decarboxylase inhibition)** — This describes carbidopa, which is always given with levodopa and is not independently associated with ICDs at this level.
- **C (Selective MAO-B inhibition)** — Selegiline/rasagiline carry a lesser ICD risk and are typically used for mild symptoms.[4][7]
- **D (COMT inhibition)** — Entacapone/tolcapone are adjuncts to levodopa, not first-line monotherapy, and are not strongly linked to ICDs.[8]

Would you like to explore the management strategies for dopamine agonist–induced impulse control disorders, including dose reduction protocols and alternative medications?

Relevant images

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Question 1266

A 45-year-old male with a history of diabetes and poorly controlled hypertension presents to his primary care physician for an annual check-up. He reports that he feels well and has no complaints. He takes enalapril and metformin. His temperature is 98.8°F (37.1°C), blood pressure is 155/90 mmHg, pulse is 80/min, and respirations are 16/min. His physician adds another anti-hypertensive medication to the patient's regimen. One month later, the patient returns to the physician complaining of new onset lower extremity swelling. Which of the following medications was likely prescribed to this patient?

Answer Choices:

(A) Metoprolol
(B) Verapamil
(C) Nifedipine
(D) Hydrochlorthiazide

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/0028fb44-240e-4724-8038-4a8bf2a2f840

OpenEvidence Explanation

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The answer is **C. Nifedipine**.

Nifedipine, a dihydropyridine calcium channel blocker (DHP CCB), is the most likely medication to cause new-onset lower extremity edema in this clinical scenario. Among the answer choices, it is the only drug strongly associated with dose-dependent peripheral edema of the lower extremities.

Mechanism: DHP CCBs like nifedipine cause peripheral edema by preferentially dilating precapillary arterioles without a corresponding effect on postcapillary venules, leading to increased intracapillary hydrostatic pressure and fluid extravasation into the interstitial space.[1] This is not a fluid-overload state, which is an important distinction — diuretics are generally ineffective for this type of edema.[2]

Why nifedipine specifically? A network meta-analysis of 71 RCTs (56,283 patients) found that **nifedipine ranked highest among all DHP CCBs for inducing peripheral edema** (SUCRA 81.8%).[1] The incidence of peripheral edema with DHP CCBs ranges from 5% to 60% at higher doses, and the weighted incidence across studies is approximately 12.3% for DHP CCBs compared to only 3.1% for non-DHP CCBs (verapamil, diltiazem).[1][3]

Why not the other options?

- **Metoprolol (A):** Beta-blockers can cause edema but far less commonly; this is not their hallmark side effect.
- **Verapamil (B):** A non-dihydropyridine CCB with a much lower incidence of peripheral edema (3.1% vs. 12.3% for DHPs). Its more characteristic side effects are constipation and bradycardia.[3][4]
- **Hydrochlorothiazide (D):** A thiazide diuretic that would be expected to reduce edema, not cause it. Its characteristic adverse effects include electrolyte imbalances (hypokalemia, hyponatremia) and hyperglycemia.[5]

Would you like to explore strategies for managing CCB-induced peripheral edema, including the evidence for combining DHP CCBs with ACE inhibitors or ARBs to mitigate this effect?

Relevant images

(CONTENT OMITTED)

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Question 1267

A 29-year-old woman comes to the physician with high-grade fever, headache, and muscle pain. A week ago, she returned from India, where she was working with an NGO to build houses in rural areas. The patient took one dose of chloroquine one week before her trip. She also took a further dose during her trip. She has no history of a serious illness. Her temperature is 39.3°C (102.7°F), pulse is 102/min, respirations are 22/min, and blood pressure is 112/78 mm Hg. Physical examination shows jaundice. The abdomen is soft and nontender. The remainder of the examination shows no abnormalities. Her hemoglobin concentration is 10 g/dL and a blood smear shows fragmented erythrocytes and occasional ring-shaped inclusion bodies within erythrocytes. Which of the following is the most likely cause of infection in this patient?

Answer Choices:

(A) Plasmodium ovale
(B) Plasmodium falciparum
(C) Chikungunya virus
(D) Hepatitis A virus

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/9d79135d-9ff8-4475-9578-7d1250b2e973

OpenEvidence Explanation

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The answer is **B. Plasmodium falciparum**. Several key features in this presentation point to *P. falciparum* as the causative organism:

Ring-shaped inclusion bodies on blood smear are characteristic of *P. falciparum*, which classically shows early ring stages (often with multiple parasites per erythrocyte) in infected erythrocytes of all sizes.[1] The **fragmented erythrocytes** reflect the hemolytic process and microvascular damage caused by sequestration of parasitized red blood cells, a hallmark of *P. falciparum* virulence.[2]

Inadequate chloroquine prophylaxis is a critical clue. The patient took only two doses of chloroquine rather than the recommended weekly regimen (starting 1–2 weeks before travel, continuing weekly during travel, and for 4 weeks after return). Moreover, ***chloroquine-resistant* P. falciparum is widespread in India, making chloroquine an inappropriate choice for prophylaxis in this region even if taken correctly.**[1]

Severity of presentation — high-grade fever, jaundice, and anemia (hemoglobin 10 g/dL) — is consistent with *P. falciparum*, which can infect erythrocytes of all ages and produce high parasitemia, leading to severe hemolysis, hyperbilirubinemia, and potentially life-threatening disease in nonimmune travelers.[2]

Why not the other options:

- **P. ovale** (A) preferentially invades young red blood cells, produces low parasitemia, and rarely causes severe disease (severe disease in ~0.03% of cases). Infected erythrocytes appear oval with fimbriae and Schüffner dots.[1]
- **Chikungunya virus** (C) causes fever and severe arthralgias/polyarthralgia but would not produce ring-shaped inclusion bodies on blood smear.
- **Hepatitis A virus** (D) can cause jaundice and fever but would not explain ring-shaped inclusions in erythrocytes or the hemolytic anemia pattern seen here.

Would you like to explore the current recommended antimalarial prophylaxis regimens for travelers to chloroquine-resistant regions such as India?

Relevant images

(CONTENT OMITTED)

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Question 1268

A 39-year-old woman presents to the clinic for her annual physical. Although she feels generally healthy she has noticed gaining about 9 kg (20 lb) over the last year. She eats a healthy, varied diet and exercises at the gym 4 days a week, including 20 minutes of aerobic exercise. On further questioning, she has also noted fatigue and constipation. She denies shortness of breath, chest pain, lightheadedness, or blood in her stool. At the clinic, the vital signs include: pulse 52/min, blood pressure 110/72 mm Hg, and oxygen saturation 99% on room air. The physical exam is notable only for slightly dry skin. The complete blood count (CBC) is within normal limits. Which of the following laboratory values is most likely elevated in this patient?

Answer Choices:

(A) Glucose
(B) Triiodothyronine (T3)
(C) Thyroxine (T4)
(D) Thyroid-stimulating hormone (TSH)

Correct Answer:

(D)

OpenEvidence Response:

(D) ✓

OpenEvidence Link: https://openevidence.com/ask/ddb28f0f-d763-4c7c-b761-5c5a1c26dfd6

OpenEvidence Explanation

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The answer is **D. Thyroid-stimulating hormone (TSH)**.

This patient's presentation — **weight gain, fatigue, constipation, bradycardia (52/min), and dry skin** — is classic for **primary hypothyroidism**. In primary hypothyroidism, the thyroid gland fails to produce adequate thyroid hormones (T3 and T4), which triggers a compensatory rise in **TSH** from the anterior pituitary via loss of negative feedback.

Why the other options are incorrect:

- **A. Glucose** – While hypothyroidism can be associated with metabolic changes, hyperglycemia is not a hallmark feature. The clinical picture here points much more strongly to a thyroid disorder.
- **B. Triiodothyronine (T3)** – T3 would be **low or low-normal** in hypothyroidism, not elevated. Elevated T3 would be seen in hyperthyroidism, which presents with weight loss, tachycardia, heat intolerance, and diarrhea — the opposite of this patient's findings.
- **C. Thyroxine (T4)** – T4 would similarly be **low** in primary hypothyroidism. Elevated T4 is characteristic of hyperthyroidism.

The most common cause of primary hypothyroidism in iodine-sufficient regions is **Hashimoto thyroiditis** (chronic lymphocytic thyroiditis), an autoimmune condition most prevalent in women aged 30–50. Diagnosis is confirmed with an elevated TSH and low free T4, and anti-thyroid peroxidase (anti-TPO) antibodies are often positive. Standard treatment is levothyroxine replacement therapy.

Would you like to explore the recommended approach to levothyroxine dosing and TSH monitoring targets in newly diagnosed hypothyroidism?

Question 1270

A 21-year-old college student comes to the physician because of daytime fatigue for 2 months. He has problems getting to sleep at night and frequently falls asleep during class. Recently he has started skipping classes altogether. He goes to bed between 11 p.m. and 1 a.m. but cannot fall asleep for 2–3 hours. When he wakes up at 8:30 a.m., he feels extremely drowsy, and he tries to overcome his fatigue by drinking 2–3 cups of coffee a day. He naps at various times during the afternoon, often for more than an hour. He stopped watching videos on his smartphone at night because of suggestions from his peers. He states that he has tried over-the-counter melatonin pills and exercising at 8 p.m. without success. He has no history of serious illness. He does not smoke. He drinks three to five beers on weekends. Physical examination shows no abnormalities. Which of the following is the most appropriate recommendation for this patient?

Answer Choices:

(A) Trial of diphenhydramine
(B) Stop evening exercise
(C) Alcoholic beverage prior to bedtime
(D) Scheduled afternoon naps

Correct Answer:

(B)

OpenEvidence Response:

(B) ✓

OpenEvidence Link: https://openevidence.com/ask/0b3e7a65-4d50-4ba7-a7e4-5c164b36749f

OpenEvidence Explanation

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The most appropriate recommendation is **B. Stop evening exercise**. Evening exercise at 8 p.m. can further **delay circadian timing** and worsen sleep onset latency, which is counterproductive in this patient who likely has **delayed sleep-wake phase disorder (DSWPD)**.

This patient's presentation — a young adult with difficulty initiating sleep at conventional bedtimes, sleep onset delayed to 1–4 a.m., morning drowsiness, and daytime sleepiness — is classic for DSWPD, the most common circadian rhythm sleep disorder in adolescents and young adults.[1] Key sleep hygiene principles apply here:

- **Evening exercise can delay circadian phase.** Evidence demonstrates that nocturnal/evening exercise delays sleep onset and worsens sleep quality, particularly when performed within 4 hours of sleep onset. In individuals with circadian rhythm disorders specifically, evening exercise appears to delay sleep onset further. The AASM found no evidence supporting timed exercise as a treatment for DSWPD, and in this patient's case, exercising at 8 p.m. is likely exacerbating his already-delayed sleep phase.[2][3][4][5]
- **Diphenhydramine (A)** is not recommended for chronic insomnia or circadian rhythm disorders due to tolerance, anticholinergic side effects, and lack of evidence for circadian phase correction.[6]
- **Alcohol before bedtime (C)** disrupts sleep architecture, reduces REM sleep, and worsens sleep quality — it is not a recommended sleep aid.
- **Scheduled afternoon naps (D)** would reduce homeostatic sleep drive and further impair the ability to fall asleep at an appropriate bedtime, worsening the cycle.

Among the available options, stopping evening exercise is the most evidence-based behavioral modification, as it removes a factor actively contributing to circadian delay.

Would you like to explore the optimal timing and dosing of melatonin for delayed sleep-wake phase disorder in young adults?

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Question 1271

A 19-year-old man is brought to the physician by his mother because she is worried about his strange behavior. Over the past 3 years, he has been dressing all in black and wears a long black coat, even in the summer. The mother reports that her son has always had difficulties fitting in. He does not have any friends and spends most of his time in his room playing online games. He is anxious at college because he is uncomfortable around other people, and his academic performance is poor. Rather than doing his coursework, he spends most of his time reading up on paranormal phenomena, especially demons. He says that he has never seen any demons, but sometimes there are signs of their presence. For example, a breeze in an enclosed room is likely the “breath of a demon”. Mental status examination shows laborious speech. The patient avoids eye contact. Which of the following is the most likely diagnosis?

Answer Choices:

(A) Social anxiety disorder
(B) Avoidant personality disorder
(C) Schizotypal personality disorder
(D) Schizophrenia

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/5270c821-8727-498d-af4d-f248cc7f3afd

OpenEvidence Explanation

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The most likely diagnosis is **C. Schizotypal personality disorder**.

This patient demonstrates multiple hallmark features of schizotypal personality disorder as defined in the DSM-5:[1][2]

- **Odd beliefs and magical thinking**: Preoccupation with paranormal phenomena (demons) and interpreting a breeze in an enclosed room as the "breath of a demon" — a classic example of magical thinking that influences behavior, consistent with Criterion A2.[1]
- **Eccentric behavior and appearance**: Dressing entirely in black with a long black coat even in summer fulfills the criterion for odd, eccentric, or peculiar behavior/appearance (Criterion A7).[1]
- **Odd speech**: Laborious speech on mental status examination aligns with the odd thinking and speech criterion (Criterion A4), which can manifest as vague, circumstantial, or idiosyncratic communication.[1]
- **No close friends**: Spending most of his time alone playing online games with no friends (Criterion A8).[1]
- **Social anxiety that does not diminish with familiarity**: Discomfort around others at college (Criterion A9).[1]
- **Avoidance of eye contact**: Consistent with the interpersonal awkwardness and constricted interaction style seen in schizotypal personality disorder.[1]

Why not the other options?

- **Social anxiety disorder (A)**: While this patient has social anxiety, it is accompanied by magical thinking, eccentric dress, odd speech, and perceptual-like experiences — features not explained by social anxiety disorder alone.[1][3]
- **Avoidant personality disorder (B)**: Avoidant personality disorder involves an active desire for relationships constrained by fear of rejection and

negative evaluation. This patient shows a **lack of desire** for relationships and persistent detachment, along with cognitive-perceptual distortions that are absent in avoidant personality disorder.[1][4]

- **Schizophrenia (D)**: The patient does not have frank psychotic symptoms — he acknowledges he has never seen demons, and his beliefs are subclinical (magical thinking rather than fixed delusions). There are no hallucinations or persistent psychotic symptoms, which are required for schizophrenia. His reality testing remains partially intact.[1]

The pervasive pattern beginning in early adulthood, combining social-interpersonal deficits with cognitive/perceptual distortions and behavioral eccentricities, is the defining feature of schizotypal personality disorder.[1]

Would you like to explore the risk of progression from schizotypal personality disorder to schizophrenia and recommended monitoring strategies?

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Question 1272

A 79-year-old man presents to the office due to shortness of breath with moderate exertion and a slightly productive cough. He has a medical history of 25 years of heavy smoking. His vitals include: heart rate 89/min, respiratory rate 27/min, and blood pressure 120/90 mm Hg. The physical exam shows increased resonance to percussion, decreased breath sounds, and crackles at the lung base. Chest radiography shows signs of pulmonary hyperinflation. Spirometry shows a forced expiratory volume in the first second (FEV1) of 48%, a forced vital capacity (FVC) of 85%, and an FEV1/FVC ratio of 56%. According to these results, what is the most likely diagnosis?

Answer Choices:

(A) Asthma
(B) Lymphangioleiomyomatosis
(C) Chronic obstructive pulmonary disease (COPD)
(D) Heart failure

Correct Answer:

(C)

OpenEvidence Response:

(C) ✓

OpenEvidence Link: https://openevidence.com/ask/e07aab32-393b-4eee-874a-23221c7ab392

OpenEvidence Explanation

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The most likely diagnosis is **C. Chronic obstructive pulmonary disease (COPD)**. Every element of this presentation — the clinical history, physical examination, imaging, and spirometry — converges on this diagnosis.

Spirometry is the reference standard for diagnosing COPD. The GOLD guidelines define airflow obstruction as an **FEV1/FVC ratio < 0.70**.[1] This patient's FEV1/FVC ratio of **56%** (0.56) clearly meets this criterion. The FEV1 of 48% predicted classifies the airflow obstruction as **GOLD Grade 3 (severe)**, corresponding to an FEV1 between 30–49% predicted.[2]

The clinical picture is classic for COPD:

- **Risk factor**: 25-year heavy smoking history, the primary risk factor for COPD[3]
- **Symptoms**: Exertional dyspnea and productive cough, the hallmark symptoms[1][4]
- **Physical exam**: Increased resonance to percussion (hyperinflation/air trapping), decreased breath sounds, and basilar crackles — all consistent with emphysematous changes[4]
- **Chest radiography**: Pulmonary hyperinflation, a characteristic radiographic finding of COPD

Why not the other options?

- **Asthma** typically presents with variable, reversible airflow obstruction, symptom variability (worse at night/early morning), and is associated with atopy, rhinitis, or eczema. Onset in a 79-year-old with fixed obstruction and heavy smoking history strongly favors COPD.[1][5]
- **Heart failure** produces volume restriction on pulmonary function testing (reduced FVC and FEV1 proportionally), not an obstructive pattern. Chest radiography would show cardiomegaly and pulmonary edema rather than hyperinflation.[1][6]
- **Lymphangioleiomyomatosis (LAM)** is exceedingly rare and occurs almost exclusively in premenopausal women, making it highly unlikely in a 79-year-old male.[1]

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Based on the available data, the GOLD COPD calculator above can be used to further classify this patient's COPD group (A, B, or E) once exacerbation history and formal symptom burden scoring (mMRC or CAT) are obtained.

Would you like to explore the initial pharmacotherapy recommendations for COPD based on GOLD group classification and the role of inhaled corticosteroids guided by blood eosinophil counts?

Relevant images

(CONTENT OMITTED)

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