MedQA

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Question 1

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?

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

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

This presentation is a classic case of **atheroembolic renal disease (cholesterol crystal embolization)** following an invasive vascular procedure. The diagnostic triad is present:[1]

1. **Precipitating event** — cardiac catheterization 2 weeks prior, which can dislodge atheromatous plaque material from the aorta

2. **Acute/subacute renal failure** — creatinine of 4.2 mg/dL with decreased urinary output
3. **Skin findings** — mottled, reticulated purplish discoloration of the feet (livedo reticularis / "blue toe syndrome")

The **intravascular spindle-shaped vacuoles** on renal biopsy are pathognomonic **cholesterol clefts** — biconvex, needle-shaped empty spaces ("ghost cells") left behind when cholesterol crystals dissolve during histological processing.[1] They are found within arcuate and interlobular arteries.

Supporting laboratory findings include **eosinophilia** (11%) and markedly **elevated ESR** (68 mm/h), both characteristic of the inflammatory response to cholesterol crystal emboli.[1][2][3] Low-grade fever and leukocytosis further reflect this systemic inflammatory state.

Why not the other choices:

- **A. Renal papillary necrosis** — associated with NSAID use and diabetes (both present here), but would not explain livedo reticularis, eosinophilia, or cholesterol clefts on biopsy. Urinalysis would typically show hematuria and sloughed papillary tissue.
- **C. Eosinophilic granulomatosis with polyangiitis (EGPA)** — can cause eosinophilia and renal disease but is associated with asthma, sinusitis, and extravascular eosinophilic granulomas, not cholesterol clefts on biopsy.
- **D. Polyarteritis nodosa** — causes medium-vessel vasculitis with fibrinoid necrosis, not cholesterol clefts. The temporal relationship to catheterization and the characteristic biopsy findings point away from PAN.

Would you like to explore the management and prognosis of atheroembolic renal disease?

References

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Question 2

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?

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

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

This presentation — **bilateral itchy, watery eyes with conjunctival injection, sneezing, and seasonal recurrence** — is classic for **seasonal allergic conjunctivitis**. The key clinical features pointing to this diagnosis include the pruritus (hallmark symptom), watery (not purulent) discharge, bilateral involvement, seasonal pattern, and unremarkable anterior chamber examination.

Topical dual-activity agents (combined antihistamine and mast cell stabilizer) such as **ketotifen** are the **standard of care and first-line pharmacotherapy** for allergic conjunctivitis.[1][2] Ketotifen blocks histamine H1 receptors, stabilizes mast cells, and prevents eosinophil accumulation, providing both acute symptom relief and prophylaxis against recurrence.[3][4] It is available over the counter and has demonstrated superiority over placebo and levocabastine in reducing itching and tearing.[5]

Why the other options are incorrect:

- **A. Erythromycin ointment** — Treats bacterial conjunctivitis, which typically presents with mucopurulent discharge and matted eyelids, not the itchy, watery, bilateral presentation seen here.[1]
- **C. Warm compresses** — Used for chalazia or hordeola. For allergic conjunctivitis, **cold** compresses (not warm) are recommended to provide vasoconstriction and symptom relief.[1]
- **D. Fluorometholone eye drops** — A topical corticosteroid reserved for refractory or severe cases, not first-line therapy. Topical steroids carry risks of cataract formation, increased intraocular pressure, and enhanced infection susceptibility, and their use should be supervised by ophthalmology.[1][6]

Would you like to explore how topical dual-action agents compare in efficacy for seasonal allergic conjunctivitis?

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Question 3

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?

A. Nifedipine
B. Enoxaparin
C. Clopidogrel
D. Spironolactone

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The correct answer is **C. Clopidogrel**.

This patient presents with an **NSTEMI** (ST depressions with elevated troponin) treated with **PCI**. After PCI for ACS, **dual antiplatelet therapy (DAPT)** with aspirin plus a **P2Y12 inhibitor** is standard of care, recommended for at least 12 months as the default strategy in patients without high bleeding risk.[1] Among the answer choices, **clopidogrel is the only P2Y12 inhibitor**. While current guidelines prefer ticagrelor or prasugrel over clopidogrel in patients with ACS undergoing PCI, clopidogrel remains a guideline-endorsed P2Y12 inhibitor and is the appropriate choice here given the available options.[1][2]

Why the other options are incorrect:

- **A. Nifedipine** — Immediate-release nifedipine causes reflex tachycardia and is contraindicated in ACS. Even extended-release nifedipine has no established role in secondary prevention after MI.[3]
- **B. Enoxaparin** — A parenteral anticoagulant used during the acute hospitalization phase of ACS management, not a discharge medication.[4]

- **D. Spironolactone** — Aldosterone antagonists are indicated post-MI in patients with **LVEF ≤40%** and either heart failure symptoms or diabetes. This patient's LVEF is **58%** (preserved), so spironolactone is not indicated.[5][6]

Notably, the patient's **asthma** is clinically relevant context — it would influence the choice of beta-blocker therapy (another standard post-ACS medication), but since beta-blockers are not among the answer choices, it serves as a distractor. The patient is already appropriately on lisinopril and atorvastatin, both part of standard post-ACS secondary prevention.[6]

Would you like to explore how to choose between ticagrelor, prasugrel, and clopidogrel after PCI for ACS?

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Question 4

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?

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

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B. Active or recurrent pelvic inflammatory disease. Acute PID is an explicit labeled contraindication to copper IUD placement, along with "conditions associated with increased susceptibility to pelvic infections," untreated acute cervicitis/vaginitis, distorted uterine cavity, pregnancy, unexplained uterine bleeding, known/suspected uterine or cervical malignancy, Wilson disease, and copper hypersensitivity.[1] Current pelvic infection is US MEC Category 4 for IUD **initiation** (though only Category 2 for continuation in an existing user).[2][3]

Why the other options are not contraindications to a copper IUD

- **A. Stroke or VTE** — the Cu-IUD is nonhormonal and carries no thrombotic risk; US MEC Category 1 for history of DVT/PE not on anticoagulation, and Category 2 if on therapeutic anticoagulation, where the concern is heavier menses rather than thrombosis. Copper IUD use in anticoagulated patients has been associated with worsened uterine bleeding, whereas LNG-IUDs reduce it.[4][5][6]
- **C. Breast cancer** — Cu-IUD is Category 1 for both current and past breast cancer; it is the LNG-IUD that is Category 4 (current) and Category 3 (past, disease-free 5 years). The copper IUD is in fact the most effective nonhormonal option recommended for breast cancer survivors.[2][4][7]
- **D. Liver neoplasm** — a concern for combined and progestin-only hormonal contraception, not for a device delivering no systemic hormone.

Practical caveats

- The distinction that matters is **active** infection. A remote history of PID, now resolved, is not an absolute barrier; the contraindication applies to current PID, current purulent cervicitis, or known untreated chlamydial/gonococcal infection. Insertion can proceed once treatment is complete, symptoms resolve, and the cervical and bimanual exams are normal.[3][8]
- **Screening should not delay placement.** STI testing per CDC criteria can be done the same day as insertion, and routine antibiotic prophylaxis is not recommended.[3][9]
- If PID develops with an IUD in situ, **removal is not required** — treat per CDC guidance and reassess at 48–72 hours, considering removal only if there is no clinical improvement.[10][11]
- For this 37-year-old switching from OCPs, counsel that the copper IUD typically produces heavier, longer, and more painful menses, a leading reason for discontinuation; NSAIDs for 5–7 days can reduce bleeding.[8]

Would you like to explore the timing and bridging strategy for switching from OCPs to a copper IUD?

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Question 5

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?

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

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

In the current CDC-recommended HIV testing algorithm, initial screening is performed with an **HIV-1/HIV-2 antigen/antibody (Ag/Ab) combination immunoassay** (4th-generation test), which detects both HIV antibodies and p24 antigen.[1][2] In urgent settings such as labor with unknown HIV status, a **rapid point-of-care test** (antibody-only or Ag/Ab) may be used for expedited screening, as described in this vignette.[3] When the initial screening is reactive, the specimen is reflexed to an **HIV-1/HIV-2 antibody differentiation immunoassay** for confirmatory/supplemental testing.[1][2][3]

This differentiation immunoassay (e.g., the Bio-Rad Geenius HIV 1/2 Confirmatory Assay) **replaced the Western blot**, which is no longer recommended due to its subjectivity, labor intensity, limited sensitivity in early infection, and inability to reliably differentiate HIV-1 from HIV-2.[1][4][5]

Why the other options are incorrect:

- **A (Southwestern blot)** — Identifies DNA-binding proteins; this is a research technique unrelated to HIV diagnostics.
- **B (Northern blot identifying RNA)** — A laboratory method for detecting specific RNA sequences, not used in clinical HIV confirmation.
- **C (Northern blot identifying DNA)** — Incorrect on two counts: Northern blots detect RNA (not DNA), and they are not part of the HIV diagnostic algorithm. (Southern blots detect DNA.)

Would you like to explore the intrapartum and neonatal zidovudine prophylaxis protocol for preventing perinatal HIV transmission?

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Question 6

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?

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

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

Standing from supine causes gravitational pooling of 500–1,000 mL of blood into the lower extremities and splanchnic vasculature, decreasing venous return, central blood volume, and cardiac filling pressures.[1][2][3] Baroreceptor-mediated compensatory responses ensue: **sympathetic activation and parasympathetic withdrawal increase heart rate by ~20%**, which directly **shortens diastolic filling time**.[4][5]

This is supported by direct measurement: diastolic time per beat decreased from **519 ± 176 ms supine to 375 ± 115 ms standing** ($p < 0.01$).[4]

The other options are incorrect:

- **A (Increase in right atrial pressure):** Right atrial pressure **decreases** by ~5 mmHg upon standing due to reduced venous return and gravitational blood pooling.[6]
- **B (Increase in pulmonary capillary wedge pressure):** PCWP also **falls** with upright posture as central blood volume drops.[5][7]
- **C (Reduction in the slope of the pacemaker potential):** The baroreflex response to standing involves sympathetic activation and vagal withdrawal, which **increases** (not reduces) the slope of phase 4 (pacemaker) depolarization in the SA node, thereby increasing heart rate.[1][2][8]

The clinical context — a **mid-systolic murmur at the 2nd left intercostal space radiating to the carotids** — is consistent with **aortic stenosis**, in which reduced diastolic filling time upon standing further decreases preload and may soften the murmur. However, the question specifically tests understanding of the normal physiological response to orthostasis, not aortic stenosis management.

Would you like to explore how standing and other maneuvers change the intensity of various cardiac murmurs?

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Question 7

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?

A. Blinding
B. Restriction
C. Randomization
D. Matching

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The answer is **D. Matching**.

In this case-control study, the pediatrician selected 75 controls (infants without BRUE) who were of **the same age, socioeconomic background, and family history** as the 75 cases (infants with BRUE). This is a textbook example of **matching** — a design-stage strategy to control confounding in observational studies by selecting controls that are similar to cases on known confounders.[1] [2]

Why the other options are incorrect:

- **A. Blinding** — Controls for information bias (e.g., detection bias, reporting bias), not confounding.[3]
- **B. Restriction** — Involves limiting the entire study population to a single category of the confounder (e.g., enrolling only one sex, or only one narrow age group), thereby eliminating variability in that factor across the study. The key distinction is that restriction narrows the

eligibility criteria uniformly, whereas matching allows variation in the confounder but ensures cases and controls share the same distribution of those variables.[1]

- **C. Randomization** — Balances both known and unknown confounders, but is a feature of experimental (RCT) designs, not observational case-control studies.[1]

As noted in the epidemiologic literature, matching in case-control studies generates subsamples of cases and controls that are similar with respect to one or more confounders, and is one of three major design-stage methods for confounding control alongside restriction and randomization.[1][2][4]

Would you like to explore the trade-offs between matching, restriction, and stratification for confounder control in case-control studies?

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Question 8

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?

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

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

This presentation is classic for **acute pericarditis**: sharp chest pain worsening when supine and improving with leaning forward, radiating to the shoulders and neck, with a pericardial friction rub (the "scratching, to-and-from" sound at the left sternal border) and expected diffuse ST elevation with PR depression on ECG. The normal chest X-ray and absence of hemodynamic compromise indicate uncomplicated disease.

Why B is correct

First-line treatment for acute idiopathic/viral pericarditis is **dual anti-inflammatory therapy** with a high-dose NSAID (ibuprofen 600–800 mg three times daily) plus **colchicine** (0.5 mg twice daily if >70 kg; 0.5 mg once daily if ≤70 kg) for 3 months.[1][2] A proton-pump inhibitor is added for gastroprotection with NSAID use.[1][3] In the **ICAP trial**, colchicine reduced the rate of incessant or recurrent pericarditis from **37.5% to 16.7%** compared with placebo, establishing its role as a critical adjunct to NSAIDs for the initial episode.[2]

> "Treatment of acute idiopathic and pericarditis after cardiac procedures or operations involves use of high-dose nonsteroidal anti-inflammatory drugs (NSAIDs), with doses tapered once chest pain has resolved and C-reactive protein level has normalized, typically over several weeks. These patients should receive a 3-month course of colchicine to relieve symptoms and reduce the risk of recurrence."
>
> —Paul C. Cremer, MD, MS 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. JAMA. October 01, 2024.
>
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Why the other options are incorrect

- **A (Indomethacin +/- omeprazole):** While indomethacin is an acceptable NSAID for pericarditis, this option omits colchicine. Guideline-recommended first-line therapy requires the addition of colchicine to reduce recurrence risk.[1]
- **C (Pericardiocentesis):** Reserved for cardiac tamponade or large effusions causing hemodynamic compromise. This patient has uncomplicated pericarditis with no effusion on chest X-ray.[2]
- **D (Pericardiectomy):** A last-resort surgical option for refractory recurrent pericarditis or constrictive pericarditis unresponsive to medical therapy — not appropriate for an initial episode.[1]

Would you like to explore the risk stratification criteria and indications for hospital admission in acute pericarditis?

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Question 9

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?

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

https://openevidence.com/ask/84c8518d-d165-4da5-8434-15a6ff6f4fe5

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

Radiation therapy is a well-established risk factor for secondary hematologic malignancies, including non-Hodgkin lymphoma (NHL). This patient received radiation for breast cancer approximately 15+ years ago, which aligns with the known latency period for radiation-induced secondary malignancies. A SEER-based study found that radiation therapy for breast DCIS was associated with a significantly increased delayed risk of NHL (HR 1.33; 95% CI 1.09–1.62).[1] Similarly, a large population study of over 1.4 million cancer survivors demonstrated an increased NHL risk after initial radiotherapy for solid cancers (RR 1.13; 95% CI 1.06–1.20).[2] Radiation dose has been specifically linked to increased incidence of mature B-cell lymphoma (RR 3.90 for 30 mGy vs. 0 mGy).[3]

Why the other options are incorrect:

- **A. Travel to Africa** — While certain endemic infections (e.g., EBV-associated Burkitt lymphoma, HIV) are more prevalent in Africa, travel alone is not a recognized risk factor for DLBCL. No specific infection is described in this patient.

- **B. Axillary lymph node involvement** — This describes the **site of disease presentation**, not a risk factor. Lymphadenopathy is a common presenting feature of DLBCL.[4][5]

- **D. Previous breast cancer** — While breast cancer survivors have a modestly increased risk of NHL, this association is largely confounded by the **treatments** received (radiation and chemotherapy) rather than the cancer diagnosis itself. The question specifically separates these options, and the direct causative risk factor is the radiation therapy.[6]

The centroblastic and immunoblastic morphology described on FNA is characteristic of DLBCL, the most common NHL subtype, representing 30–40% of adult lymphomas.[4][7] The long latency (over a decade), the prior radiation exposure, and the anatomical proximity to the irradiated field all point to radiation therapy as the responsible risk factor.

Would you like to explore the recommended workup and first-line treatment for newly diagnosed DLBCL?

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Question 10

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?

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

https://openevidence.com/ask/6b24562e-afaf-47d4-a042-eef111324a87

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

Several features of this case converge on acute pulmonary histoplasmosis:

- **Endemic geography**: The patient was hiking in **Mississippi**, within the Mississippi River valley, which is a hyperendemic area for *H. capsulatum*.[1][2]
- **Classic presentation**: Dry cough, chest discomfort, fever, chills, myalgias, arthralgias, and headache developing **~10 days after exposure** align with acute pulmonary histoplasmosis, which typically presents 2–3 weeks after inhalation of conidia with symptoms mimicking community-acquired pneumonia.[1][3]
- **Urinary polysaccharide antigen positivity**: The *Histoplasma* urinary antigen (EIA detecting galactomannan) is a major rapid diagnostic tool, with sensitivity of **75–81% in immunocompetent patients with acute pulmonary infection**.[4][5]
- **BAL with GMS/PAS staining showing macrophages filled with a dimorphic fungus**: This is the histopathologic hallmark of histoplasmosis — **small (2–4 μm) oval intracellular yeasts found within phagocytic cells**, staining strongly with GMS and PAS. The term "dimorphic

fungus with septate hyphae" describes the organism's dual morphology (yeast form in tissue, mold with septate hyphae at ambient temperature).[1][3][6]

Why not the other options?

- **A (Legionella)**: A bacterium, not a dimorphic fungus; would not appear as intracellular yeast on silver/PAS staining.
- **B (Pneumocystis)**: Not a classic dimorphic fungus with septate hyphae; does not produce a positive urinary polysaccharide antigen.
- **D (Blastomyces)**: Also endemic to the Mississippi River valley, but *Blastomyces* appears as **large (8–15 µm) broad-based budding yeasts** — too large to be characteristically described as "filling macrophages". The finding of small intracellular organisms within macrophages is the key distinguishing feature favoring *Histoplasma*.[6]

The mother's lung disease treated with methotrexate is a clue pointing toward **sarcoidosis**, which is common in African American women and can mimic or coexist with histoplasmosis in endemic regions, further contextualizing the geographic risk.

Would you like to explore the treatment approach for acute pulmonary histoplasmosis based on disease severity?

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Question 11

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?

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

https://openevidence.com/ask/7077ec95-5856-4e58-b623-d9c8a317fd76

The answer is **A. Intubate with mechanical ventilation**.

This child is exhibiting classic signs of **impending respiratory failure** despite maximal pharmacotherapy. The critical findings after treatment are:

- **Silent chest** (absence of wheezing): This does not indicate improvement. A quiet chest on auscultation indicates **minimal ventilation, insufficient to produce a wheeze**, and portends impending respiratory failure.[1][2]
- **Altered mental status** (limp, lethargic): Drowsiness and confusion are features of **cerebral hypoxemia** and are hallmarks of life-threatening asthma.[1][3][4]

- **Declining respiratory rate** (40 → 22/min): In the setting of a severe exacerbation, a falling respiratory rate with worsening mental status reflects **respiratory muscle fatigue**, not clinical improvement.[2][3]

This child has already received the full escalation of medical therapy — **inhaled SABA, ipratropium, IV methylprednisolone, and IV magnesium sulfate** — and has continued to deteriorate. Endotracheal intubation and mechanical ventilation should not be delayed when clinical improvement is not achieved with conservative therapies.[2][5]

Why not the other options:

- **B. Needle thoracostomy** — Tension pneumothorax would present with **unilateral** absent breath sounds, hypotension, tracheal deviation, and JVD. This child has bilateral absence of wheezing with relatively stable hemodynamics, consistent with severe bronchospasm rather than pneumothorax.

- **C. Bronchoscopy** — No role in acute asthma exacerbation management. Foreign body aspiration is unlikely given the known asthma history and clear precipitant (missed medications).

- **D. Additional methylprednisolone** — IV steroids have already been administered. Systemic corticosteroids take **hours** to produce clinical effect and will not address imminent respiratory arrest. The problem here is airway failure, not inadequate steroid dosing.

Would you like to explore ventilator strategies for mechanically ventilated children with status asthmaticus?

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Question 12

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?

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

https://openevidence.com/ask/690e68b4-0063-4bf4-88c3-8db529944f35

D. Steeple sign.

The presentation — barking cough, hoarse voice, inspiratory stridor, low-grade fever, and retractions in a 3-year-old — is classic viral croup (laryngotracheobronchitis).[1][2][3] Subglottic inflammatory edema produces **symmetric narrowing of the tracheal air column for ≥5–10 mm below the vocal cords on the AP view (steeple/wine-bottle sign)**.[4] Note that this is best seen on an AP neck film rather than a chest radiograph, and imaging is not required — croup is a clinical diagnosis, and radiographs are reserved for atypical presentations or when alternative diagnoses are suspected.[1][2][5]

Why the other options are wrong

- **C. Thumbprint sign (lateral view)** — indicates epiglottitis, from an enlarged epiglottis and thickened aryepiglottic folds. The tripod/forward-leaning posture in this vignette is a distractor, but the barking cough and hoarseness point to croup; epiglottitis characteristically presents with drooling, muffled "hot potato" voice, dysphagia, high fever, and a toxic appearance without a barking cough.[2][4][6]
- **A. Increased interstitial markings** — suggests viral pneumonitis/bronchiolitis; does not explain stridor with a normal-sounding chest.

- **B. Lobar consolidation** — bacterial pneumonia; would produce focal crackles/bronchial breath sounds, not inspiratory stridor and hoarseness.

One caveat on radiographic reliability: the steeple sign is neither sensitive nor specific — croup radiographs can be normal, and bacterial tracheitis produces similar subglottic narrowing but with a ragged tracheal contour or an intraluminal membrane.[2][4] If imaging is obtained in a child with respiratory distress, the child must be monitored throughout by personnel equipped for airway management.[2]

Management here (moderate croup with stridor at rest and retractions) is **dexamethasone 0.6 mg/kg orally, max 12 mg, plus nebulized epinephrine**.[1][7]

Would you like to explore admission versus discharge criteria after nebulized epinephrine for moderate croup?

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Question 13

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?

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

https://openevidence.com/ask/59bebc24-c38f-4bcd-b67c-2f2313707e60

The most likely diagnosis is **A. Psoriatic arthritis (PsA)**.

This presentation has several hallmark features of PsA:

- **Nail pitting** is one of the most characteristic findings, present in **80–90% of patients with PsA** and a key component of the CASPAR classification criteria.[1][2]
- **Dandruff requiring special shampoos** likely represents **scalp psoriasis**, a common but easily overlooked location; the occipital scalp and behind the ears are sites clinicians are specifically advised to examine.[3][4]
- **Asymmetric oligoarthritis** (right knee now, left knee weeks ago) is one of the five classic Moll and Wright subtypes of PsA.[3]
- **Back pain (axial involvement)** occurs in **over 40% of PsA patients** and typically coexists with peripheral arthritis.[3][5]

Why not the other options:

- **Arthritis mutilans (B)** is a rare, severely destructive *subtype* of PsA characterized by osteolysis, telescoping digits, and flail joints — features not described here.[3]

- **Rheumatoid arthritis (C)** typically presents with **symmetric** proximal joint involvement, spares distal interphalangeal joints, and is not associated with nail pitting or psoriatic skin disease. Spinal involvement is uncommon in RA.[3]
- **Mixed connective tissue disease (D)** is characterized by overlapping features of SLE, polymyositis, and scleroderma with anti-U1 RNP antibodies — none of which are present in this vignette.

Would you like to explore treatment guidelines for psoriatic arthritis with combined peripheral and axial disease?

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Question 14

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?

A. 0.375
B. 0.5
C. 2.5
D. 2.67

https://openevidence.com/ask/b5df0fe1-282a-4780-865f-f92e608807b8

D. 2.67

Calculation. The therapeutic index is the ratio of the dose producing toxicity in 50% of subjects to the dose producing the desired effect in 50% (TD50/ED50; in preclinical work often LD50/ED50).[1][2]

- **ED50 ≈ 30 mg**: 26/53 = 49% improved, the dose closest to a 50% response (10 mg = 10%, 20 mg = 39%, 40 mg = 90%)
- **TD50 ≈ 80 mg**: 23/47 = 49% with a treatment-related adverse event (20 mg = 10%, 40 mg = 22%, 60 mg = 36%, 100 mg = 90%)
- **TI = 80/30 = 2.67**

Why the other options are wrong

- **A (0.375)** inverts the ratio (30/80) — ED50/TD50 rather than TD50/ED50.
- **B (0.5)** uses 20/40, pairing the wrong points on the two curves (the 10% response dose over the 22% toxicity dose).
- **C (2.5)** comes from 100/40, i.e., using the TD90 and ED90 rather than the median values.

Caveats worth noting for interpretation. ED50 is a hybrid PK/PD quantity that depends on clearance and bioavailability as well as intrinsic potency, so it is formulation- and route-dependent, unlike EC50.[3] Defining TD50 from "any treatment-related adverse event" is a crude toxicity endpoint; a meaningful clinical TI requires a prespecified toxicity of defined severity (e.g., grade ≥3 or dose-limiting toxicity). In actual drug development the TI is more often framed as an exposure ratio — the highest exposure producing no toxicity relative to the exposure producing efficacy — and integrates in vitro, animal, and human data rather than a single dose-response pair.[1]

Most cytotoxic chemotherapeutics have steep dose-response curves and narrow therapeutic windows with substantial interindividual PK variability, which is the pharmacologic rationale behind dose-optimization efforts in oncology.[4][5]

Would you like to explore how Project Optimus has changed dose selection in early-phase oncology trials?

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Question 15

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?

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

https://openevidence.com/ask/9a3db3a4-5b2d-4d6b-ae08-1797be87e177

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

This presentation describes **conduction aphasia** — characterized by **fluent speech, intact comprehension, but impaired verbal repetition**.[1][2] In the classic Wernicke-Geschwind model, this syndrome results from a disconnection between the posterior receptive language area (Wernicke's area in the superior temporal gyrus) and the anterior expressive language area (Broca's area in the inferior frontal gyrus) via damage to the **arcuate fasciculus**, the white matter tract that connects them.[1][3][4]

The key to the localization is that fluent speech rules out significant damage to Broca's area (inferior frontal gyrus), and intact comprehension rules out damage to Wernicke's area (superior temporal gyrus). The isolated repetition deficit points to an interruption of the pathway linking these two intact cortical regions — the arcuate fasciculus.[1][5]

As Damasio described in the NEJM:

> "Patients with conduction aphasia can comprehend essential sentences as well as produce intelligible speech. However, they cannot repeat sentences verbatim or assemble phonemes effectively (they thus produce many phonemic paraphasias)."
>
> —Antonio R. Damasio, M.D., University of Iowa College of Medicine. Aphasia. N Engl J Med. February 20, 1992.

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Why not the other options:

- **B (Superior temporal gyrus)** — Damage here would produce **Wernicke's aphasia** with impaired comprehension and fluent but often nonsensical speech, which this patient does not have.
- **C (Inferior frontal gyrus + superior temporal gyrus)** — Combined damage to both Broca's and Wernicke's areas would produce **global aphasia** with deficits in both production and comprehension.
- **D (All three structures)** — This would also produce global aphasia, not an isolated repetition deficit.

While modern neuroimaging research has nuanced the classic model — implicating temporoparietal cortex (particularly the supramarginal gyrus and area Spt) in addition to the arcuate fasciculus itself — the arcuate fasciculus remains the classic and board-relevant answer for conduction aphasia.[2][6][7]

Would you like to explore how conduction aphasia is distinguished from the transcortical aphasias?

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Question 16

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?

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

https://openevidence.com/ask/1726233f-cadb-4f71-a98a-e637ddd2e1e9

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

This patient's presentation is classic for PCOS, fulfilling the **Rotterdam diagnostic criteria**, which require at least two of three features: (1) **oligomenorrhea/anovulation**, (2) **clinical and/or biochemical hyperandrogenism**, and (3) polycystic ovarian morphology on ultrasound.[1][2][3] This patient clearly meets two criteria — making ultrasound unnecessary for diagnosis:[2][4]

- **Oligomenorrhea**: menstrual cycles occurring every 45 days (normal 21–35 days)
- **Clinical hyperandrogenism**: severe inflammatory acne, hirsutism (facial hair on the upper lip, dark coarse hairs on the back)

The associated findings further support PCOS:

- **Obesity** (BMI ~33 kg/m²) — present in 30–70% of women with PCOS[5]

- **Impaired glucose tolerance** (2-hour OGTT 160 mg/dL, where 140–199 mg/dL defines IGT) — PCOS is strongly associated with insulin resistance, metabolic syndrome, and increased risk of type 2 diabetes[6][7][8]

- **Elevated blood pressure** (138/80 mmHg) — consistent with the metabolic cardiovascular risk profile of PCOS[7][9]

Why not the other options:

- **A. Hypothyroidism** — Does not cause hirsutism or acne. While thyroid disease can cause oligomenorrhea, the hyperandrogenic features (hirsutism, acne) are not explained. Thyroid disease should be excluded as part of the PCOS workup, but the overall clinical picture is far more consistent with PCOS.[9]

- **B. Idiopathic hirsutism** — Defined as hirsutism in **eumenorrheic** women without hyperandrogenemia or other signs of a hyperandrogenic endocrine disorder. This patient has oligomenorrhea, acne, obesity, and glucose intolerance — features that point to a systemic endocrine disorder, not isolated idiopathic hirsutism.[10][11]

- **D. Ovarian hyperthecosis** — Often described as a **severe or extreme form** of PCOS, typically presenting with markedly elevated testosterone (>150 ng/dL / >5.2 nmol/L), frank virilization (clitoromegaly, voice deepening), and is more common in postmenopausal women. This patient's presentation — with acne, mild hirsutism, and oligomenorrhea — fits the typical PCOS spectrum rather than the more severe hyperandrogenism of hyperthecosis.[12]

Has this patient had serum androgen levels (total and free testosterone), thyroid function, prolactin, or 17-hydroxyprogesterone testing to formally exclude other causes of hyperandrogenism?

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Question 17

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?

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

https://openevidence.com/ask/8659551f-726a-424b-b12c-ddde9fa32969

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

This patient presents with **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 ankle-brachial pressure index (1.1)** effectively rules out peripheral arterial disease.

Glycemic optimization is the cornerstone measure to prevent DPN progression. The ADA 2026 Standards of Care recommend optimizing glucose management to slow neuropathy progression in type 2 diabetes.[1] While the evidence is strongest in type 1 diabetes (78% risk reduction per the DCCT), trials in type 2 diabetes — including UKPDS and ACCORD — have demonstrated that improved glycemic control provides a modest but meaningful reduction in neuropathy incidence and progression.[2][3] This patient's HbA1c of 8.1% with inconsistent medication use represents a clear opportunity for improvement.

Why the other options are incorrect:

- **A. Atorvastatin** — Lipid management is a component of comprehensive metabolic risk reduction but is not the primary intervention for preventing DPN progression.[1]
- **B. Femoro-ileal artery bypass** — Indicated for symptomatic peripheral arterial disease, which is excluded here by the normal ABPI of 1.1.
- **D. Lower limb amputation** — Reserved for non-salvageable limbs (e.g., gangrene, critical ischemia, non-healing ulcers). There is no such indication in this patient.

Would you like to explore first-line pharmacologic options for managing this patient's neuropathic pain?

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Question 18

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?

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

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The answer is **A. Duodenal atresia**. This neonate's presentation — **bilious vomiting on day 1 of life, failure to pass meconium, and polyhydramnios** — in the setting of a quad screen classic for **Trisomy 21** makes duodenal atresia the most likely etiology.

Connecting the quad screen to Down syndrome

The maternal quad screen shows **decreased AFP, increased beta-hCG, decreased unconjugated estriol, and increased inhibin A** — the hallmark pattern for Trisomy 21.[1][2] Advanced maternal age (36 years) further increases baseline risk. The mother declined first-trimester screening and no diagnostic testing (amniocentesis/CVS) was performed, so the diagnosis remains unconfirmed but strongly suspected.

Duodenal atresia and Trisomy 21

Duodenal atresia is the **most common structural GI defect in Down syndrome**, occurring in approximately 1–5% of affected individuals.[3][4] Conversely, **approximately 30–40% of all infants with duodenal atresia have Trisomy 21**.[5][6] It classically presents with **bilious vomiting within the first 1–2 days of life**.[7][8] Prenatal polyhydramnios (AFI 28 cm; normal <25 cm) results from impaired intestinal transit and absorption of swallowed amniotic fluid due to the obstruction.[8]

Why not the other choices:

- **B. Meconium ileus** — Associated with **cystic fibrosis**, not Down syndrome. The quad screen pattern does not point to CF, and no family history of CF is described.
- **C. Necrotizing enterocolitis (NEC)** — Predominantly a disease of **premature infants**; this is a near-term (38-week) neonate on day 1 of life, making NEC unlikely.
- **D. Pyloric stenosis** — Presents at **2–6 weeks of age** with **non-bilious** projectile vomiting. This infant has bilious vomiting on day 1, which is inconsistent with pyloric stenosis.

The abdominal radiograph in this case would be expected to show the classic "**double bubble**" **sign** — a dilated, air-filled stomach and proximal duodenum with no distal gas — which is highly predictive of duodenal atresia.[7][8]

Would you like to explore the surgical management and outcomes of duodenal atresia in neonates with Trisomy 21?

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Question 19

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.)

A. 5
B. 16
C. 20
D. 50

https://openevidence.com/ask/1c4add0c-c6e8-44e8-83a6-d3c446889445

The answer is **C. 20**.

The **number needed to treat (NNT)** is calculated as the **reciprocal of the absolute risk reduction (ARR)**:[1][2][3]

$$NNT = \frac{1}{ARR}$$

Step-by-step calculation:

- **Event rate, Medication 1 (treatment):** 134 / 1,500 = **8.93%**
- **Event rate, Medication 2 (control):** 210 / 1,500 = **14.0%**
- **ARR** = 14.0% − 8.93% = **5.07%**
- **NNT** = 1 / 0.0507 = **19.7 ≈ 20**

This means approximately **20 patients** need to be treated with Medication 1 instead of Medication 2 to prevent one additional cardiac death at 45 days. A smaller NNT indicates a more

effective treatment.[4] The statistically significant p-value of 0.03 for this primary endpoint confirms the treatment effect is unlikely due to chance.

Would you like to explore how NNT compares with relative risk reduction in interpreting clinical trial outcomes?

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Question 20

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?

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

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The answer is **A. Femoropopliteal artery stenosis**.

This presentation is classic for **chronic peripheral arterial disease (PAD) localized to the femoropopliteal segment**. Three key findings localize the disease:

- **Calf claudication** (cramping on treadmill incline, relieved by rest within minutes) is typically caused by disease in the **superficial femoral artery**. By contrast, aortoiliac disease causes **buttock, hip, and thigh** claudication.[1][2][3]
- **Palpable femoral pulses with absent right pedal pulses** indicate preserved aortoiliac inflow with obstruction distal to the femoral artery. As the TASC II consensus states, "a normal femoral, but absent pedal, pulse suggests significant arterial disease in the leg with preserved inflow," whereas "a diminished or absent femoral pulse suggests aorto-iliac artery occlusive disease".[4]
- **Elevation pallor** on straight leg raise is a sign of arterial insufficiency (Buerger's sign), not a neurologic finding — notably, there is no back pain.[5][6][7]

Why the other choices are incorrect:

- **B. Acute popliteal vein thrombosis** — Deep venous thrombosis presents with swelling, warmth, and pain at rest, not exercise-induced calf cramping relieved by rest with elevation pallor and absent arterial pulses.
- **C. Lumbar spinal stenosis** — Neurogenic claudication classically requires postural change (sitting or spinal flexion) for relief, not just cessation of walking. The absence of back pain argues against this, but the decisive features are objective arterial signs: elevation pallor and absent pedal pulses are not explained by spinal pathology.[4][6]
- **D. Aortoiliac artery stenosis** — Aortoiliac disease (Leriche syndrome in its classic form) presents with **buttock/thigh claudication, diminished or absent femoral pulses**, and erectile dysfunction. The preserved femoral pulses and calf-predominant symptoms strongly favor femoropopliteal disease instead.[1][3][4]

The patient's significant risk factors — **68 pack-year smoking history, diabetes mellitus, and hypertension** — are the strongest risk factors for PAD.[6]

Would you like to explore the recommended initial workup and management for symptomatic femoropopliteal PAD?

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Question 21

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

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

https://openevidence.com/ask/1e02ad87-f7ed-4dd4-a770-012986de331b

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

DNA double-strand breaks (DSBs) are the primary lethal lesion produced by ionizing radiation. Approximately **40 DSBs are induced per Gray** in a typical cell, and even a single unrepaired DSB can trigger the damage-sensing process and lead to cell death.[1] Ionizing radiation damages DNA through both **direct mechanisms** (radiation particles colliding with DNA molecules) and **indirect mechanisms** (radiolysis of water generating reactive oxygen species that subsequently damage DNA).[2][3] DSBs are particularly consequential because they are difficult to repair accurately; failed or erroneous repair leads to chromosomal aberrations, mitotic catastrophe, and cell death.[1][2]

The other answer choices represent distinct mechanisms:

- **A (Thymidine dimers):** Thymine dimers are the signature lesion of **ultraviolet (UV) radiation**, not ionizing radiation. UV causes adjacent pyrimidines to form covalent bonds (cyclobutane dimers), a fundamentally different photochemical process.
- **B (Disulfide bonds):** Disulfide bond formation is a normal protein-folding event and is not a recognized mechanism of radiation-induced DNA damage.
- **C (Deamination of cytosine):** Spontaneous hydrolytic deamination of cytosine (producing uracil) is an endogenous process, not a characteristic effect of ionizing radiation.

Would you like to explore the standard chemoradiation protocol and expected toxicities for anal carcinoma?

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Question 22

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?

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

https://openevidence.com/ask/68d0bab4-2fea-44e8-ba93-b0ec9ee1d0d7

A. Aldosterone excess (primary aldosteronism).

The combination of **resistant hypertension** (174/111 mmHg on three agents, including a thiazide and an ACE inhibitor), **hypokalemia** (K^+ 3.3 mEq/L), and **metabolic alkalosis** (HCO_3^- 33 mEq/L) with a high-normal sodium is the classic biochemical triad of renin-independent aldosterone excess.[1][2][3] Excess mineralocorticoid receptor activation drives distal nephron sodium reabsorption with volume expansion and hypertension, while promoting renal potassium and hydrogen ion secretion — producing exactly this hypokalemic metabolic alkalosis.[1][2] The symptoms are also typical: fatigue and muscle cramps are recognized hypokalemia-related presentations of primary aldosteronism.[3] Mild hyperglycemia (129 mg/dL) fits as well, since

impaired glucose tolerance and metabolic dysfunction are more prevalent in primary aldosteronism than in essential hypertension.[3][4]

Why not the others

- **Catecholamine-secreting mass (pheochromocytoma):** would be expected to produce episodic/paroxysmal hypertension with headache, palpitations, diaphoresis, and tachycardia. The pulse is 70/min, and catecholamine excess does not explain hypokalemic metabolic alkalosis.
- **Cortisol excess:** hypokalemic alkalosis can occur with very high cortisol (mostly ectopic ACTH), but there are no Cushingoid features — no central obesity, striae, proximal myopathy, or marked hyperglycemia — making this less likely than aldosteronism in a patient whose only findings are resistant hypertension and hypokalemia.
- **Impaired kidney perfusion (renovascular hypertension):** secondary hyperaldosteronism from renal artery stenosis can cause hypokalemia, but it is typically less prominent, the BUN/creatinine would more often be deranged, and the abdominal exam is free of a bruit. The absence of an acute change and the classic triad favor a primary adrenal source. Note that in secondary hyperaldosteronism renin is high, whereas in primary aldosteronism renin is suppressed — the distinguishing test.

Confirmatory workup

Both the 2025 AHA/ACC hypertension guideline and the 2025 Endocrine Society guideline recommend screening with a **morning, seated plasma aldosterone concentration plus plasma renin activity (or direct renin concentration) and the aldosterone-to-renin ratio**.[5][6] Key practical points:

- **Do not stop most antihypertensives** before screening; only mineralocorticoid receptor antagonists need withdrawal (≥4 weeks).[5]
- **Correct hypokalemia first** and maintain unrestricted sodium intake, since low potassium suppresses aldosterone and can cause a false-negative screen.[5][6]
- A positive screen generally requires **suppressed renin (PRA ≤1 ng/mL/h or DRC ≤8.2 mU/L) with aldosterone ≥10 ng/dL by immunoassay** (≥7.5 ng/dL by LC-MS/MS) and an elevated ARR (>20 by immunoassay units; the AHA/ACC cites the most commonly used cutoff as 30, with alternatives of 20 or 40).[5][6]
- Confirmatory testing (saline suppression or oral salt loading) is generally required, though it may be omitted in patients with spontaneous hypokalemia, undetectable renin, and

aldosterone >20 ng/dL; subtyping then proceeds with adrenal CT ± adrenal venous sampling if surgery is contemplated.[5][7]

Would you like to explore medical management options when adrenal venous sampling shows bilateral disease?

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Question 23

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?

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

https://openevidence.com/ask/b357a6ec-5c10-4ac9-b8df-98b1979baff3

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

The urinalysis pattern of **elevated urine bilirubin with low urobilinogen** is the hallmark of **obstructive/cholestatic jaundice**. The clinical reasoning is as follows:

- **Elevated urine bilirubin** indicates conjugated (direct) hyperbilirubinemia, since only conjugated bilirubin is water-soluble and can be filtered by the kidneys into urine. When bile excretion is impaired, conjugated bilirubin accumulates in the blood and spills into the urine.[1]
- **Low urine urobilinogen** indicates that bilirubin is not reaching the intestines, where gut bacteria normally convert it to urobilinogen. Low or absent urobilinogen signifies a **blockage in bile flow** from the liver or gallbladder to the intestines.[2]
- **Generalized pruritus** further supports cholestasis, caused by bile salt deposition in the skin.

The ACG guideline notes that the absence of urobilinogen gives stool its classic **clay-colored appearance** in those with impaired bile flow, and that elevated conjugated bilirubin indicates hepatocellular dysfunction or cholestasis.[3]

Why the other options are incorrect:

- **A (Absent UDP-glucuronosyltransferase activity):** This describes Crigler-Najjar syndrome, which produces **unconjugated** hyperbilirubinemia. Unconjugated bilirubin is water-insoluble and would **not** appear in urine.
- **B (Increased hemoglobin breakdown):** Hemolytic anemia causes unconjugated hyperbilirubinemia with **no urine bilirubin** and **increased** (not decreased) urobilinogen, since more bilirubin reaches the gut.[2][4]
- **C (Increased intestinal bilirubin reabsorption):** This does not correspond to a recognized mechanism for the urinalysis pattern described.

Would you like to explore the most common causes of obstructive jaundice in this age group and the recommended diagnostic workup?

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Question 24

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?

A. Bethanechol
B. Metoclopramide
C. Atropine
D. Oxybutynin

https://openevidence.com/ask/3bd6bbc7-fd08-45f9-9844-eacfbad40f62

The answer is **C. Atropine**.

Galantamine is an **acetylcholinesterase inhibitor** used for mild-to-moderate Alzheimer's dementia. By inhibiting acetylcholinesterase, it increases acetylcholine at synapses, which produces therapeutic cognitive effects but also predictable **muscarinic side effects** — most commonly **nausea, vomiting, diarrhea, abdominal pain**, and decreased appetite.[1] The FDA label explicitly states these GI effects are "a predictable consequence of its pharmacological properties".[1]

This patient's symptoms represent **cholinergic (muscarinic) excess** in the GI tract. **Atropine**, a **nonselective muscarinic receptor antagonist**, directly counteracts these effects by competitively blocking acetylcholine at muscarinic receptors on smooth muscle and exocrine glands.[2][3]

Why the other options are incorrect:

- **A. Bethanechol** — A direct-acting **muscarinic agonist** (parasympathomimetic); it would **worsen** the cholinergic GI symptoms, not treat them.
- **B. Metoclopramide** — A **dopamine D2 antagonist/prokinetic** that increases GI motility; it does not address muscarinic excess and would exacerbate diarrhea and cramping.
- **D. Oxybutynin** — While antimuscarinic, it is specifically indicated for **overactive bladder** and has significant **CNS penetration**, which would antagonize the central muscarinic

activity that galantamine is designed to enhance, potentially negating its therapeutic benefit for dementia.

The key pharmacological principle is recognizing cholinesterase inhibitor side effects as muscarinic overstimulation and selecting a **peripheral muscarinic antagonist** as the antidote.[4] [5]

Would you like to explore strategies for managing cholinesterase inhibitor GI side effects while preserving their cognitive benefits?

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Question 25

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?

A. Tardive dyskinesia
B. Acute dystonia
C. Pseudoparkinsonism
D. Palsy

https://openevidence.com/ask/fe2eead8-95f9-484b-8889-9391d304c9d2

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

This presentation is classic for **tardive dyskinesia (TD)** — characterized by **repetitive, involuntary orofacial movements** including **lip smacking, pursing, and rapid eye blinking** that emerge after prolonged exposure to dopamine receptor-blocking agents.[1][2] The DSM-5 specifies that TD develops during or after at least **3 months of antipsychotic exposure** (or 1 month in patients ≥60 years), with an **insidious onset** that is often initially mild and unnoticed by the patient.[2] This patient's age (61), use of **haloperidol** (a first-generation antipsychotic with among the highest TD risk), months-long treatment duration, and gradual symptom emergence all fit precisely.[1][3]

Why the other options are incorrect:

- **B. Acute dystonia** — Presents with **sudden-onset sustained muscle contractions** (torticollis, oculogyric crisis, trismus), typically within **hours to days** of starting or increasing an antipsychotic, not after months of stable treatment.[4]
- **C. Pseudoparkinsonism (drug-induced parkinsonism)** — A **hypokinetic** disorder manifesting as **resting tremor (3–6 Hz), rigidity, and bradykinesia**, which is mechanistically opposite to the hyperkinetic involuntary movements seen here. The

rhythmic tremor of parkinsonism is distinctly different from the choreiform/stereotypic orofacial movements of TD.[2][5]

- **D. Palsy** — Refers to **paralysis or weakness** of a muscle group (e.g., Bell's palsy, cerebral palsy), not involuntary repetitive movements. Nothing in this presentation suggests motor weakness.

The orobuccal-lingual movements described — lip smacking, pursing, and excessive blinking — are the **hallmark and most common manifestation** of classic TD, present in most affected individuals.[3][4][6]

Would you like to explore the evidence-based treatment options for tardive dyskinesia?

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Question 26

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?

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

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A. KOH examination of lesion scrapings.

The presentation is classic tinea cruris: a pruritic, erythematous, well-demarcated patch with an active peripheral scaling border involving the medial thigh, pubic area, and perineum in an adolescent athlete after summer workouts, with sparing of the scrotum — a feature that helps distinguish dermatophytosis from candidal intertrigo and other groin eruptions.[1] Diagnosis is usually clinical, and confirmation is by **direct microscopy of skin scrapings taken from the advancing scaly edge, mounted in 10–20% KOH**, which dissolves keratinocytes and reveals septate branching hyphae.[1][2][3] KOH microscopy is the most frequently used confirmatory test for dermatophytes, is performed at the bedside, and yields results within about an hour.[4][5] In a study of 100 patients with tinea cruris, the conventional scrape-KOH method was positive in 91%.[4]

Why the other options are wrong

- **B. Nikolsky's sign** — epidermal shearing with lateral pressure, seen in pemphigus vulgaris, staphylococcal scalded skin syndrome, and SJS/TEN. It has no role in a localized scaly groin patch.

- **C. Gram stain** — would be relevant for bacterial intertrigo or erythrasma, but erythrasma (Corynebacterium minutissimum) is diagnosed by coral-red fluorescence on Wood lamp or culture, and it lacks the raised active scaly border seen here.[6][7]
- **D. AFB stain** — used for mycobacteria (e.g., cutaneous TB, atypical mycobacterial infection), which present as chronic nodules, ulcers, or plaques, not an acute pruritic annular groin rash.

Additional points

- **Confirmatory alternatives** when KOH is negative but suspicion persists: fungal culture (Trichophyton rubrum, Epidermophyton floccosum), calcofluor/Blankophor fluorescence microscopy, PAS-stained biopsy, or dermatophyte PCR. Wood lamp does not fluoresce most dermatophytes causing tinea cruris and is mainly useful to exclude erythrasma.[1][8][9][10]
- **Vital signs**: the stated temperature is internally inconsistent (38.1°C corresponds to 100.6°F, not 98.7°F; 98.7°F ≈ 37.1°C). Tinea cruris is a superficial, afebrile infection, so a true fever of 38.1°C would prompt a search for another source rather than being attributed to the rash.
- **Practical management**: topical allylamine (terbinafine) or azole for 2–4 weeks, plus examination of the feet — concurrent tinea pedis is a common reservoir for reinfection. Avoid topical steroid/antifungal combinations, which can produce tinea incognito.[1][2]

Would you like to explore return-to-play rules for athletes with dermatophyte skin infections?

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Question 27

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?

A. Agranulocytosis
B. Shortened QT interval
C. Gynecomastia
D. Weight loss

https://openevidence.com/ask/88186db9-b004-4234-b36a-1ad1dfcc56b3

The answer is **C. Gynecomastia**.

Risperidone causes the highest degree of prolactin elevation among second-generation antipsychotics, a well-established and prominently labeled adverse effect.[1][2] The FDA label specifically 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 in patients receiving the drug.[1] In men, hyperprolactinemia characteristically manifests as **gynecomastia**, erectile dysfunction, and impaired spermatogenesis.[3][4]

A large cohort study confirmed that risperidone (HR 2.70) and amisulpride (HR 2.76) carry the highest risk of prolactin elevation among SGAs, while clozapine, quetiapine, and aripiprazole carry the lowest.[5] A network meta-analysis of over 25,000 participants similarly ranked risperidone among the top prolactin-elevating antipsychotics.[6]

Why the other options are incorrect:

- **A. Agranulocytosis** — This is the hallmark adverse effect of **clozapine**, not risperidone. Clozapine requires mandatory absolute neutrophil count (ANC) monitoring through a REMS program.
- **B. Shortened QT interval** — Antipsychotics are associated with QTc **prolongation**, not shortening. Among SGAs, sertindole, amisulpride, and ziprasidone carry the greatest risk of QTc prolongation.[7]

- **D. Weight loss** — Risperidone is associated with **weight gain**, not weight loss. Among antipsychotics, olanzapine and clozapine cause the most weight gain, but risperidone also contributes meaningfully.

Would you like to explore the recommended monitoring and management of risperidone-induced hyperprolactinemia?

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Question 28

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?

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

https://openevidence.com/ask/5b2392b8-e4c8-4fd2-bb38-bd3558e3f648

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

This presentation is classic for **typhoid (enteric) fever**. The key features that converge on this diagnosis:

- **Travel to Indonesia** (Southeast Asia), a highly endemic region for typhoid[1][2]
- **Incubation period of ~7–14 days**, consistent with the typical 6–30 day incubation for S. typhi[1][3]
- **Biphasic illness**: initial low-grade fever with **constipation** transitioning to high fever with **diarrhea** — constipation is characteristic early in the disease course, while diarrhea is more common in children[1][3]
- **Hepatosplenomegaly**, a hallmark finding as the organism disseminates to the liver, spleen, and lymphoid tissue[3][4]
- **Salmon-colored maculopapular rash on the trunk/abdomen** — these are the classic "**rose spots**", blanching erythematous lesions 2–4 mm in diameter seen in 5–30% of cases, typically on the abdomen and chest[3][5]

"A few rose spots, blanching erythematous maculopapular lesions approximately 2 to 4 mm in diameter, are reported in 5 to 30 percent of cases. They usually occur on the abdomen and chest and more rarely on the back, arms, and legs."

—Christopher M. Parry, M.B. et al., University of Oxford and other institutions. Typhoid Fever. N Engl J Med. November 28, 2002.

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Why the other options are incorrect:

- **Giardia lamblia** causes watery, foul-smelling diarrhea and bloating but does not produce high fever, hepatosplenomegaly, or rose spots.
- **Schistosoma mansoni** can cause hepatosplenomegaly (Symmers fibrosis), but acute schistosomiasis (Katayama fever) presents with urticaria, eosinophilia, and pulmonary symptoms — not rose spots or the stepwise fever pattern described here.
- **Clostridium perfringens** causes acute, self-limited food poisoning (watery diarrhea and cramping within 6–24 hours of ingestion), not a prolonged febrile illness with organomegaly.

Would you like to explore the current antibiotic treatment recommendations for typhoid fever, particularly regarding resistance patterns in Southeast Asia?

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Question 29

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:

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

https://openevidence.com/ask/4c19502f-6329-4566-a768-bffa91b89e8a

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The answer is **A. Acetaldehyde**.

This question describes the classic **disulfiram-like reaction** between metronidazole and alcohol. The traditional teaching holds that metronidazole, like disulfiram, **inhibits aldehyde dehydrogenase (ALDH)** in the ethanol degradation pathway, leading to **accumulation of acetaldehyde** in the bloodstream.[1] Acetaldehyde is the toxic intermediate of ethanol metabolism responsible for symptoms including **facial flushing, nausea, tachycardia, dyspnea, headache, and abdominal cramps** — exactly the constellation described in this vignette.[1][2]

Why the other options are incorrect:

- **B. Uric acid** — Elevated uric acid is associated with gout, tumor lysis syndrome, or chronic alcohol use, but does not explain this acute symptom complex following a single alcohol exposure while on metronidazole.
- **C. Cytochrome P-450 enzymes** — While metronidazole does interact with the CYP450 system (e.g., inhibiting CYP3A4 and potentiating warfarin), CYP450 enzyme levels do not acutely rise to cause these symptoms.[3]
- **D. Amylase** — Elevated amylase suggests pancreatitis. Although chronic heavy alcohol use can cause pancreatitis, a single episode of drinking does not explain this presentation, which is classic for an acetaldehyde-mediated reaction.

It is worth noting that more recent evidence has questioned the strength of this interaction — some controlled studies found that metronidazole did **not** raise blood acetaldehyde or produce objective disulfiram-like signs in volunteers, and animal data suggest the mechanism may involve intracolonic rather than systemic acetaldehyde or possibly serotonergic pathways.[4][5][6] Nonetheless, the acetaldehyde accumulation model remains the standard exam-tested explanation and the basis for the longstanding recommendation to avoid alcohol during metronidazole therapy.[1][7]

Would you like to explore the evolving evidence on whether the metronidazole-alcohol interaction is truly clinically significant?

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Question 30

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?

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

https://openevidence.com/ask/6cd332c5-820c-404d-ae97-f59aa4633760

A. Insert a "straight cath" into the patient's bladder.

This is acute postoperative urinary retention (POUR), and in-and-out catheterization is both diagnostic and therapeutic when the bladder scan is nondiagnostic. Catheterization remains the mainstay of POUR management, with the immediate goal of emptying the bladder to prevent overdistension, detrusor injury, stasis-related infection, and hydronephrosis.[1] The inpatient urinary retention algorithm developed by RAND/UCLA appropriateness methods explicitly endorses intermittent straight catheterization when a bladder scanner is unavailable or its data cannot be used, and prefers intermittent over indwelling catheterization for initial management.[2]

Why this patient is high risk

- **Antimuscarinic premedication** — atropine and scopolamine block detrusor contraction; anticholinergic use is an independent risk factor for POUR after inguinal hernia repair

(adjusted OR 2.38, 95% CI 1.02–5.52), and glycopyrrolate carries similar risk in ambulatory general surgery (adjusted OR 3.48).[3][4]

- **Opioid exposure** — morphine impairs detrusor contractility and bladder sensation.[5]
- **Advanced age and likely BPH** — age is independently associated with POUR (adjusted OR 1.02 per year), and elderly men are the group most prone to drug-induced retention.[3][5]
- **Timing** — 14 hours without voiding plus suprapubic/pelvic discomfort meets any reasonable threshold for intervention; symptomatic patients warrant treatment at lower volumes than asymptomatic ones.[2]

Why the other options are wrong

- **B. Aggressive IV fluids** — does not address outlet/detrusor failure and risks further bladder overdistension; higher perioperative IV fluid volume (>500 mL) has itself been implicated as a POUR risk factor. If catheterization returns little or no urine, then true oliguria should be worked up with volume status, creatinine/electrolytes, and targeted fluid resuscitation only if hypovolemia is demonstrated.[3]
- **C. Digital rectal exam** — reasonable adjunct to assess prostate size and rule out fecal impaction contributing to retention, but it is not a treatment and does not decompress the bladder.
- **D. Renal ultrasound** — indicated only if the bladder is empty on catheterization, if AKI persists after decompression, or if upper-tract obstruction is suspected.

Practical points after the cath

- Record the drained volume; it establishes the diagnosis retrospectively and guides whether repeat intermittent catheterization or an indwelling catheter is needed. Transition to an indwelling catheter is appropriate if catheterization is required more often than every 4 hours or output exceeds 500 mL every 4 hours, though these cutoffs are protocol-derived rather than universal.[2]
- Anticipate **post-obstructive diuresis** after a large-volume drain and monitor urine output and electrolytes.
- Hold or minimize further anticholinergics and opioids. Alpha-blockers may facilitate a subsequent trial of void, but evidence for pharmacologic treatment of established POUR is weak, and tamsulosin should be used selectively in an 80-year-old with SBP 100 mm Hg given orthostasis and fall risk.[1]

- If resistance is met, avoid repeated blind attempts — consider a coudé-tip catheter or urology assistance.
- Separately, **SpO_2 90%** in an obese elderly patient on opioids 14 hours postop deserves independent evaluation (opioid-induced hypoventilation, OSA, atelectasis, PE), not just observation.

Would you like to explore how to conduct a trial of void and whether alpha-blockers help after POUR?

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Question 31

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?

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

https://openevidence.com/ask/84e7f693-26f9-41e5-b39d-6792c8e38e76

C. Perform emergency laparotomy. This child has a surgical abdomen — bilious vomiting, obstipation, peritoneal signs, and dilated bowel loops — and treatment of an emergency medical condition must not be delayed while attempting to reach a parent or guardian.[1]

Why the other options fail

- **Brother's consent (A):** A 14-year-old sibling is himself a minor with no legal authority to consent. Only parents, custodial guardians, or a documented legal surrogate (consent by proxy) may give permission, and no such documentation exists here.[1][2]
- **Patient's consent (B):** A 4-year-old lacks decisional capacity and legal standing. Mature-minor doctrines, where recognized, generally apply to adolescents roughly 12 and older.[1]
- **Delaying for parental consent (D):** Delay in the face of a likely obstruction with peritonitis risks perforation, sepsis, and death. EMTALA and the emergency exception rule (doctrine of implied consent) presume that a guardian, if present, would consent to care in the child's best interest.[1][3]

Operational points

- Continue **good-faith attempts to contact the parents** in parallel with resuscitation and transport to the OR; obtain formal consent when reached.[1]
- **Document** the nature and immediacy of the emergency, why delay would cause serious harm, the impossibility of obtaining consent, and the attempts made to contact the guardians.[1][3]
- Concurrent management while mobilizing the OR: NPO, IV crystalloid resuscitation, nasogastric decompression, analgesia, broad-spectrum antibiotics, and type and screen.
- The intraoperative extension of this exception also applies — any procedure that becomes necessary for a condition discovered during the operation that poses an immediate threat may be performed.[3]
- Seek **assent** from the child in a developmentally appropriate way, recognizing it is not legally sufficient.[1][4]

Would you like to explore the differential and workup for acute bowel obstruction with peritonitis in a preschool-aged child?

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Question 32

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?

A. Phentolamine
B. Prazosin
C. Nifedipine
D. Nadalol

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

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

Why nadolol?

Non-selective beta-blockers (NSBBs) are the cornerstone of secondary prophylaxis for variceal bleeding. The 2024 AASLD guidance specifies that **propranolol, nadolol, and carvedilol** may all be used, and recommends combining NSBBs with endoscopic band ligation (EBL) for secondary prophylaxis.[1] NSBBs reduce portal pressure through two mechanisms: **beta-1 blockade** decreases cardiac output, and **beta-2 blockade** produces unopposed alpha-1 splanchnic vasoconstriction, reducing portal inflow.[2][3] Without prophylaxis, the 1-year rebleeding rate is up to **60%**.[1]

Why not the other options?

- **A. Phentolamine** (non-selective alpha-blocker) — would cause splanchnic vasodilation and worsen portal hypertension.
- **B. Prazosin** (selective alpha-1 blocker) — similarly would reduce splanchnic vascular tone and is not indicated.
- **C. Nifedipine** (calcium channel blocker) — causes splanchnic vasodilation and has no role in variceal prophylaxis.

Note the likely intentional misspelling: the answer choice reads "Nadalol" but refers to **nadolol**, a well-established NSBB used in this setting.

Would you like to explore the dosing and monitoring parameters for nadolol in variceal bleeding prophylaxis?

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Question 33

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?

A. Spontaneous bacterial peritonitis
B. Metabolic alkalosis
C. Portal vein thrombosis
D. Hypoglycemia

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

This patient presents with **overt hepatic encephalopathy** (progressive somnolence, unresponsive to commands, oriented x0, asterixis, hyperreflexia) in the setting of alcoholic liver cirrhosis with significant ascites. The question is what precipitated this decompensation.

Why SBP is the most likely precipitant:

- The key clinical clue is the **low-grade fever (38.0°C)** in a cirrhotic patient with ascites. **Infections — particularly SBP — are among the most common precipitants of hepatic encephalopathy** in cirrhosis. SBP had an adjusted odds ratio of **5.13** (95% CI 3.03–8.69) for precipitating HE in one large case-control study.[1][2][3]
- SBP presentation is notably heterogeneous: up to **one-third of patients may be asymptomatic or present with only encephalopathy and/or AKI**, without classic peritoneal signs. Per AASLD guidance, bacterial infection should be suspected whenever a cirrhotic patient deteriorates with encephalopathy, and **diagnostic paracentesis should be performed in all cirrhotic patients admitted with ascites**.[4][5]

Why the other options are eliminated:

- **B. Metabolic alkalosis** — The ABG is entirely normal (pH 7.4, pCO2 40, HCO3 26). Although alkalosis is a recognized HE precipitant, there is no alkalosis here.[1]
- **C. Portal vein thrombosis** — The abdominal ultrasound showed no changes aside from cirrhosis and ascites, making this unlikely.
- **D. Hypoglycemia** — Serum glucose is 90 mg/dL, which is normal.

Would you like to explore the empiric antibiotic regimen and albumin use for SBP management?

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Question 34

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?

A. Cardiac contusion
B. Hemorrhage
C. Pulmonary contusion
D. Takotsubo cardiomyopathy

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The answer is **A. Cardiac contusion**.

This presentation is classic for **blunt cardiac injury (myocardial contusion)** following high-energy blunt chest trauma. The key features that distinguish this diagnosis are:

- **Mechanism**: Unrestrained driver in a head-on collision — the anterior chest strikes the steering wheel, compressing the heart between the sternum and spine[1][2]
- **Elevated troponins**: Directly reflect myocardial cell injury/necrosis from the contusion. Troponin is the primary biochemical marker for diagnosing myocardial contusion[3][4]
- **Elevated pulmonary capillary wedge pressure (PCWP)**: Reflects impaired myocardial compliance and diastolic dysfunction from the contused myocardium — this is a hallmark of cardiac (not pulmonary or hypovolemic) pathology
- **Chest wall bruising**: Consistent with a direct sternal/anterior chest impact
- **Sinus tachycardia**: The most common ECG finding in blunt cardiac injury; arrhythmias and conduction abnormalities can also occur[1][5]

Why not the other choices:

- **B. Hemorrhage** — Would cause **low** PCWP (hypovolemia), not elevated, and would not explain elevated troponins. The patient's blood pressure improved with fluids, which is inconsistent with ongoing hemorrhage as the primary diagnosis.
- **C. Pulmonary contusion** — Would present with hypoxemia, respiratory distress, and pulmonary infiltrates. It would not explain elevated troponins or elevated PCWP. This patient's oxygen saturation is 98% on room air.
- **D. Takotsubo cardiomyopathy** — Predominantly affects **postmenopausal women** and is triggered by emotional or catecholamine-mediated stress, not direct mechanical trauma. It would be highly unusual in a 27-year-old man with a clear traumatic mechanism.

The ACCF expert consensus document notes that troponin elevations in trauma patients are more likely with thoracic injuries and that progressively higher levels are associated with increasing mortality.[6] The ACR Appropriateness Criteria recommend that hemodynamically stable patients with abnormal ECG findings or elevated cardiac troponins undergo echocardiography as the first-line imaging modality to assess ventricular function, wall motion abnormalities, and structural injury.[7]

Would you like to explore monitoring and management strategies for blunt cardiac injury?

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Question 35

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?

A. Adding dopamine to his treatment regimen
B. Adding lisinopril to his treatment regimen
C. Liver transplantation
D. Transjugular intrahepatic portosystemic shunting

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The answer is **C. Liver transplantation**.

This patient with **decompensated cirrhosis** (ascites, scleral icterus, hepatomegaly) complicated by **spontaneous bacterial peritonitis (SBP)** — PMN count >250 cells/mm³ with positive E. coli culture — is now developing **hepatorenal syndrome–acute kidney injury (HRS-AKI)**. The key features supporting this diagnosis include a doubling of serum creatinine (0.9 → 1.8 mg/dL), oliguria despite adequate fluid intake, low urine sodium (prerenal pattern), and bland urine

sediment (no blood or protein), all in the absence of nephrotoxic medications or structural renal disease.[1]

Why liver transplantation is the best answer:

Liver transplantation is the definitive treatment for HRS-AKI because the underlying liver failure drives the splanchnic vasodilation and renal hypoperfusion that cause the syndrome.[2][3][4] The AASLD 2021 guidance states that restoring liver function by transplant is the "ultimate therapy" for HRS-AKI, and the AGA expert review calls it the "optimal treatment" because vasoconstrictors do not address the underlying liver disease.[2][4] All patients with cirrhosis and AKI should be considered for **urgent liver transplant evaluation** given high short-term mortality, even among responders to vasoconstrictors.[4]

In clinical practice, **vasoconstrictor therapy (terlipressin or norepinephrine) plus albumin** serves as the pharmacological bridge to transplant, with an average ~50% HRS reversal rate.[4][5] However, these agents are not among the answer choices.

Why the other options are incorrect:

- **A. Dopamine** — "Renal-dose" dopamine has not been shown to improve outcomes in HRS-AKI and is not recommended by any guideline for this indication.[6]
- **B. Lisinopril** — **ACE inhibitors are contraindicated** in cirrhosis with ascites. They further reduce systemic vascular resistance and renal perfusion pressure, worsening renal function.
- **D. TIPS** — While TIPS can be considered for refractory ascites, it is **not a recommended treatment for HRS-AKI** and is generally contraindicated in the setting of active infection such as SBP.[6]

Would you like to explore the comparative efficacy of terlipressin versus norepinephrine as bridge therapy for HRS-AKI?

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Question 36

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?

A. Glucocorticoids
B. Methimazole
C. Propranolol
D. Radioiodine therapy

https://openevidence.com/ask/c7b89f9b-4fb3-49b7-a0ce-2488e8c3e3cb

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The answer is **B. Methimazole**.

This patient presents with a classic **hyperthyroidism** syndrome — unintentional weight loss, heat intolerance, tachycardia (110/min), widened pulse pressure (146/78), warm/moist skin, and fine tremor — most consistent with **Graves' disease**, the most common cause of hyperthyroidism in young women.[1]

Methimazole is the first-line antithyroid drug for overt hyperthyroidism in non-pregnant patients.[1][2][3] It inhibits thyroid peroxidase, thereby decreasing thyroid hormone synthesis, and a **12- to 18-month course** achieves remission in 30%–50% of patients with Graves' disease.[4] Practice patterns have shifted to favor antithyroid drugs over radioiodine as initial treatment, consistent with current guidelines.[1][3]

Why not the other options:

- **Propranolol (C):** Provides symptomatic relief of hyperadrenergic symptoms (tachycardia, tremor) but **does not treat the underlying hyperthyroidism**. It is used as an adjunct, not as definitive monotherapy.[1]
- **Radioiodine therapy (D):** A valid definitive treatment, but results in **permanent hypothyroidism in >80%** of patients with Graves' disease and carries a risk of inducing or

worsening Graves' ophthalmopathy. In a young woman of childbearing age, pregnancy must be deferred at least 6 months after treatment. Methimazole is generally preferred as the initial approach.[1][4][5]

- **Glucocorticoids (A):** Not a primary treatment for uncomplicated hyperthyroidism. Their role is limited to thyroid storm, severe subacute thyroiditis, or management of Graves' ophthalmopathy.

Would you like to explore the key safety monitoring and adverse effect counseling when starting methimazole?

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Question 37

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?

A. 5
B. 7
C. 18
D. 21

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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 deletion on the short arm of **chromosome 5** (5p-).[1][2] The hallmark features presented in this vignette include:

- **High-pitched, mewing (cat-like) cry** — the pathognomonic feature, resulting from abnormal laryngeal development; the syndrome's name literally means "cry of the cat"[1][3]
- **Microcephaly** and **epicanthal folds** — characteristic craniofacial dysmorphisms[4][5]
- **Severe developmental and speech delay** — most patients have significant intellectual disability, and approximately 50% never develop expressive language[6][7]
- **Ventricular septal defect (VSD)** — the holosystolic murmur at the left 5th intercostal space near the sternum localizes to the tricuspid area/left lower sternal border, consistent with a VSD. Per an AHA scientific statement, **30–60% of patients with 5p deletion have congenital heart disease**, with **VSD being the most common** cardiac lesion, followed by ASD, PDA, and tetralogy of Fallot[8][9]

Why not the other choices:

- **B (Chromosome 7)** — Williams syndrome (7q11.23 deletion) features elfin facies, supravalvular aortic stenosis, and hypercalcemia, not a cat-like cry.
- **C (Chromosome 18)** — Edwards syndrome (trisomy 18) presents with clenched fists, rocker-bottom feet, and multiple organ defects; it is typically lethal in infancy.
- **D (Chromosome 21)** — Down syndrome (trisomy 21) features hypotonia, upslanting palpebral fissures, and atrioventricular septal defects, but no cat-like cry.

Would you like to explore early intervention and speech therapy strategies for children with Cri-du-chat syndrome?

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Question 38

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?

A. Coarctation of the aorta
B. Persistent truncus arteriosus
C. Transposition of great vessels
D. Tricuspid atresia

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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 no effective oxygenation of systemic blood.[1][2] Several features in this vignette are pathognomonic:

- **Severe cyanosis at birth** — deoxygenated systemic venous blood is recirculated through the aorta without passing through the lungs, causing profound hypoxemia.[3]
- **Single loud S2** — the aortic valve is positioned anteriorly (closer to the chest wall), making its closure sound louder and the pulmonary component inaudible.[2]
- **Machine-like murmur at the left upper sternal border** — consistent with a **patent ductus arteriosus (PDA)**, which in TGA serves as one of the few communications allowing mixing between the parallel circulations.[2]
- **Egg-shaped (or "egg on a string") cardiac silhouette** on chest radiograph — a hallmark of TGA, resulting from the narrow superior mediastinum (the great arteries are stacked anteroposteriorly rather than side-by-side) and cardiomegaly.[2][4]

- **Balloon atrial septostomy (Rashkind procedure)** — the initial palliative intervention of choice for TGA, creating an atrial-level communication to allow mixing of oxygenated and deoxygenated blood while awaiting the definitive **arterial switch operation**.[3][5][6]

Why the other choices are incorrect:

- **A. Coarctation of the aorta** — presents with differential cyanosis (lower extremity only), diminished femoral pulses, and hypertension in the upper extremities; chest X-ray shows a "figure of 3" sign, not an egg-shaped heart.[4]
- **B. Persistent truncus arteriosus** — produces a single S2 (from a single semilunar valve) but presents with mild cyanosis and signs of heart failure from excessive pulmonary blood flow, not an egg-shaped heart.
- **D. Tricuspid atresia** — causes cyanosis but characteristically shows a **boot-shaped heart** on radiography (similar to tetralogy of Fallot) and decreased pulmonary vascularity; atrial septostomy may be performed but the overall constellation (egg-shaped heart, loud single S2, machine-like murmur) points to TGA.

Would you like to explore the long-term outcomes and complications following the arterial switch operation for d-TGA?

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Question 39

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:

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

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

This clinical presentation — a 68-year-old heavy smoker (60 pack-years) with **daily productive cough** and **chronic lower extremity edema** — is classic for **chronic bronchitis**, a component of COPD. Chronic bronchitis is defined clinically by productive cough for at least 3 months per year for 2 consecutive years.[1] The lower extremity edema in this context suggests **cor pulmonale** from long-standing pulmonary disease.

The **pathological hallmark of chronic bronchitis** is enlargement of bronchial submucosal mucous glands.[2][3][4] The **Reid Index** — the ratio of mucous gland thickness to the total bronchial wall thickness (measured from the epithelial basement membrane to the perichondrium of the cartilage) — is elevated above 50% (>0.5) in chronic bronchitis, compared to normal values of approximately 0.36–0.41.[2][5][6] Reid originally used this ratio as a "diagnostic yardstick for the pathological diagnosis of chronic bronchitis".[2]

The other options are incorrect:

- **A. Hypereosinophilia** — characteristic of **asthma** or eosinophilic lung diseases, not chronic bronchitis. In COPD, the inflammatory infiltrate is predominantly neutrophilic.[3][7]
- **C. Non-caseating granulomas** — the hallmark of **sarcoidosis**, which does not fit this clinical scenario.
- **D. Necrotizing infection** — no features suggest necrotizing pneumonia; the chronic, indolent nature of this patient's symptoms points to an obstructive process rather than an infectious one.

Would you like to explore the pathological distinctions between the classic COPD phenotypes (blue bloater vs. pink puffer)?

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Question 40

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?

A. Desmoplastic
B. Nodular
C. Acral lentiginous
D. Superficial spreading

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

Acral lentiginous melanoma (ALM) is the most common specific histologic subtype of melanoma in Black patients. In a National Cancer Database analysis of 2,464 Black patients with cutaneous melanoma, ALM was the most common defined subtype (20.3%), followed by superficial spreading melanoma (9.4%).[1] A single-institution case series in JAMA Dermatology similarly found that **75% of cutaneous melanomas in Black patients occurred on acral skin** (palms, soles, nail beds).[2]

ALM accounts for **33%–36% of melanomas in Black individuals** compared to only ~1% in non-Hispanic White individuals.[3] While superficial spreading melanoma (choice D) is the most common melanoma subtype overall and in fair-skinned populations, ALM constitutes a disproportionately higher fraction of melanomas in darker-skinned populations, including those of African, Asian, and Hispanic descent.[4][5]

Critically, ALM is **not related to ultraviolet radiation exposure** — it arises on non-sun-exposed glabrous skin and lacks UV-associated mutational signatures.[3][5] This distinguishes it from the other subtypes listed: superficial spreading and lentigo maligna melanoma are strongly UV-associated, and desmoplastic melanoma typically arises on chronically sun-damaged skin. For this African-American woman, despite her Caribbean travel (high sun exposure), the greatest melanoma risk relates to ALM on the palms, soles, or nail beds rather than UV-driven subtypes.

Would you like to explore screening and early detection strategies for acral lentiginous melanoma in patients with skin of color?

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Question 41

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?

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

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A. Jaw claudication.

This presentation is classic polymyalgia rheumatica — a woman over 50 with bilateral shoulder girdle pain and morning stiffness severe enough to impair combing her hair, neck stiffness, low-grade fever, preserved muscle strength, and markedly elevated ESR/CRP.[1][2] Because PMR and giant cell arteritis lie on a single disease spectrum, every patient diagnosed with PMR must be actively questioned and examined for cranial GCA features, of which jaw claudication is among the most discriminating.[3]

Why GCA screening is mandatory here

- **16–21% of PMR patients have concurrent GCA**, and subclinical large-vessel involvement is found on imaging in 3–46% of PMR patients.[1][4]
- **Jaw claudication carries the highest positive likelihood ratio of any GCA symptom** (LR+ 4.90, 95% CI 3.74–6.41) in a JAMA Internal Medicine meta-analysis, with limb claudication LR+ 6.01.[5]
- New temporal headache, jaw claudication, or temporal artery abnormality in a PMR patient is **highly predictive of cranial GCA**.[4]
- **Vision loss occurs in up to 20% of GCA patients**, and ischemic complications typically occur before glucocorticoids are started.[6]

Screening should therefore include jaw claudication, new-onset temporal headache, scalp tenderness, visual disturbance or amaurosis fugax, limb claudication, and palpation of temporal, radial, and pedal arteries.[2][3] If any cranial feature is present, start high-dose glucocorticoids (40–60 mg prednisone equivalent daily; IV methylprednisolone for visual loss) immediately and arrange temporal artery biopsy or vascular ultrasound — treatment must not be delayed for the biopsy, though yield is highest when the biopsy is obtained promptly.[6][7] For isolated PMR, prednisone 12.5–25 mg/day with gradual taper is standard.[1][6]

Why the other options are wrong

- **Heliotrope rash** — dermatomyositis, which produces objective proximal weakness with elevated CK; strength is intact here.
- **Gastroesophageal reflux** — a feature of systemic sclerosis/myositis overlap, not PMR.
- **Pink plaques with silvery scales** — psoriasis; psoriatic arthritis presents with peripheral or axial inflammatory arthritis, not isolated girdle stiffness with this inflammatory profile.

Two caveats on the labs

- The CRP is reported as 44 mg/dL (i.e., 440 mg/L), almost certainly a unit transcription for 44 mg/L. If the value were literal, that degree of elevation would be atypical for uncomplicated PMR and would warrant exclusion of infection, malignancy, or another severe inflammatory process — mimickers that account for roughly one third of provisional PMR diagnoses being reclassified.[1]
- Hemoglobin 12.9 g/dL and hematocrit 37.7% are within normal limits; the MCV of 82.2 fL is low-normal and not itself diagnostic.

Would you like to explore whether all new PMR patients should get vascular ultrasound to screen for subclinical GCA?

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Question 42

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?

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

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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**, **cyclic pelvic/back pain**, and **painful diarrhea** recurring monthly for 4–6 days — a pattern corresponding to menses and reflecting cyclic inflammation from ectopic endometrial implants.[1] Partial response to ibuprofen is consistent, as NSAIDs reduce prostaglandin-mediated pain from these lesions.[2] Importantly, a **normal pelvic exam and normal hysterosalpingogram do not exclude endometriosis** — physical examination and imaging can be entirely normal, particularly in superficial or minimal disease.[1][2]

Endometriosis causes infertility through multiple mechanisms even with patent tubes, including **impaired ovarian function, altered peritoneal environment** (elevated inflammatory cytokines, prostaglandins), **dysfunction of uterine endometrium** with progesterone resistance, and adverse effects on oocyte quality and embryo implantation.[1][2][3] Approximately 25–40% of women with infertility have endometriosis.[4]

Why the other options are incorrect:

- **A. Loss of fallopian tube function following infection** — Pelvic inflammatory disease (PID) typically causes tubal occlusion visible on HSG, which was normal here. PID also does not produce cyclic symptoms tied to menses.
- **B. Smooth muscle tumor arising from the myometrium** — Leiomyomas would likely be detected on bimanual examination and do not cause cyclic diarrhea.
- **D. Increased secretion of androgens and LH** — Polycystic ovary syndrome (PCOS) presents with **oligomenorrhea/anovulation** and hyperandrogenic features (hirsutism, acne), not regular 29-day cycles with cyclic pain and diarrhea.

Would you like to explore the diagnostic workup and treatment strategies for endometriosis-associated infertility?

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Question 43

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?

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

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

This patient presents with classic features of **infective endocarditis (IE)** on a prosthetic tricuspid valve: fever, malaise, splinter hemorrhages (nail bed hemorrhages), and a major predisposing condition (prosthetic valve replacement 1 year prior). **Vegetations** — friable, irregular masses composed of platelets, fibrin, inflammatory cells, and microorganisms adherent to the valve — are the hallmark pathological finding of IE and a **major diagnostic criterion** in the modified Duke criteria.[1]

Echocardiographically, vegetations appear as **irregularly shaped, oscillating intracardiac masses**, typically on the inflow side of the affected valve, with density similar to myocardium.[2][3] In prosthetic valve endocarditis, these masses form when organisms adhere to foreign material, triggering platelet aggregation and thrombus formation.[4][5] They are characteristically friable, leading to embolization — which explains this patient's splinter hemorrhages.[6]

The other options are incorrect:

- **A. Bicuspid valve** — A congenital predisposition to native valve IE, not 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 is not diagnostic of it.

Would you like to explore empiric antibiotic therapy for prosthetic valve endocarditis?

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Question 44

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?

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

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The answer is **C. Laparoscopy**.

This presentation — **cyclic pelvic pain, dyspareunia, and rectovaginal tenderness** with a normal transvaginal ultrasound and negative cervical/urethral swabs — is classic for **endometriosis**, particularly superficial peritoneal or deep infiltrating disease not visualized on ultrasound.[1][2] Transvaginal ultrasound has high sensitivity for endometriomas but **low sensitivity for superficial peritoneal lesions** (65%).[2] Critically, this patient is **already on combined oral contraceptives** — a first-line hormonal treatment for endometriosis — yet remains symptomatic, and her pain is unrelieved by analgesics.[2]

Diagnostic laparoscopy is appropriate here because it allows both **definitive diagnosis** (via visualization and histological confirmation) and **concurrent surgical treatment** of lesions. ACOG guidelines state that laparoscopy should be considered when empiric medical therapy fails, when the clinical diagnosis is unclear, or as part of a stepwise approach.[1] It can identify disease even when physical examination and imaging are negative.[1]

Why not the other options:

- **A. CA-125** — ACOG **strongly recommends against** using biomarkers to diagnose endometriosis. CA-125 has **poor sensitivity (~40–52%)** at the standard cutoff of >30–35 U/mL, particularly for minimal-mild disease, and a normal level does not exclude the diagnosis.[1][3]
- **B. Hysterectomy** — This is reserved for refractory endometriosis after other medical and surgical treatments have failed, and approximately 25% of patients who undergo hysterectomy for endometriosis experience recurrent pain. It is not appropriate as a next step in a 30-year-old without prior surgical evaluation.[2]
- **D. Hysteroscopy** — This evaluates the **uterine cavity** (for polyps, submucosal fibroids, intrauterine adhesions) and would not identify endometriosis, which is defined by endometrial-like tissue **outside** the uterus.

Would you like to explore the stepwise management approach for endometriosis after first-line hormonal therapy fails?

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Question 45

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?

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

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The answer is **C. Thoracic aortic rupture**.

This presentation is classic for **blunt traumatic aortic injury (BTAI)** following a high-speed deceleration mechanism. The chest X-ray findings in this case — **widened mediastinum, depression of the left mainstem bronchus, and rightward deviation of the nasogastric tube** — constitute the hallmark radiographic triad of traumatic aortic rupture.[1][2][3]

Why these findings point to aortic rupture:

- **Widened mediastinum** results from mediastinal hemorrhage surrounding the injured aorta. The 2022 ACC/AHA guidelines list this as the leading CXR sign of acute aortic injury. [1]
- **Nasogastric tube deviation to the right** occurs because the periaortic hematoma displaces the esophagus rightward. Per the 2010 ACCF/AHA guidelines, a CXR with nasogastric tube

displacement has approximately **80% sensitivity** for suggesting traumatic aortic rupture.[4][5]

- **Depression of the left mainstem bronchus** results from mass effect of the hematoma inferior to the aortic arch. Marnocha et al. identified this as one of the most helpful findings for suspecting aortic rupture.[3]
- **Left second rib fracture** reflects a high-energy mechanism consistent with deceleration injury to the aortic isthmus.

Why not the other choices:

- **A. Diaphragmatic rupture** — Would present with bowel sounds in the chest, elevated hemidiaphragm, or NG tube coiling above the diaphragm. It does not produce a widened mediastinum or NG tube deviation.
- **B. Traumatic bronchial rupture** — Typically manifests with pneumothorax, persistent air leak, pneumomediastinum, or subcutaneous emphysema rather than a widened mediastinum with NG tube deviation.[6]
- **D. Tension pneumothorax** — Would produce **hyperresonance** to percussion (not dullness), absent breath sounds, and contralateral tracheal deviation. The dullness at the left base here suggests hemothorax accompanying the aortic injury, not tension physiology.

The hemodynamic instability (tachycardia, hypotension) and low oxygen saturation are consistent with hemorrhagic shock from contained aortic rupture with associated hemothorax. The next step would be **CT angiography** of the chest if hemodynamically permissible, as this is the diagnostic standard for confirming BTAI.[6][7]

Would you like to explore the management of traumatic thoracic aortic injury, including endovascular versus open repair?

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Question 46

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?

A. Methimazole
B. Propylthiouracil
C. Radioiodine therapy
D. Thyroidectomy

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The answer is **B. Propylthiouracil (PTU)**.

This patient at **10 weeks gestation** presents with classic findings of **Graves' disease** — diffusely enlarged thyroid with bruits, tachycardia, diaphoresis, anxiety, insomnia, and markedly suppressed TSH with elevated FT4. In the **first trimester**, PTU is the preferred antithyroid drug. [1][2][3]

Why PTU over the other options:

- **Methimazole (A)** is avoided in the first trimester due to its association with a characteristic embryopathy including **aplasia cutis, choanal atresia, esophageal atresia, and abdominal wall defects**. A meta-analysis found a higher congenital anomaly rate with methimazole compared to PTU (adjusted RR 1.28 vs. 1.16 relative to controls). PTU-associated anomalies (facial/neck cysts, urinary tract abnormalities) are milder and less frequent.[1][3]

- **Radioiodine therapy (C)** is **absolutely contraindicated** in pregnancy — it crosses the placenta and destroys the fetal thyroid gland, causing permanent neonatal hypothyroidism.[4][5]
- **Thyroidectomy (D)** is reserved for cases where antithyroid drugs are contraindicated or cannot control hyperthyroidism; if needed, it is preferably performed in the **second trimester** to minimize anesthetic teratogenicity.[4]

Per the ATA 2026 guidelines and ACOG, PTU should be used at the **lowest effective dose** to maintain maternal FT4 at or just above the upper reference limit, with typical initial dosing of **200–400 mg daily divided into three doses**.[2][3] After the first trimester, some clinicians switch to methimazole to reduce the risk of PTU-associated hepatotoxicity, though this transition carries a risk of transient poor thyroid control.[2]

Would you like to explore the monitoring and dose adjustment approach for PTU throughout pregnancy?

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Question 47

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?

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

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D. Freshwater snails.

This is intestinal/hepatosplenic schistosomiasis caused by **Schistosoma mansoni**, acquired through skin contact with freshwater containing cercariae released by **Biomphalaria** snails, the obligate intermediate host.[1][2][3] Uganda (Lake Victoria basin) is highly endemic.

Why the findings fit S. mansoni

- **Lateral-spined oval eggs in stool** are the diagnostic hallmark of S. mansoni; S. haematobium eggs have a terminal spine and appear in urine.[4][5]
- **Granulomatous inflammation with periportal fibrosis** (Symmers' pipestem fibrosis) results from the Th2-driven granulomatous response to eggs embolized to presinusoidal periportal spaces, producing hepatomegaly, presinusoidal portal hypertension, and splenomegaly.[3][6][7]
- **Eosinophilia (12%)**, intermittent diarrhea, abdominal pain, and weight loss are typical of intestinal schistosomiasis; eosinophilia may be present in both acute and chronic infection.[1][8]

- Timing fits: the prepatent period is ~5–7 weeks from cercarial penetration to egg production, consistent with symptom onset around the time of migration.[1]

Why the other options are wrong

- **Undercooked pork** — Taenia solium (cysticercosis) or Trichinella; neither produces lateral-spined eggs or pipestem fibrosis.
- **Undercooked fish** — Clonorchis/Opisthorchis (small operculated eggs, biliary disease, cholangiocarcinoma), Diphyllobothrium latum, or Anisakis.
- **Dog feces** — Echinococcus granulosus (hydatid cysts, not periportal fibrosis) or Toxocara canis (visceral larva migrans, no eggs in stool).

Management point: treat with **praziquantel**, first-line for all Schistosoma species.[9] Praziquantel acts on adult worms and is less effective against juvenile stages, so treatment initiated during early infection may require a repeat course several weeks later.[5][9] Established periportal fibrosis and portal hypertension can persist despite cure, so screening for esophageal varices should be considered in hepatosplenic disease.[10]

Would you like to explore praziquantel dosing and the timing of repeat treatment in newly arrived migrants?

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Question 48

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?

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.

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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 clinical scenario describes classic **tetralogy of Fallot (TOF)** — the four cardinal features being pulmonary outflow obstruction, right ventricular hypertrophy, VSD, and overriding aorta. The key concept tested here relates to hematologic complications of chronic cyanosis.

Why B is correct

Chronic hypoxemia in cyanotic congenital heart disease triggers **secondary erythrocytosis** — a physiologic increase in red cell mass. This process depletes bone marrow iron stores. Because erythrocytosis elevates hemoglobin above typical population norms, a patient with TOF can be iron-deficient yet still show a hemoglobin that falls within the "normal" reference range. The 2025 ACC/AHA Guideline for Management of Adults with Congenital Heart Disease states that iron deficiency screening is indicated because "**deficiency can occur even when hematocrit levels are either normal or elevated**".[1] Additionally, classic red cell indices are unreliable: the AHA scientific statement notes that **hypochromia and microcytosis are rare** in cyanotic CHD because chronic cyanosis itself causes macrocytosis, and MCV is not a reliable screening test.[2][3] Diagnosis requires **serum iron, ferritin, and transferrin saturation**.[2][3]

Why the other options are incorrect

- **A** — The **tricuspid valve is not** the most commonly affected valve in uncorrected TOF endocarditis. In right-sided endocarditis overall, the tricuspid valve is frequently involved (particularly in IV drug use), but TOF-associated endocarditis more typically involves the right ventricular outflow tract, pulmonary valve, or VSD margins.[4][5]
- **C** — In cyanotic CHD, **cerebral venous thrombosis is more common** than cerebral arterial thrombosis. As specifically noted in the literature, CVA complicating cyanotic congenital heart disease is "**most frequently attributed to cerebral venous thrombosis, only rarely to in situ cerebral arterial thrombosis**". Risk factors include polycythemia, dehydration, and iron deficiency.[6][7][8]
- **D** — **Heart failure is not a common complication** of uncorrected TOF. The large nonrestrictive VSD allows the right ventricle to decompress at systemic pressure, preventing volume overload. The predominant complications are cyanosis, hypercyanotic ("tet") spells, polycythemia/hyperviscosity, cerebrovascular events (stroke, brain abscess), and endocarditis.[9]

Would you like to explore the acute management of hypercyanotic (tet) spells in infants with TOF?

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Question 49

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?

A. Dementia
B. Opioid intoxication
C. Delirium
D. Urinary tract infection

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The answer is **C. Delirium**.

This presentation is classic for **postoperative delirium**, which occurs in **10–65% of elderly patients hospitalized with hip fracture**.[1] The key diagnostic features, based on DSM-5 and the Confusion Assessment Method (CAM), are all present here:[2]

- **Acute onset** following surgery (not a chronic, insidious decline)
- **Fluctuating course** — unarousable during the day but awake and impulsive at night, reflecting a disrupted sleep-wake cycle
- **Inattention** on neurologic exam (a hallmark of delirium)
- **Disorientation** to place and time with altered level of consciousness

Why not the other options:

- **Dementia (A):** Dementia has an **insidious onset over months to years**, with attention generally preserved until advanced stages. This patient was previously healthy, and the acute, fluctuating course is inconsistent with dementia.[3]

- **Opioid intoxication (B):** While opioids are a recognized precipitant of delirium, pure opioid intoxication would present primarily with **sedation, respiratory depression, and miosis** — not the fluctuating agitation, impulsivity, and disorientation described. The overall syndrome here is delirium, which opioid use may be contributing to as a precipitating factor.

- **UTI (D):** The **normal urine dipstick** makes UTI unlikely. Moreover, UTI would be a precipitating cause of delirium rather than a distinct diagnosis explaining this clinical picture.

This patient's **advanced age (79 years)** and **opioid use** are well-established predisposing and precipitating factors for postoperative delirium.[3][4][5] Management priorities include identifying and treating reversible precipitants, minimizing opioid and other deliriogenic medications, ensuring fluid/electrolyte balance, early mobilization, and frequent reorientation.[1]

Would you like to explore evidence-based management strategies for postoperative delirium after hip fracture?

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Question 50

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?

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

https://openevidence.com/ask/6cb2a1b4-d73d-4975-b0de-aae02fd93773

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

This patient presents with **atlantoaxial subluxation (AAS) causing cervical myelopathy**, and rheumatoid arthritis (RA) is the predisposing risk factor.

Key findings supporting the diagnosis:

- **Upper motor neuron signs** — new-onset spasticity, 3+ hyperreflexia, and a positive Babinski sign indicate **cervical myelopathy** from spinal cord compression at the craniocervical junction.
- **The "clunk" with anterior-posterior shear force** describes the **Sharp-Purser test**, a clinical maneuver for atlantoaxial instability. A palpable clunk indicates excessive anterior translation of C1 on C2 that reduces with the maneuver.[1]
- **Symmetric swelling and deformities of the hands** are characteristic of RA, which causes synovial inflammation, pannus formation, and ligamentous destruction at the C1-C2 joint.

Why RA causes atlantoaxial instability:

Cervical spine involvement occurs in **up to 86% of RA patients**.[2] Chronic synovial inflammation at the atlantoaxial joint erodes the transverse ligament and odontoid process, leading to AAS. This allows the odontoid or posterior arch of C1 to impinge on the spinal cord, producing myelopathy.[2][3] AAS is the most common form of cervical instability in RA, and it can progress to cause catastrophic spinal cord compression or even sudden death from medullary compression.[4]

Why not the other choices:

- **Down syndrome (C)** is also a known risk factor for atlantoaxial instability due to ligamentous laxity, but the HEENT exam explicitly notes **normal facial features**, making this diagnosis unlikely. The hand deformities further point toward RA.
- **Diabetes mellitus (B)** and **cerebral palsy (A)** are not recognized risk factors for atlantoaxial instability.

Would you like to explore the surgical indications and management of atlantoaxial instability in rheumatoid arthritis?

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Question 51

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?

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

https://openevidence.com/ask/c507e2e7-54dc-4189-aaf8-91e18b04abe5

The answer is **D. MR angiography of the brain**.[1][2][3]

This presentation — **resistant hypertension, bilateral palpable flank masses, elevated creatinine, and a family history of early kidney transplantation** — is classic for **autosomal dominant polycystic kidney disease (ADPKD)**. The most critical extrarenal complication to screen for is **intracranial aneurysm (ICA)**, which has a prevalence of approximately **12.9%** in ADPKD patients, representing a 4–5-fold increased risk compared to the general population.[4][5] Rupture of an ICA causes subarachnoid hemorrhage with significant morbidity and mortality.

Why MR angiography?

The 2025 KDIGO guidelines and the AHA/ASA recommend **time-of-flight MR angiography (MRA) without gadolinium** as the preferred screening modality for intracranial aneurysms in ADPKD.[1][3] High-resolution CT angiography is an acceptable alternative. Screening is particularly recommended in patients with a family history of ICA, subarachnoid hemorrhage, or unexplained sudden death, and should also be discussed in those with de novo ADPKD, unknown family history, or before kidney transplantation.[1] If negative, rescreening is individualized to every **5–10 years** based on risk factors.[1][6]

Why not the other options?

- **A (Colonoscopy):** While colonic diverticulosis can be associated with ADPKD, it is not a standard screening recommendation.
- **B (EGD):** Esophageal varices from polycystic liver disease are rare (~1.5%) and not a routine screen.[2]
- **C (Liver function tests):** Hepatic cysts are very common in ADPKD (>90% by age 35–46) but are typically detected on imaging; liver synthetic function is usually preserved, making LFTs a low-yield screening test.[2]

Would you like to explore the management of hypertension and disease-modifying therapy in ADPKD?

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Question 52

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?

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

https://openevidence.com/ask/e54caf84-a419-48bd-8ea8-b1e008ba3be1

B. Antigenic variation.

The organism is *Neisseria gonorrhoeae* — intracellular gram-negative diplococci within PMNs on urethral smear is >99% specific and >95% sensitive for gonococcal urethritis in symptomatic men, and growth on Thayer-Martin (selective, antibiotic-containing chocolate agar) confirms it.[1][2] Repeat gonococcal infection after successful treatment reflects the gonococcus's failure to induce durable protective immunity, driven largely by high-frequency antigenic and phase variation of surface-exposed antigens.[3][4]

Mechanism

- **Pilin (type IV pilus) antigenic variation** is the classic example: the single expressed locus *pilE* undergoes unidirectional gene conversion from multiple promoterless silent *pilS* copies, generating a new PilE variant at >4×10^{-3} events per cell per generation — the highest reported antigenic variation rate for any bacterial gene. Antibody generated against the prior pilin type does not recognize the new variant.[5][6][7]
- **Opa proteins and lipooligosaccharide** additionally undergo phase and antigenic variation, further eroding any anamnestic response.[5][6]
- Contributing mechanisms include complement evasion, PorB-mediated suppression of dendritic-cell–induced $CD4^{+}$ T-cell proliferation, and a TGF-β/Treg–driven Th17-skewed

response that suppresses Th1/Th2 adaptive immunity and specific antibody. Natural infection produces only modest antibody titers.[3][4][8][9]

Why the other options are wrong

- **A. Exotoxin release** — *N. gonorrhoeae* does not produce a disease-defining exotoxin; its pathology is mediated by LOS endotoxin, peptidoglycan fragments, and neutrophilic inflammation. Exotoxin-driven lack of immunity would instead suggest organisms like *C. diphtheriae* or *C. tetani*, and even those elicit neutralizing antitoxin after vaccination.
- **C. Polysaccharide capsule** — the gonococcus is unencapsulated (unlike *N. meningitidis*), which is precisely why there is no polysaccharide-conjugate vaccine for gonorrhea; the meningococcal serogroup B OMV vaccines that show partial cross-protection work via outer-membrane proteins, not capsule.[3][4]
- **D. Bruton's agammaglobulinemia** — XLA presents in infancy with recurrent sinopulmonary and enteroviral infections and absent B cells/immunoglobulins, not a single recurrence of an STI in an otherwise well 26-year-old. Terminal complement (C5–C9) deficiency, not XLA, is the immunodeficiency classically associated with recurrent *Neisseria* infection, and it predisposes to disseminated/meningococcal disease rather than isolated urethritis.

Practice points

Recurrence at one year in this patient is almost certainly reinfection from an untreated or new partner rather than treatment failure. Retest for gonorrhea and chlamydia at 3 months after treatment, obtain culture with susceptibility testing if true treatment failure is suspected (NAAT cannot provide susceptibilities), and address partner treatment and HIV/syphilis screening.[2]

Would you like to review current CDC treatment recommendations and the approach to suspected ceftriaxone treatment failure in gonorrhea?

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Question 53

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?

A. Lateral cervical film
B. Cervical immobilization
C. IV methylprednisolone
D. Observation overnight

https://openevidence.com/ask/c388b0b4-a893-4794-a563-f95404d1db5a

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The correct answer is **B. Cervical immobilization**.

Cervical spine motion restriction is the standard of care as the initial step for any trauma patient with neck pain and a mechanism concerning for cervical spine injury.[1][2] The American College of Surgeons Best Practices Guidelines state that indications for spinal motion restriction include **midline neck pain/tenderness**, focal neurologic deficits, altered consciousness, and distracting injuries.[1] This patient reports significant neck pain after a rear-end MVC, making immobilization the immediate priority before any further workup.

Why not the other options:

- **A. Lateral cervical film** — While imaging may be needed after immobilization and clinical assessment, plain radiographs have a **sensitivity of only ~36%** for cervical injuries and have been supplanted by CT as the preferred modality. Additionally, imaging is a subsequent step — immobilization must come first.[3]
- **C. IV methylprednisolone** — High-dose methylprednisolone for spinal cord injury is **no longer recommended** by major guidelines (AANS/CNS). Furthermore, this patient has no neurological deficits, making this intervention inappropriate.
- **D. Observation overnight** — Passive observation alone does not address the risk of an unstable cervical spine and is insufficient as the initial management step.

After immobilization, clinical evaluation using validated decision tools (NEXUS or Canadian C-Spine Rule) guides the need for imaging.[1] Notably, the Canadian C-Spine Rule identifies a **simple rear-end MVC** as a low-risk factor, so depending on clinical examination (ability to rotate the neck 45° bilaterally, absence of high-risk features), this patient could potentially be cleared clinically.[1][4] If imaging is required, **CT is the appropriate modality** rather than plain films.[3][5]

Would you like to explore the comparison between NEXUS and Canadian C-Spine Rule criteria for cervical spine clearance?

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Question 54

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?

A. Amantadine
B. Ribavirin
C. Levodopa
D. Zidovudine

https://openevidence.com/ask/6e667761-e65e-4677-93cc-d23fc2c17253

The answer is **A. Amantadine**.

The clinical presentation — **rigidity, bradykinesia, resting tremor, and shuffling gait without arm swing** — is classic for **Parkinson's disease**. The question's key qualifier is that the prescribed drug is an **antiviral agent**.

Amantadine was originally developed as an antiviral for **influenza A** prophylaxis and treatment, and was serendipitously discovered to have antiparkinsonian activity.[1][2] It is FDA-approved for both indications.[3] Its mechanism in Parkinson's disease involves **weak non-competitive NMDA receptor antagonism**, along with effects on dopamine release, reuptake blockade, and possible anticholinergic activity.[1][3] Placebo-controlled trials have demonstrated improvement in **akinesia, rigidity, and tremor**.[1]

The other options do not fit:

- **Levodopa (C)** is the most effective symptomatic treatment for Parkinson's disease but is **not an antiviral drug**.
- **Ribavirin (B)** is an antiviral used for hepatitis C and RSV — it has no role in Parkinson's disease.
- **Zidovudine (D)** is an antiretroviral (NRTI) for HIV — it has no antiparkinsonian activity.

Would you like to explore the comparative role of amantadine versus levodopa in early Parkinson's disease management?

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Question 55

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?

A. Histrionic personality disorder
B. Borderline personality disorder
C. Dependent personality disorder
D. Narcissistic personality disorder

https://openevidence.com/ask/445d1974-2397-4f49-8631-215c3335b931

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

This patient meets **at least 6 of the 9 DSM-5 diagnostic criteria** for BPD:[1][2]

- **Frantic efforts to avoid abandonment** — self-harm triggered by the threat of a breakup
- **Unstable, intense interpersonal relationships** — longstanding pattern of turbulent romantic and family relationships
- **Impulsivity** — described by family as "very impulsive"
- **Recurrent self-mutilating behavior** — wrist-slitting suicide attempt
- **Affective instability** — rapid alternation between sobbing and anger during hospitalization
- **Inappropriate, intense anger** — spitting at staff, angry outbursts

Only **5 of 9 criteria** are required for diagnosis.[1][3]

Why not the other options?

- **Histrionic personality disorder (A):** Also features attention-seeking, manipulative behavior, and rapidly shifting emotions. However, BPD is distinguished by **self-destructiveness, angry disruptions in close relationships, and chronic feelings of emptiness** — all prominent in this vignette.[2]
- **Dependent personality disorder (C):** Involves excessive need for others to assume responsibility and difficulty with decisions, but lacks the impulsivity, self-harm, and intense anger seen here.[2]
- **Narcissistic personality disorder (D):** Centers on grandiosity, need for admiration, and lack of empathy; angry reactions may occur but without the self-destructive behaviors, abandonment fears, or affective lability characteristic of BPD.[2]

Would you like to explore evidence-based treatment options for borderline personality disorder?

References

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Question 56

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?

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

https://openevidence.com/ask/f9a37e1a-3449-4b71-bf5f-fe9263df1224

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 SCFE include the patient's **age (13 years), obesity, hip/groin/knee pain, inability to bear weight, and limited hip range of motion**.[1][2] SCFE occurs between ages 8–16, has a male predominance (1.5:1), and obesity is the strongest modifiable risk factor, increasing risk up to 17-fold in severe obesity.[1][3]

Why surgical pinning (answer D):

The definitive treatment for SCFE is **in situ screw fixation**, which halts further slippage and prevents complications such as **avascular necrosis, chondrolysis, and femoroacetabular impingement**.[2][4][5] This patient's inability to bear weight classifies the SCFE as **unstable**, which carries a higher complication rate and warrants **urgent surgical fixation, ideally within 24 hours**.[1][2] Patients should be placed on non-weight-bearing status immediately and referred urgently to orthopedic surgery.[2]

Why the other answers are incorrect:

- **A. Casting and crutches** — Non-operative management does not prevent slip progression in SCFE. A spica cast has historically been attempted but is inferior to screw fixation.[5]

- **B. Pavlik harness** — This is used for **developmental dysplasia of the hip (DDH) in infants**, not for SCFE in adolescents.
- **C. Supportive therapy and observation** — SCFE always requires surgical intervention; delayed treatment increases the risk of avascular necrosis and permanent deformity.[1][2]

Would you like to explore whether prophylactic pinning of the contralateral hip is recommended in SCFE?

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Question 57

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?

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

https://openevidence.com/ask/d64ebf8b-aa73-4b97-baec-5722ca70455a

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

This patient has **decompensated cirrhosis** (untreated hepatitis C, scleral icterus, spider angiomas, hypoalbuminemia, ascites) complicated by **spontaneous bacterial peritonitis (SBP)** and **hepatic encephalopathy** (confusion, hand tremors). The ascitic fluid confirms the diagnosis:

- **SAAG** = 2.6 − 0.8 = **1.8 g/dL** (≥1.1 → portal hypertension)[1]
- **Absolute PMN count** = 1,900 × 0.60 = **1,140/mm³**, far exceeding the **>250/mm³ threshold** diagnostic of SBP[1]

Bacterial translocation — the passage of enteric bacteria across the intestinal wall to mesenteric lymph nodes and then into the ascitic fluid — is the established pathogenic mechanism of SBP.[2][3][4] Portal hypertension leads to intestinal mucosal edema and increased permeability, while cirrhosis-associated immune dysfunction and bacterial overgrowth (from reduced bile acid and gastric acid secretion) facilitate translocation of gram-negative Enterobacteriaceae.[1][2] The AASLD 2021 guidance confirms that bacterial translocation, together with decreased host defenses, is central to the pathogenesis of spontaneous infections in cirrhosis.[1]

> "Bacterial translocation is usually monomicrobial, with invasive species belonging to Enterobacteriaceae or Streptococcaceae, and can result in spontaneous bacterial peritonitis and bacteremia."
>
> —Jasmohan S. Bajaj, M.D. et al., Virginia Commonwealth University and other institutions. The Evolving Challenge of Infections in Cirrhosis. N Engl J Med. June 17, 2021.
>
> Used under license from The New England Journal of Medicine.

Why the other options are less likely:

- **A (Aseptic peritoneal inflammation):** An elevated PMN count >250/mm³ with fever and clinical signs of infection indicates a bacterial process, not sterile inflammation.
- **B (Neoplastic growth):** No features suggest malignancy (no weight loss, lymphadenopathy, or low-SAAG ascites); the high SAAG and clinical context point to portal hypertension from cirrhosis.
- **D (Perforated viscus):** Secondary peritonitis from perforation classically presents with ascitic fluid **glucose <50 mg/dL**, **total protein >1 g/dL**, and **elevated LDH**, along with polymicrobial cultures and peritoneal signs such as guarding and rigidity. Here, glucose is 62 mg/dL (above the 50 mg/dL cutoff), and there is **no guarding** — findings more consistent with SBP. SBP is characteristically **monomicrobial** and occurs without a surgically identifiable intra-abdominal source.[5][6][7][8]

Would you like to explore the empiric treatment protocols for SBP, including antibiotic selection and albumin co-administration?

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Question 58

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?

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

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C. JAK/STAT.

The clinical picture — normocytic (MCV 90), hypoproliferative (reticulocyte 0.5%) anemia with adequate iron stores (ferritin 325 ng/mL) in a patient with diabetic nephropathy (Cr 2.2, BUN 45) — is anemia of CKD from inadequate renal erythropoietin production.[1] Treatment is an erythropoiesis-stimulating agent (epoetin alfa or darbepoetin alfa) after correctable causes such as iron deficiency are addressed.[2][3]

Mechanism: The EPO receptor is a type I cytokine receptor with no intrinsic kinase activity. EPO binding induces EPOR homodimerization, activating receptor-associated **JAK2**, which autophosphorylates and phosphorylates cytoplasmic EPOR tyrosines (notably Y343 and Y401). These serve as SH2 docking sites for **STAT5**, which is then phosphorylated, dimerizes, and translocates to the nucleus to induce anti-apoptotic genes such as BCL2L1 in erythroid progenitors.[4][5][6][7]

Why the other options are wrong:

- **PI3K/Akt/mTOR** and **MAP kinase (RAS/MEK/ERK)** are activated by EPOR, but as secondary/downstream branches contingent on JAK2 activation, not as the direct, canonical transduction pathway of the receptor.[8][9]
- **IP3** signaling is a GPCR/Gq-phospholipase C pathway (e.g., angiotensin II, vasopressin V1, alpha-1 adrenergic) and has no role in EPOR signaling.

Two practice points relevant to this case: ESAs should not be pushed to normalize hemoglobin — targeting higher Hb increases risk of stroke, hypertension, and vascular access thrombosis; typical practice is to initiate at Hb 9–10 g/dL and maintain 10–11.5 g/dL.[1][10] Also, metformin warrants review at this level of renal function, and blood pressure must be monitored with ESA initiation and dose changes.[3]

Would you like to explore how HIF-prolyl hydroxylase inhibitors differ mechanistically from ESAs in anemia of CKD?

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Question 59

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?

A. Acyclovir
B. Atorvastatin
C. Metformin
D. Metoprolol

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The answer is **C. Metformin**.

The laboratory values reveal a **high anion gap metabolic acidosis (HAGMA)** most consistent with **metformin-associated lactic acidosis (MALA)** in the setting of significant renal impairment.

Computed value for Anion Gap: 31 mEq/L

The **anion gap of 31 mEq/L** (normal ~12) with a **bicarbonate of 11 mEq/L** indicates a severe HAGMA. In a patient with type 2 diabetes (evidenced by diabetic nephropathy) and a **creatinine of 3.1 mg/dL** (estimated eGFR likely <30 mL/min/1.73 m²), this pattern is characteristic of MALA.

Why metformin:

- MALA is characterized by **elevated blood lactate (>5 mmol/L), anion gap acidosis, and arterial pH <7.35**. It is fundamentally an **accumulation disorder** — metformin is renally cleared, and at eGFR <30 mL/min/1.73 m², drug levels rise, inhibiting **mitochondrial complex I** in hepatocytes and impairing hepatic lactate clearance.[1][2]
- Metformin is **contraindicated at eGFR <30 mL/min/1.73 m²** per FDA labeling. This patient's creatinine of 3.1 with diabetic nephropathy strongly suggests he falls below this threshold.[3][4]
- The presenting symptoms — **abdominal pain, nausea, and vomiting** — are classic nonspecific symptoms of MALA, described on the FDA label as having a "subtle onset" accompanied by "malaise, myalgias, abdominal pain, respiratory distress, or increased somnolence".[4]

Why not the other choices:

- **Acyclovir (A):** Can cause crystal nephropathy and AKI but does not produce a profound HAGMA with an anion gap of 31.
- **Atorvastatin (B):** May rarely cause rhabdomyolysis or hepatotoxicity, neither of which explains this acid-base derangement.
- **Metoprolol (D):** Does not cause high anion gap metabolic acidosis.

Would you like to explore the management of metformin-associated lactic acidosis, including indications for emergent hemodialysis?

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Question 60

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?

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

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The answer is **D. Chronic obstructive pulmonary disease (COPD)**.

The PFT findings in this case demonstrate a classic **obstructive pattern with hyperinflation**, which is the hallmark of COPD:

- **FEV1/FVC ratio of 60% (< 0.7)** confirms airflow obstruction, meeting the GOLD diagnostic criterion for COPD.[1][2]
- **FEV1 of 50% predicted** places this at the boundary of **GOLD grade 2–3** severity.[1]
- **TLC of 110% predicted** (elevated) indicates **hyperinflation**, characteristic of emphysema/COPD.[3]
- **RV of 115% predicted** (elevated) reflects **air trapping**, a hallmark of obstructive physiology.[3]

- **DLCO of 60% predicted** (reduced) suggests an **emphysema component**, reflecting loss of alveolar-capillary surface area. DLCO values < 60% predicted in COPD are associated with increased symptoms, decreased exercise capacity, and increased mortality.[1]

The **36 pack-year active smoking history** is the dominant risk factor, and the physical exam finding of a **prolonged expiratory phase without crackles** is consistent with obstructive lung disease.

Why the other options are incorrect:

- **A. Asbestosis** and **B. Idiopathic pulmonary fibrosis** both produce a **restrictive pattern** on PFTs — decreased FVC, decreased TLC, low RV, and a normal or elevated FEV1/FVC ratio. This patient's elevated TLC/RV and reduced FEV1/FVC are the opposite. Additionally, IPF and asbestosis typically present with **Velcro-like crackles** on auscultation, which are absent here.[4][5][6][7]

- **C. Bronchiectasis** can produce an obstructive pattern, but it typically presents with **chronic productive cough, recurrent infections, and crackles** — none of which are described. The overall clinical picture (heavy smoking, hyperinflation, reduced DLCO) fits COPD far better.[8]

Would you like to explore the recommended initial pharmacotherapy for this patient's COPD severity?

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Question 61

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?

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

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C. Avoid exposure to birds.

This is bird fancier's lung, the avian-antigen form of hypersensitivity pneumonitis (HP). **Complete antigen avoidance is the mainstay of treatment**.[1][2][3]

Why the presentation fits

- **Episodic, exposure-timed symptoms**: dry cough, fever, chills, and malaise recurring 4–8 hours after avian antigen exposure and resolving over hours is the classic acute/subacute HP pattern.[3]
- **Occupational avian exposure** as a zookeeper caring for birds supplies the inciting antigen; HP most commonly derives from bird proteins and fungi.[1]
- **Bibasilar diffuse haziness** on chest radiograph corresponds to the interstitial/ground-glass pattern seen in ~79% of bird fancier's lung patients, with ground-glass (68%) and mosaic attenuation (61%) on CT.[4]
- **Negative PPD** and absence of travel argue against tuberculosis. Note that HP is type III/IV (immune-complex and T-cell) mediated, not IgE-mediated — the atopic history and family

asthma are distractors, and the delayed, febrile, non-wheezing pattern with radiographic infiltrates does not fit asthma.

Why the other options are wrong

- **A. Thoracocentesis** — HP produces parenchymal infiltrates, not pleural effusion; there is nothing to drain.
- **B. Inhaled beclomethasone** — inhaled corticosteroids treat airway inflammation in asthma and have no established role in parenchymal HP. Systemic (not inhaled) corticosteroids are the pharmacologic adjunct when used.
- **D. Isoniazid for 6 months** — a negative PPD with no epidemiologic risk excludes latent TB treatment.

Practical management points

- **Removal from exposure alone frequently produces resolution.** In one series of acute bird-related HP with abnormal baseline function, FVC improved in 28% and normalized in 50% an average of 3.4 ± 2.4 months after avian contact ceased, with no substantial difference between those who did and did not receive corticosteroids. Continued exposure carries a materially worse prognosis, including progression to fibrosis and respiratory failure.[3][5]
- **Systemic corticosteroids are adjunctive, not curative.** In non-fibrotic HP, corticosteroids reversed monthly FVC decline (−0.35%/month to +0.84%/month, $P < .01$) without a DLCO effect; in fibrotic HP, no significant benefit was observed. A randomized trial showed faster early recovery of FVC and DLCO with prednisone but equivalent lung function at trial end. Corticosteroids likely do not alter long-term prognosis. Reasonable to use for symptomatic or hypoxemic acute disease while avoidance is implemented.[3][5][6]
- **Confirmatory workup** if not already done: HRCT (centrilobular nodules, ground-glass, mosaic attenuation), serum specific IgG to avian antigens, PFTs with DLCO, and BAL lymphocytosis (>20–25%) if the diagnosis remains uncertain. Note that serum avian IgG is common in asymptomatic exposed bird handlers (87% of pigeon breeder controls) and so indicates exposure, not disease.[2][3][4]
- If avoidance is incompatible with the job, **respiratory protection is inadequate as sole management** — occupational reassignment away from birds should be discussed, and lung function should be followed to confirm recovery.[7]

Would you like to explore corticosteroid dosing and taper regimens for acute non-fibrotic hypersensitivity pneumonitis?

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Question 62

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?

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

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D. Uterine artery

The ureter passes directly beneath the uterine artery approximately 1.5–2 cm lateral to the cervix at the level of the internal os ("water under the bridge"), and this crossover is where ureteral injury during hysterectomy most often occurs — 80% of ureteral injuries in a prospective universal-cystoscopy series were at the ureter–uterine artery junction, with transection and kinking the predominant mechanisms.[1][2] Ligation or thermal injury at this pedicle produces unilateral obstruction with ipsilateral flank pain, oliguria, hematuria, and a modest creatinine rise — the mean increase with unilateral suture entrapment was 0.8 mg/dL, closely matching the 1.0 → 1.4 mg/dL change here.[3][4]

Why the ultrasound is normal

A normal renal ultrasound does not exclude ureteral ligation in the immediate postoperative period. Hydronephrosis takes time to develop and may be absent early or with partial/kinking injury; unilateral obstruction may also leave creatinine near-normal because of contralateral compensation.[5] Cadaveric measurements place the ureter a median 1.7 cm from the uterine

isthmus (as close as 1.0 cm) and only 0.5 cm from the cervix in ~3% of women, so even standard extrafascial technique can catch it.[2][6] A uniformly enlarged uterus, as in this patient, distorts the pedicle and further shortens that margin.

Why not the others

- **Artery of Sampson** — a small vessel running along the round ligament; ligation causes no urologic consequence, and the round ligament is remote from the ureter.
- **Ovarian artery** — the ureter does cross the infundibulopelvic ligament near the pelvic brim, so this is the second most common site of injury, but obstruction there would be proximal and the pedicle is taken well away from the classic crossover; the uterine pedicle remains the far more likely culprit.[1]
- **Superior vesical artery** — arises from the internal iliac and supplies the bladder dome; it is sacrificed only in class IV radical hysterectomy, not simple laparoscopic hysterectomy. Injury here would cause bladder rather than ureteral symptoms.[7]

Practical next step

Ureteral injuries are recognized postoperatively in roughly 60% of cases and carry worse outcomes than those found intraoperatively (pooled OR for management failure 0.22 for intraoperative vs postoperative detection).[8][9] CT urography (or retrograde pyelography) rather than repeat ultrasound is the appropriate confirmatory study, followed by cystoscopy with attempted retrograde stent placement; suture entrapment often requires percutaneous nephrostomy or deligation, since retrograde stenting frequently fails in ligated ureters.[3][10]

Would you like to explore the optimal timing and approach for repairing a ureteral injury discovered postoperatively?

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Question 63

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?

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

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The answer is **A. Epstein-Barr virus (EBV)**, the only virus among the options with a well-established causal association with Hodgkin lymphoma.

EBV is detected in approximately **40–60% of classical Hodgkin lymphoma (cHL)** cases in developed countries and up to 80% in developing countries.[1][2][3] The EBV genome is found within the malignant Hodgkin and Reed-Sternberg (HRS) cells themselves, and is monoclonal, supporting a direct pathogenic role rather than bystander infection.[3][4] The key oncogenic mechanism involves EBV-encoded proteins **LMP-1 and LMP-2A**: LMP-1 mimics a constitutively active CD40 receptor, activating NF-κB and upregulating anti-apoptotic genes, while LMP-2A provides survival signals that substitute for the B-cell receptor, rescuing pre-apoptotic germinal center B cells from programmed cell death.[5] A large Danish-Swedish cohort study demonstrated that the risk of EBV-positive cHL was significantly increased after EBV infection (relative risk 4.0; 95% CI 3.4–4.5), with a median incubation time of approximately 4.1 years.[6][7]

The other options are incorrect because each is associated with different malignancies:

- **HTLV-1** (option B) causes **adult T-cell leukemia/lymphoma**, not Hodgkin lymphoma.

- **HHV-8** (option C) is implicated in **Kaposi sarcoma and primary effusion lymphoma**.[8]
- **HPV-16** (option D) is associated with **cervical, oropharyngeal, and anogenital squamous cell carcinomas**, not lymphomas.

Would you like to explore the clinical and prognostic differences between EBV-positive and EBV-negative classical Hodgkin lymphoma?

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Question 64

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?

A. Dengue virus
B. Rubella virus
C. Toxoplasmosis
D. Zika virus

https://openevidence.com/ask/b691bb5a-9a59-4343-81d9-2341ad88d2e8

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

This presentation is classic for **congenital Zika syndrome**. Several features converge to make Zika the most likely etiology:

- **Epidemiologic exposure**: Travel to Brazil, an endemic area for Zika virus, with evening outdoor activity and no mosquito repellent use. Zika is transmitted primarily by *Aedes* mosquitoes.[1]
- **Maternal illness**: The first-trimester syndrome of **fever, headache, myalgias, arthralgias, and pruritic maculopapular rash** is the hallmark of symptomatic Zika virus infection. An estimated 50–80% of Zika infections are asymptomatic; when symptomatic, the illness is typically mild and self-limited. Zika is specifically characterized by a **fine, pruritic maculopapular rash**, which distinguishes it from dengue (which more often presents with petechiae and the "white islands in a sea of red" pattern).[1][2][3]
- **Fetal microcephaly**: Zika virus has a **specific neurotropism** and is causally linked to microcephaly and other CNS anomalies. The risk of congenital Zika syndrome is **greatest**

with first-trimester infection, with approximately 11% of fetuses/infants affected when exposure occurs in the first trimester.[4][5]

Why not the other options?

- **A. Dengue virus** — While also transmitted by *Aedes* mosquitoes in Brazil, dengue is **not associated with congenital microcephaly**. The pruritic rash is also more characteristic of Zika than dengue.[2][6]
- **B. Rubella virus** — The patient received all recommended childhood vaccinations, which includes MMR. Congenital rubella syndrome can cause microcephaly, but prior vaccination makes this exceedingly unlikely.
- **C. Toxoplasmosis** — Directly ruled out by **negative IgM and IgG titers**.

Would you like to explore the recommended diagnostic workup and prenatal surveillance for suspected Zika virus infection in pregnancy?

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Question 65

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?

A. Hypotonia
B. Diarrhea
C. Umbilical hernia
D. Macroglossia

https://openevidence.com/ask/1d852380-7256-419e-8943-b575d07918b8

The answer is **B. Diarrhea**.

Congenital hypothyroidism is characterized by a **hypometabolic state** that produces **constipation**, not diarrhea. Diarrhea is a manifestation of **hyperthyroidism**, in which increased gut motility accelerates gastrointestinal transit.[1] The classic clinical features of congenital hypothyroidism include all three of the other answer choices:

- **Hypotonia** — with delayed reflexes[2][3][4]
- **Umbilical hernia** — one of the most common signs[2][4][5]
- **Macroglossia** — also among the most common signs[2][4][5]

Additional expected findings include prolonged jaundice, lethargy, poor feeding, constipation, hoarse cry, large posterior fontanelle, hypothermia, bradycardia, mottled skin, and myxedematous/coarse facies.[2][4][5] The AAP guidelines specifically list **constipation** (the opposite of diarrhea) as a clinical feature that should prompt serum TSH and free T4 measurement even if newborn screening results were normal.[5]

Would you like to explore the treatment protocol and neurodevelopmental monitoring for neonates with congenital hypothyroidism?

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Question 66

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?

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

https://openevidence.com/ask/6d41fe1c-a3fc-4c62-beac-ba0070736475

The answer is **C. Natural killer cells**.[1][2][3]

The question describes the hallmark features of **NK cell-mediated "missing-self" recognition**. NK cells are innate lymphocytes that detect and lyse cells with downregulated or absent MHC class I molecules — precisely the abnormality described in these monoclonal plasma cells.[1][2] Their key distinguishing characteristic is the ability to kill target cells **spontaneously, without prior sensitization, priming, or antigen presentation**.[3][4]

Mechanism: NK cells express inhibitory receptors — primarily killer immunoglobulin-like receptors (KIRs) and CD94/NKG2A — that bind MHC class I molecules on normal cells, delivering an inhibitory signal that prevents lysis. When MHC class I is downregulated (as on these plasma cells), the inhibitory signal is lost and activating receptors (NKp46, NKp30, NKG2D) predominate, triggering cytotoxicity.[1][5][6] This is the basis of the **"missing-self" hypothesis** proposed by Kärre.[2]

Why the other options are incorrect:

- **A. Bone marrow-derived macrophages** — Macrophages rely heavily on opsonization (via Fc receptors and complement receptors) and do not selectively target MHC class I-deficient cells.
- **B. CD4+ T lymphocytes** — These are adaptive immune cells requiring antigen presentation via MHC class II and prior priming; they are not cytolytic in this context.
- **D. Band neutrophils** — Immature granulocytes involved in acute inflammation; they do not perform missing-self recognition.

Clinical relevance: NK cells play a critical role in immune surveillance of monoclonal plasma cell disorders. Early-stage myeloma cells often have low MHC class I expression, making them susceptible to NK killing, while progression to advanced disease is associated with upregulation of MHC class I and NK cell evasion.[7][8]

Would you like to explore how myeloma cells evade NK cell-mediated killing during disease progression?

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Question 67

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?

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

https://openevidence.com/ask/f5b4313b-2680-4c14-96cc-da4679135081

The correct answer is **A. Decreased acetylcholine release**.

This presentation is classic for **foodborne botulism**: GI prodrome (nausea, vomiting, diarrhea) followed by cranial nerve findings including **fixed mydriasis**, **ophthalmoplegia** (difficulty depressing the eyes), and **vertical diplopia** — in an afebrile patient who consumed homemade pickles (home-canned foods provide the anaerobic, low-acid environment for *Clostridium botulinum* spore germination and toxin production).[1][2] The concurrent illness in his friend further supports an outbreak.

Mechanism: Botulinum neurotoxin (BoNT) binds irreversibly to **presynaptic cholinergic nerve terminals** at the neuromuscular junction. The toxin's light chain acts as a zinc-dependent metalloprotease that **cleaves SNARE proteins** (SNAP-25, syntaxin, and synaptobrevin), which are essential for synaptic vesicle fusion with the presynaptic membrane. This prevents acetylcholine vesicle exocytosis, blocking neuromuscular transmission and producing **descending flaccid paralysis**.[2][3][4]

Why the other options are incorrect:

- **B. Overactivation of adenylate cyclase** — This is the mechanism of **cholera toxin** (and heat-labile enterotoxin of *E. coli*), which ADP-ribosylates the Gs alpha subunit, causing persistent cAMP elevation and secretory diarrhea.
- **C. Release of interferon-gamma** — Not relevant to this toxin-mediated syndrome.
- **D. Inhibition of GABA release** — This describes the mechanism of **tetanus toxin** (tetanospasmin), which cleaves synaptobrevin in inhibitory interneurons of the spinal cord, preventing glycine and GABA release and causing spastic paralysis — the clinical opposite of botulism.

Would you like to explore the management of foodborne botulism, including antitoxin timing and supportive care?

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Question 68

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?

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

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

This presentation is classic: a **4-week-old term infant** who appears otherwise healthy with **progressive conjugated hyperbilirubinemia** (direct bilirubin 12.3 mg/dL, comprising ~82% of total), **pale (acholic) stools**, **hepatomegaly**, and a markedly **cholestatic biochemical pattern** (ALP 2007 U/L, GGT 154 U/L) with only mildly elevated transaminases.[1] Biliary atresia is the most common cause of cholestatic jaundice in infancy (25–40% of cases), and infants with biliary

atresia characteristically **appear well and grow normally**, which often misleads parents and clinicians into attributing the jaundice to benign causes such as breast milk jaundice.[2]

Why the other choices are incorrect:

- **Breast milk jaundice (D):** Causes **unconjugated** hyperbilirubinemia only, is nonpathologic, and is **not associated with direct hyperbilirubinemia, pale stools, or elevated GGT/ALP**. The parents' assumption that switching to formula would help was incorrect — the conjugated fraction here indicates true hepatobiliary disease.[1][3]
- **Crigler–Najjar syndrome (C):** Results from deficient UDP-glucuronosyltransferase activity and causes severe **unconjugated** hyperbilirubinemia. There would be no elevation in direct bilirubin, ALP, or GGT.
- **Galactosemia (A):** Can cause neonatal cholestasis, but affected infants typically appear **acutely ill** with vomiting, poor feeding, hepatic dysfunction, cataracts, and susceptibility to E. coli sepsis — not the well-appearing infant described here.[2]

The **elevated GGT** is a particularly useful distinguishing feature, as it tends to be higher in biliary atresia than in most other causes of neonatal cholestasis.[1] Timely diagnosis is critical because **Kasai portoenterostomy performed before 30 days of life** yields the best chance of delaying or preventing the need for liver transplantation.[4]

Would you like to explore the diagnostic workup and optimal surgical timing for biliary atresia?

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Question 69

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?

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

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

This patient presents with classic **post-thyroidectomy hypocalcemia** due to hypoparathyroidism — the most common complication of total thyroidectomy, typically peaking **48–72 hours** after surgery.[1][2] The constellation of **perioral numbness, nausea, diarrhea**, and a **positive Trousseau sign** (carpal spasm during blood pressure cuff inflation) is pathognomonic for hypocalcemia-induced neuromuscular excitability.[3][4]

Why QT prolongation (B) is correct

Hypocalcemia prolongs the QT interval primarily by **lengthening the ST segment**, without affecting the QRS complex or T-wave morphology.[5] Lower extracellular calcium delays calcium-dependent inactivation of the L-type calcium channel, prolonging ventricular repolarization.[6] In a study of chronic hypoparathyroidism patients, **13.6% had prolonged QTc**, with a significant inverse correlation between QTc and serum calcium ($r = -0.43$); for every 1 mg/dL decrease in calcium, QTc increased by ~13 ms.[7]

Why the other options are less likely

- **A. Torsade de pointes** — While QT prolongation from hypocalcemia can theoretically lead to torsade de pointes, this association is **rare** compared to hypokalemia or

hypomagnesemia. QT prolongation is the expected and far more common ECG finding in this setting.[5][8]

- **C. Peaked T waves** — This is the hallmark of **hyperkalemia**, not hypocalcemia.
- **D. PR prolongation** — Associated with first-degree AV block (e.g., from hyperkalemia, digoxin, or conduction disease), not a typical feature of hypocalcemia.

Would you like to explore the management protocol for post-thyroidectomy hypocalcemia?

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Question 70

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?

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

https://openevidence.com/ask/fbb2a973-1cb4-4a23-ad66-943abaaa91e5

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

This patient presents with the **classic triad of acute diverticulitis**: **left lower quadrant pain, fever, and leukocytosis**.[1][2][3] Key features supporting this diagnosis include:

- **Age >65 years**, a major risk factor for diverticular disease[1]
- **Crampy LLQ pain worsening with defecation**, consistent with sigmoid colon inflammation — approximately 70% of patients with acute diverticulitis present with LLQ pain[1]

- **Low-grade fever** (37.8°C) and **tachycardia** (102/min), both characteristic findings (tachycardia occurs in ~27% of cases)[1]
- **Leukocytosis with a left shift** (WBC 16,000, 89% neutrophils, 5% bands), indicating an acute inflammatory/infectious process
- **Chronic constipation**, which is present in approximately 50% of patients with diverticulitis and is a risk factor for diverticular disease[4]

Why the other options are less likely:

- **Hypothyroidism (B):** Can cause constipation but does not produce acute LLQ pain, fever, or marked leukocytosis with neutrophilia.
- **Adenocarcinoma of the colon (C):** Typically presents more insidiously with weight loss, iron-deficiency anemia, or occult blood — this patient denies weight change and has normal hemoglobin. Acute leukocytosis with left shift and fever would be atypical as the primary presentation of colon cancer.[5]
- **Irritable bowel syndrome (D):** A functional disorder that does not cause fever, leukocytosis, or localized tenderness on exam.[3]

Has this patient had a prior CT-confirmed episode of diverticulitis, or would this be a first presentation requiring confirmatory imaging?

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Question 71

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?

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

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The 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 bone disorder (CKD-MBD) with secondary hyperparathyroidism**, also known as renal osteodystrophy. The expected laboratory profile follows directly from the pathophysiology of progressive renal failure:[1][2]

1. **Decreased calcitriol** — Declining renal mass reduces 1-alpha hydroxylase activity, impairing conversion of 25-hydroxyvitamin D to 1,25-dihydroxyvitamin D (calcitriol). This is one of the earliest detectable abnormalities, beginning as early as CKD stage 2.[2]

2. **Increased phosphate** — As GFR falls, renal phosphate excretion becomes inadequate, leading to hyperphosphatemia. Retained phosphate further inhibits 1-alpha hydroxylase.[1][3]

3. **Decreased calcium** — Calcitriol deficiency reduces intestinal calcium absorption, causing hypocalcemia. Hyperphosphatemia also directly lowers ionized calcium through calcium-phosphate complexation.[1][4]

4. **Increased PTH** — The combination of hypocalcemia, hyperphosphatemia, and decreased calcitriol all independently stimulate parathyroid hormone secretion, producing **secondary hyperparathyroidism**.[1][2][5]

The elevated PTH drives increased osteoclast-mediated bone resorption (high-turnover bone disease/osteitis fibrosa), which accounts for this patient's **bone pain**.[4][6] This constellation —

high PTH, low calcium, high phosphate, low calcitriol — is the classic biochemical signature of CKD-MBD.

Why the other options are incorrect:

- **B** (decreased PTH, increased calcium) — This pattern suggests hypoparathyroidism or vitamin D toxicity, not CKD.
- **C** (decreased PTH) — Low PTH would not be expected; the hypocalcemia and hyperphosphatemia of CKD stimulate, rather than suppress, PTH secretion.
- **D** (all normal) — A patient with CKD severe enough to cause bone pain would have significant mineral metabolism derangements.

Would you like to explore the current guideline-based management of secondary hyperparathyroidism in CKD?

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Question 72

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?

A. Partially occluded coronary artery
B. Umbilical hernia
C. Gastroesophageal junction incompetence
D. Intestinal metaplasia at the gastroesophageal junction

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

This patient's presentation is classic for **gastroesophageal reflux disease (GERD)**: chest pain worsened by **large meals and spicy foods**, relieved by **calcium carbonate** (an antacid), with a **normal ECG** and no exertional dyspnea.[1][2] The underlying pathophysiology of GERD is dysfunction of the antireflux barrier at the gastroesophageal junction — specifically, **incompetence of the lower esophageal sphincter (LES)** — which allows retrograde flow of acidic gastric contents into the esophagus.[2][3][4]

Why the other answers are incorrect:

- **A. Partially occluded coronary artery** — Coronary artery disease can cause chest pain, and the family history (father dying of MI at 62) is notable. However, the symptom pattern — provocation by food and spice, relief with antacids, no exertional component, and a normal ECG — points away from ischemia.[1]
- **B. Umbilical hernia** — An umbilical hernia presents as a periumbilical bulge and would not cause chest pain with the described features.
- **D. Intestinal metaplasia at the gastroesophageal junction** — This describes **Barrett's esophagus**, a complication of chronic GERD in which squamous epithelium is replaced by specialized intestinal-type columnar epithelium. Barrett's esophagus itself is typically asymptomatic and is not the *cause* of reflux symptoms — rather, it is a consequence of prolonged acid exposure from GEJ incompetence.[2][5]

The key distinction between C and D is that **GEJ incompetence is the mechanism causing reflux symptoms**, whereas intestinal metaplasia is a downstream histologic consequence of chronic reflux that does not independently produce pain.

Would you like to explore when endoscopy is indicated versus empiric acid suppression in GERD?

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Question 73

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?

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

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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 (MNE)** — isolated nighttime bedwetting without daytime lower urinary tract symptoms in a child who has never achieved a sustained dry period of ≥6 months.[1] The normal neurologic exam, normal urinalysis, negative urine culture, and **concentrated first-morning urine (specific gravity 1.035)** effectively exclude structural, infectious, and concentrating-defect etiologies (such as diabetes insipidus).

Why an enuresis alarm is first-line:

- Per AAFP, ICCS, EAU-ESPU, and AAP guidelines, **enuresis alarms and desmopressin** are the recommended first-line interventional therapies after behavioral modification. Alarms are typically offered in children **older than 6 years** and are most effective when family motivation is high.[1][2][3]

- Alarms provide a **higher sustained cure rate** and **lower relapse rate** than desmopressin (relapse: 46% vs. 65%). A Cochrane review found approximately two-thirds of children became dry with alarm therapy.[1][4][5]
- Parental reassurance is essential — approximately **14% of children** have spontaneous resolution annually, and families should understand bedwetting is not the child's fault.[1]

Why the other options are incorrect:

- **A. MRI of the spine** — Not indicated. There are no neurologic abnormalities, no daytime incontinence, and no lower-extremity findings to suggest spinal pathology such as tethered cord.
- **C. Oral oxybutynin** — **Not recommended as monotherapy** for MNE. It may be used adjunctively with desmopressin in refractory cases, particularly with reduced bladder capacity, but only after first-line therapies have failed.[1][6]
- **D. Oral imipramine** — A **second-line agent** reserved for cases refractory to alarms and desmopressin. It carries significant adverse effects including **cardiotoxicity**, requiring ECG screening before initiation.[1]

Would you like to explore how management differs when nocturnal enuresis is nonmonosymptomatic?

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Question 74

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?

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

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

Vincristine is a vinca alkaloid that **binds to the β-subunit of tubulin heterodimers, preventing their polymerization into microtubules**.[1] This causes cytoskeletal disorganization and microtubule disorientation within axons, inhibiting vesicle-mediated axonal transport and leading to axonal degeneration — a process termed **"dying back" neuropathy**.[1][2] The FDA label for vincristine states that its mechanism of action is related to inhibition of microtubule formation in the mitotic spindle, resulting in metaphase arrest.[3]

The clinical presentation described — **distal symmetric sensory loss with decreased deep tendon reflexes** — is characteristic of vincristine-induced peripheral neuropathy, which is the most common dose-limiting toxicity of this agent.[3][4] The neuropathy is length-dependent, initially sensory (paresthesias, numbness), with motor involvement occurring later with continued treatment.[2][3]

Why the other options are incorrect:

- **B (Free radicals unwinding DNA)** — Describes the mechanism of **bleomycin**, which generates reactive oxygen species that cause DNA strand breaks.
- **C (Inhibition of dihydrofolate reductase)** — This is the mechanism of **methotrexate**, which blocks folate metabolism and nucleotide synthesis.

- **D (Incorporation of false pyrimidine analogues)** — Describes antimetabolites such as **5-fluorouracil** or **cytarabine**, which are incorporated into DNA/RNA as fraudulent nucleotides.

Would you like to explore prevention and management strategies for vincristine-induced peripheral neuropathy?

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Question 75

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?

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

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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)**: a healthy adolescent with short stature, **delayed bone age** (11 years at chronologic age 14), a **family history** of late growth (father was short as a teenager but reached normal adult height of 177 cm), and **early pubertal development already underway** (Tanner stage 2 breasts).[1][2][3] CDGP is the most common cause of short stature and delayed puberty, accounting for over 60% of cases, and often follows an autosomal dominant inheritance pattern.[2][4][5] The absent pubic and axillary hair reflects delayed adrenarche, which commonly accompanies CDGP.

The delayed bone age indicates significant remaining growth potential, and as puberty progresses, catch-up growth is expected, though serial monitoring of growth velocity and pubertal progression is important to confirm this trajectory.[1][2]

> "If puberty has started, clinically or biochemically, and stature is not a major concern, reassurance with realistic adult height prediction is frequently sufficient."
>
> —Mark R. Palmert, M.D., Ph.D. et al., Hospital for Sick Children and other institutions. Delayed Puberty. N Engl J Med. February 02, 2012.

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Why not the other options:

- **A. Pelvic ultrasound** — While Turner syndrome should be considered in girls with short stature, a pelvic ultrasound does not diagnose it (karyotype does), and the clinical picture here strongly favors CDGP. Turner syndrome remains a consideration but does not make ultrasound the best next step among these choices.
- **B. DHEA-S levels** — The absent pubic/axillary hair is consistent with delayed adrenarche in the setting of CDGP and does not require specific hormonal workup as the next step.
- **D. MRI of the brain** — Brain MRI is indicated when there is concern for CNS pathology (e.g., neurologic symptoms, multiple pituitary deficits, or failure to progress through puberty as expected). In a patient with begun pubertal development, positive family history, and classic CDGP features, MRI is not warranted initially.[1]

Would you like to explore how to distinguish constitutional delay from permanent hypogonadotropic hypogonadism?

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Question 76

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?

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

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

This patient meets **DSM-5 criteria for kleptomania**: recurrent failure to resist impulses to steal objects not needed for personal use or monetary value, pleasure/relief at the time of the theft, subsequent guilt and shame, and inability to stop despite the desire to do so.[1] The stolen items are trivial, discarded afterward, and the stealing is not motivated by anger, vengeance, or monetary gain.[1]

CBT is the first-line psychotherapeutic intervention for kleptomania.[2] Techniques commonly employed include covert sensitization, imaginal desensitization, and exposure and response prevention (ERP), which has shown treatment response in kleptomania.[3][4] Pharmacological agents — particularly **naltrexone** (which has RCT evidence supporting efficacy in reducing stealing urges and behavior) and SSRIs — are used as adjuvants to CBT or when psychotherapy alone is insufficient.[2][5]

Why not the other options:

- **A. Lithium** — A mood stabilizer primarily indicated for bipolar disorder. It has no established role in kleptomania management.
- **B. Interpersonal therapy** — Designed for depression and focuses on interpersonal relationships; it does not target the impulse control mechanisms underlying kleptomania.
- **C. Psychodynamic psychotherapy** — While historically applied to kleptomania, it lacks demonstrated efficacy and is not recommended as first-line treatment. The shift over the past century has been away from psychodynamic approaches toward CBT and pharmacotherapy.[2]

Would you like to explore the evidence for naltrexone as pharmacotherapy for kleptomania?

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Question 77

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?

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

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B. Frontotemporal dementia — specifically the behavioral variant (bvFTD). The defining feature is that **early, prominent change in personality and social conduct preceded the cognitive decline**: disinhibition with foul language and grabbing strangers, inappropriate laughter reflecting impaired social cognition and loss of empathy, with memory impairment, word-finding difficulty, inattention, and loss of self-care emerging later.[1][2] Peak prevalence is in the seventh decade, matching this patient's age.[3]

Why bvFTD fits

- **Diagnostic criteria**: possible bvFTD requires 3 of 6 discriminating features — disinhibition, apathy/inertia, loss of sympathy/empathy, perseverative or compulsive behavior, hyperorality, and a dysexecutive neuropsychological profile with relatively spared memory and visuospatial function. This patient demonstrates disinhibition, loss of social awareness/empathy, and executive-attentional dysfunction.[2]
- **Disinhibition phenotype**: tactless, socially inappropriate behavior including approaching strangers without respect for physical boundaries, embarrassing personal remarks, and new criminal or sexually inappropriate behaviors is the classic early presentation.[1]

- **Language and attention**: naming deficits, reduced single-word comprehension, and diminished spontaneous speech are common in bvFTD, present in roughly 60% of cases.[4]

Why not the others

- **Alzheimer dementia (A)**: onset is typically amnestic, with episodic memory and visuospatial deficits preceding behavioral change; frontal behavioral features appear later. A behavioral-predominant AD variant does exist and accounts for 7–20% of clinically diagnosed bvFTD at autopsy, but in that variant cognitive symptoms usually pre-date behavioral change and apathy predominates over disinhibition.[5][6][7]
- **Klüver-Bucy syndrome (C)**: requires the characteristic cluster of hyperorality, hypersexuality, hyperphagia, placidity, visual agnosia, and hypermetamorphosis, usually from bilateral temporal lobe pathology (CNS infection 27%, TBI 14%, autoimmune 12%). Isolated grabbing behavior without hyperorality, placidity, or visual agnosia does not meet even partial criteria. Note that advanced FTD can secondarily produce KBS-like features.[8]
- **Vascular dementia (D)**: the isolated BP of 162/103 mmHg is a distractor. VaD characteristically shows stepwise decline with focal neurologic deficits and imaging evidence of cerebrovascular disease, absent here; the described course is insidiously progressive.[6]

Confirmatory evaluation

MRI showing frontal and anterior temporal atrophy, often asymmetric, supports probable bvFTD, and FDG-PET may show frontotemporal hypometabolism — though structural MRI can lack sensitivity early and FDG-PET lacks specificity.[3][9] Amyloid and tau biomarkers distinguish bvFTD from behavioral-variant AD.[7] Because the reported course is only a few months, secondary and rapidly progressive causes (medication/toxic effects, metabolic derangement, subdural hematoma or other structural lesion, autoimmune encephalitis, prion disease) warrant exclusion before a neurodegenerative label is applied.

Would you like to explore the role of neurofilament light chain in separating bvFTD from primary psychiatric disorders?

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Question 78

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?

A. Levofloxacin
B. Trimethoprim/sulfamethoxazole
C. Amoxicillin
D. Rifampin

https://openevidence.com/ask/e0839144-1bb3-4805-8365-44cc9e2a3c63

The answer is **A. Levofloxacin**.

This presentation is classic for **Legionnaires' disease** (*Legionella pneumophila* pneumonia). The key diagnostic clues include:

- **Dry cough** with bilateral patchy infiltrates (atypical pneumonia pattern)
- **Watery diarrhea** — present in 19–47% of cases[1]

- **Hyponatremia** (Na^+ 131 mEq/L) — occurs more frequently in Legionnaires' disease than in other pneumonias[2][3]
- **Relative bradycardia** (pulse 65/min despite fever)[1][4]
- **Low-grade fever** with a subacute 6-day course

A classic clinical prediction framework suggests that a combination of **dry cough, diarrhea, and hyponatremia** in a patient with pneumonia is strongly suggestive of Legionnaires' disease.[5]

Why levofloxacin? *Legionella* is an **intracellular pathogen**, so effective antibiotics must achieve high intracellular concentrations within macrophages. **Fluoroquinolones** (levofloxacin) and **macrolides** (azithromycin) are first-line therapy.[1][6] Beta-lactams such as amoxicillin (option C) are ineffective against Legionella.[1] The IDSA recommends **levofloxacin 750 mg daily** for 5–14 days.[1][6]

Why not the other options?

- **Trimethoprim/sulfamethoxazole (B)** — not a recommended agent for Legionella pneumonia
- **Amoxicillin (C)** — a beta-lactam; ineffective because it does not penetrate intracellularly[1]
- **Rifampin (D)** — has in vitro activity against Legionella but is used only as **adjunctive therapy** in combination with a fluoroquinolone or macrolide in severe cases, never as monotherapy[2][7]

Would you like to explore the diagnostic workup for Legionella pneumonia, including urinary antigen testing and its limitations?

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Question 79

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?

A. Chocolate cysts
B. Corpus luteum cysts
C. Yolk sac tumor
D. Theca leutein cysts

https://openevidence.com/ask/7bd47489-d53a-446b-b368-91a9ff110a16

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

The ultrasound findings describe a **complete hydatidiform mole** — an intrauterine heteroechoic mass with numerous anechoic spaces (the classic "bunch of grapes" or vesicular pattern) and absence of fetal tissue or amniotic fluid.[1][2][3] Complete moles are characterized by marked trophoblastic proliferation producing **very high serum β-hCG levels** (often >100,000 IU/L).[4][5]

Theca lutein cysts result from **ovarian hyperstimulation by markedly elevated circulating hCG**.[5][6] They present as bilateral, enlarged, multiloculated, thin-walled cysts — exactly as described in this vignette. They are reported in **20–46% of patients with complete moles** depending on whether detection is clinical or sonographic.[5][7] Theca lutein cysts typically regress spontaneously after molar evacuation as hCG levels normalize, though they may persist for weeks even after hCG regression.[8]

Why the other options are incorrect:

- **A. Chocolate cysts (endometriomas)** — These are thick-walled cysts containing old hemorrhagic material ("ground glass" echogenicity on ultrasound), associated with endometriosis, not with molar pregnancy.
- **B. Corpus luteum cysts** — These are typically unilateral, single, thick-walled cysts with internal hemorrhage, arising from a single ovulatory follicle. They do not present as bilateral, multiple, thin-walled septated cysts.

- **C. Yolk sac tumor** — This is a malignant ovarian germ cell tumor that produces AFP (not hCG-driven) and presents as a solid-cystic mass, typically unilateral. It does not produce the bilateral multicystic ovarian enlargement described here.

Would you like to explore post-evacuation hCG surveillance and risk stratification for gestational trophoblastic neoplasia?

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Question 80

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?

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

https://openevidence.com/ask/97bfd23d-f660-4786-9a66-2c4375d20bcf

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

The virus described — **helical capsid, segmented genome**, causing fever, headache, malaise, and dry cough spreading through a household — is **influenza**. Influenza viruses possess a helical ribonucleoprotein complex and 8 segments of negative-sense single-stranded RNA.[1]

Anti-hemagglutinin (anti-HA) antibodies are the primary established correlate of protection against influenza. These antibodies prevent viral attachment and entry into host cells by neutralizing the HA surface glycoprotein.[2] The son most likely has pre-existing serum anti-HA antibodies from prior vaccination or natural infection, accounting for his lack of symptoms despite household exposure. An HAI titer ≥1:40 is generally regarded as conferring meaningful protection.[2][3]

The other options can be eliminated based on the viral identity:

- **B. Downregulation of ICAM-1 expression** — ICAM-1 is the receptor for **major-group rhinoviruses**, not influenza. Rhinoviruses have an icosahedral (not helical) capsid and a non-segmented genome.[4][5]
- **C. Protease-resistant antibodies in nasal secretions** — This refers to **secretory IgA**, which does contribute to mucosal defense against influenza. However, serum anti-HA antibodies

remain the most well-established and widely accepted correlate of protection, making A the stronger answer.[2]

- **D. Homozygous CCR5 mutation** — The CCR5Δ32 mutation confers resistance to **macrophage-tropic HIV-1**, not influenza.[6]

Would you like to explore how influenza antigenic drift and shift affect vaccine effectiveness?

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Question 81

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?

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

https://openevidence.com/ask/a404d67c-753b-4421-9bab-6cad35a63e62

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

A prior suicide attempt is consistently identified as the single strongest risk factor for completed suicide. This patient deliberately overdosed on sleeping pills three years ago, which constitutes a clear prior attempt. Multiple authoritative sources converge on this:

> "Suicide attempts are the most powerful known risk factor for completed suicide. During the first year after a suicide attempt, the risk for completed suicide varies from 0.8% to 3.0% for men and from 0.3% to 1.9% for women."
>
> —Mark Olfson, MD, MPH et al., Department of Psychiatry, College of Physicians and Surgeons, Columbia University, New York, New York and other institutions. National Trends in Suicide Attempts Among Adults in the United States. JAMA Psychiatry. November 01, 2017.
>
> Used under license from JAMA Network.

A Lancet review similarly states that "in most studies of risk factors for suicide, a history of self-harm or suicide attempts is the strongest factor, present in at least 40% of cases".[2] The DSM-5 identifies "a past history of suicide attempts or threats" as the most consistently described risk

factor for suicide in major depressive disorder.[3] Risk following a suicide attempt persists for decades, though it is greatest in the first 1–2 years.[4][5]

Why not the other options:

- **B. History of psychosis** — Psychotic features do increase suicide risk (HR elevated in long-term follow-up), and psychotic disorders approximately double the mortality rate compared with non-psychotic conditions. However, psychosis is a weaker predictor than a prior attempt.[5][6]
- **C. Sleeping disorder** — Sleep disturbances are a recognized risk factor and may increase suicidal ideation independent of depression, but carry a weaker association than a prior attempt.[7]
- **D. Age** — Older age (particularly elderly white males) is associated with higher completed suicide rates, but again is a lesser predictor than a documented prior attempt.[8]

This patient carries a notably high-risk profile overall: prior attempt, older male, living alone, bereavement, psychotic depression, sleep disturbance, and access to lethal means at a hunting club. However, among the four options listed, the **previous suicide attempt** stands as the strongest individual risk factor.

Would you like to explore evidence-based interventions for reducing suicide risk in patients with a prior attempt?

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Question 82

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?

A. Glycopyrrolate
B. Benztropine
C. Levodopa
D. Dantrolene

https://openevidence.com/ask/dcfdcaa4-884c-4cca-ade0-ca4872696504

The answer is **B. Benztropine**.

This presentation is classic for an **acute dystonic reaction** — specifically **cervical dystonia (torticollis)** — caused by an antipsychotic medication. The key features supporting this diagnosis include:

- **Young male** with schizophrenia on an antipsychotic (the unnamed medication)
- **Acute onset** of involuntary neck flexion and rotation, with contracted sternocleidomastoid and trapezius
- **Temporal relationship**: symptoms began approximately one hour after taking an extra dose of his antipsychotic for auditory hallucinations

Acute dystonic reactions are more common in **young men**, develop rapidly after drug dosing (especially with dose increases), and characteristically involve the neck, jaw, or arms.[1][2] The

clinical features include cervical and truncal dystonia, oculogyric crisis, blepharospasm, and oromandibular dystonia.[2]

Why benztropine?

Anticholinergic medications (benztropine or diphenhydramine) are the standard treatment, producing relief within minutes when given IV or IM.[2][3] The FDA-approved indication for benztropine includes **control of extrapyramidal disorders due to neuroleptic drugs**, with a recommended dose of **1–2 mg IM/IV for acute dystonic reactions**.[4]

Why not the other options?

- **A. Glycopyrrolate** — a peripheral anticholinergic that does not cross the blood-brain barrier, so it cannot treat central dystonic reactions.
- **C. Levodopa** — used for Parkinson disease, not for acute drug-induced dystonia.
- **D. Dantrolene** — a direct-acting skeletal muscle relaxant used for **neuroleptic malignant syndrome (NMS)** and malignant hyperthermia. This patient lacks the hallmarks of NMS (high fever, severe rigidity, altered mental status, markedly elevated CK). The low-grade temperature, tachycardia, and diaphoresis here are attributable to anxiety and the dystonic reaction itself.

Would you like to explore risk factors and prophylactic strategies to prevent recurrent acute dystonic reactions from antipsychotics?

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Question 83

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?

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

https://openevidence.com/ask/d2780b6e-d785-4de1-9a43-3e305cf77f31

The answer is **B. Bartter's syndrome**.

This presentation — **hypokalemia, normal blood pressure despite hyperreninemia and hyperaldosteronism, hypercalciuria, polyuria, polydipsia, failure to thrive, and constipation** — is classic for Bartter syndrome. Bartter syndrome is a salt-wasting tubulopathy caused by defective sodium-potassium-chloride reabsorption in the thick ascending limb of the loop of Henle, characterized by hypokalemic hypochloremic metabolic alkalosis, elevated plasma renin activity and aldosterone, yet **normal or low blood pressure**.[1][2][3]

Why not the other options:

- **Gitelman syndrome (D):** Also presents with hypokalemic metabolic alkalosis and hyperreninemic hyperaldosteronism, but is distinguished from Bartter syndrome by **hypocalciuria** (not hypercalciuria) and **hypomagnesemia**. Gitelman syndrome also typically presents **later in life** (school age or adulthood), often with tetany or muscle cramps rather than failure to thrive.[4][5][6]
- **Renal artery stenosis (A):** Causes secondary hyperaldosteronism but is associated with **hypertension**, which is absent here.[2]
- **Pheochromocytoma (C):** Presents with episodic **hypertension**, tachycardia, headache, and diaphoresis — none of which are present in this patient.

The **elevated urinary calcium excretion** is the critical distinguishing feature in this case: Bartter syndrome causes calcium wasting (hypercalciuria) due to impaired paracellular calcium reabsorption in the thick ascending limb, whereas Gitelman syndrome is characterized by hypocalciuria.[5][6]

Would you like to explore the treatment approach and long-term prognosis for pediatric Bartter syndrome?

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Question 84

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?

A. Gastric carcinoma
B. Non-Hodgkin lymphoma
C. Invasive ductal carcinoma of the breast
D. Adenocarcinoma of the lung

https://openevidence.com/ask/29b32ccd-f7cc-4cc3-9774-1ee83c633e51

The answer is **B. Non-Hodgkin lymphoma**.

This patient's presentation — severe xerostomia, xerophthalmia, bilateral parotid gland tenderness, and high-titer **anti-Ro (SSA) and anti-La (SSB) antibodies** — is classic for **primary Sjögren syndrome**. The most serious long-term complication of this disease is the development of **non-Hodgkin lymphoma (NHL)**, particularly **B-cell subtypes**.

The risk of B-cell lymphoma is **15- to 20-fold higher** in patients with primary Sjögren syndrome compared to the general population, with a lifetime risk of **5–10%**.[1] This is the highest lymphoma risk among all autoimmune diseases.[2] Approximately 98% of Sjögren-associated lymphomas originate from B cells, and over 90% are **mucosa-associated lymphoid tissue (MALT) lymphoma** or **diffuse large B-cell lymphoma**.[2] MALT lymphomas most commonly arise in the salivary glands, the primary extranodal site in ~70% of cases.[1][2]

This patient has several features that further increase her lymphoma risk, including **parotid gland enlargement** and **positive anti-Ro/SSA and anti-La/SSB antibodies**, both of which have been identified as independent predictors of NHL development in Sjögren syndrome.[2][3] A 40-

year cohort study found lymphoma in 9.9% of Sjögren patients, with parotid swelling carrying a relative risk of 5.53 for lymphoma.[3]

The chronic B-cell activation central to Sjögren pathogenesis drives the lymphomagenesis process: persistent antigen stimulation leads to polyclonal B-cell expansion, with subsequent acquisition of driver mutations promoting monoclonal proliferation and malignant transformation.[2][4]

The other answer choices — gastric carcinoma, invasive ductal carcinoma of the breast, and adenocarcinoma of the lung — are not strongly associated with Sjögren syndrome.

Would you like to explore recommended surveillance strategies for lymphoma risk in Sjögren syndrome?

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Question 85

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?

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

https://openevidence.com/ask/f3c6cea3-5824-4787-a171-a3aea5dcbe87

The correct answer is **C. Linear IgG staining on immunofluorescence**.

This patient presents with a classic **pulmonary-renal syndrome** — hemoptysis, dyspnea, and dark urine (hematuria) — with positive anti-GBM serologies, establishing a diagnosis of **anti-GBM disease (Goodpasture syndrome)**. The hallmark histopathologic finding is **intense, diffuse linear deposition of polyclonal IgG along the glomerular basement membrane** on immunofluorescence microscopy.[1][2] This pattern is essentially pathognomonic and distinguishes anti-GBM disease from immune-complex glomerulonephritis (which shows granular deposits) and pauci-immune GN (negative to trace staining).[1] The KDIGO guidelines confirm that in patients with negative serologies, diagnosis can still be established by kidney biopsy demonstrating linear IgG deposition.[3]

The other answer choices are specific to different conditions:

- **A. Granulomatous inflammation and necrotizing vasculitis** — characteristic of **granulomatosis with polyangiitis (GPA)**, an ANCA-associated vasculitis, not anti-GBM disease.
- **B. Positive cryoglobulins** — associated with **cryoglobulinemic vasculitis**, often linked to hepatitis C infection.

- **D. Longitudinal splitting and thickening of the GBM** — the classic "basket-weave" pattern seen on electron microscopy in **Alport syndrome**, a hereditary type IV collagen disorder.

Notably, this patient's heavy smoking history is a recognized risk factor for the pulmonary manifestations of Goodpasture syndrome, as smoking is thought to increase alveolar capillary permeability and expose the alveolar basement membrane to circulating anti-GBM antibodies.[3]

Would you like to explore the current treatment protocol for anti-GBM disease?

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Question 86

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?

A. Positive latex agglutination test
B. Positive PCR for HSV-2 DNA
C. Presence of tachyzoites
D. Increased adenosine deaminase concentration

https://openevidence.com/ask/cd0f49e2-0f6d-4192-ab6c-81c0139e5ce4

The answer is **A. Positive latex agglutination test**.

This presentation — an **HIV-positive patient with subacute meningitis, elevated CSF opening pressure (32 cm H2O), and a pathogen that grows on Sabouraud agar** — is classic for **cryptococcal meningitis** caused by *Cryptococcus neoformans*. Sabouraud dextrose agar is a fungal culture medium, and visible *Cryptococcus* colonies typically appear within 7 days.[1] The **latex agglutination test detects cryptococcal antigen (CrAg)** in CSF with sensitivity exceeding 90% in HIV-associated cryptococcal meningitis.[2][3]

Supporting this diagnosis:

- **Elevated opening pressure** (≥25 cm H_2O) is present in **60–80% of HIV-associated cryptococcal meningitis** cases.[1][4]
- The **subacute course** (2-week progressive headache, vomiting, fever, meningismus) is characteristic.[5]
- CSF typically shows mildly elevated protein, low-to-normal glucose, and variable lymphocytic pleocytosis.[1][3]

The other options are incorrect because:

- **B (PCR for HSV-2 DNA):** HSV-2 meningitis is viral and would not grow on Sabouraud agar.
- **C (Tachyzoites):** *Toxoplasma gondii* causes ring-enhancing brain abscesses in HIV, not meningitis, and is not cultured on Sabouraud agar.
- **D (Increased adenosine deaminase):** Elevated ADA suggests **tuberculous meningitis**; *Mycobacterium tuberculosis* is a bacterium that does not grow on Sabouraud agar.

Would you like to explore the recommended induction treatment regimen for HIV-associated cryptococcal meningitis?

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Question 87

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?

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

https://openevidence.com/ask/b708e310-b483-45d9-8751-2ac277bfff74

The answer is **A. Viral reactivation in dorsal root ganglia**.

This presentation is classic for **herpes zoster (shingles)**: a 70-year-old woman with burning pain followed by a unilateral, dermatomal vesicular rash with erythema and crusting extending from the back to below the right breast (consistent with a thoracic dermatome). The underlying mechanism is **reactivation of latent varicella-zoster virus (VZV) from dorsal root ganglia**.[1]

Primary VZV infection (chickenpox) seeds multiple sensory ganglia, where the virus establishes lifelong latency. With advancing age and the normal decline in VZV-specific T-cell immunity, the virus reactivates within a single dorsal root ganglion, replicates, and spreads along the sensory nerve to the corresponding dermatome, producing the characteristic unilateral vesicular eruption that does not cross the midline.[1][2] The thoracic dermatomes are the most commonly affected, accounting for up to 50% of cases.[3]

Key features distinguishing this from the other choices:

- **IgA deposits in the upper dermis (B)** would suggest dermatitis herpetiformis, which presents with intensely pruritic papulovesicles symmetrically distributed on extensor surfaces, not a unilateral dermatomal pattern.
- **Bacterial lymphatic infection (C)** describes erysipelas/cellulitis, which presents with a well-demarcated, warm, erythematous plaque — not vesicles in a dermatomal band.
- **Bloodsucking parasite infestation (D)** (e.g., scabies, pediculosis) does not produce dermatomal vesicular eruptions with preceding neuropathic pain.

Would you like to explore current guidelines on antiviral treatment timing and postherpetic neuralgia prevention for herpes zoster?

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Question 88

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?

A. Berylliosis
B. Silicosis
C. Asbestosis
D. Talcosis

https://openevidence.com/ask/e6d45728-7827-4bf3-a36f-2d6196518743

B. Silicosis.

The combination of **20 years of glass manufacturing work** (silica-containing raw materials), **progressive exertional dyspnea**, **bilateral reticulonodular interstitial fibrosis**, and **eggshell calcification of hilar/mediastinal lymph nodes** is characteristic of chronic silicosis.[1][2] Classic chronic silicosis typically follows low-to-moderate silica exposure over 20 or more years, and eggshell calcification of enlarged hilar nodes is the near-signature radiographic finding.[2]

Why the others are less likely

- **Berylliosis** — beryllium exposure occurs in aerospace, electronics, nuclear, and ceramics work. Chronic beryllium disease is a granulomatous process that radiographically and physiologically mimics sarcoidosis, and eggshell nodal calcification is not a defining feature.[3][4]
- **Asbestosis** — arises from shipbuilding, insulation, construction, and demolition. Imaging shows small irregular/linear opacities with lower-zone and subpleural predominance plus pleural plaques, resembling UIP rather than upper-zone nodularity with calcified nodes.[3][5]

- **Talcosis** — occurs with talc mining/milling or IV drug use; CT shows small centrilobular and subpleural nodules or conglomerate masses containing high-attenuation foci of talc deposition, without eggshell adenopathy.[3]

Caveats worth noting

Eggshell calcification is suggestive but not pathognomonic — it is also described in sarcoidosis, irradiated Hodgkin lymphoma, scleroderma, amyloidosis, histoplasmosis, and blastomycosis, and in coal workers' pneumoconiosis.[1][3] Diagnosis of silicosis rests on adequate documented exposure, compatible radiographic findings, and exclusion of mimics; HRCT is more sensitive than plain film.[1][2]

Clinically, this patient warrants **screening for tuberculosis and nontuberculous mycobacterial infection** (silicosis substantially increases susceptibility), spirometry with DLCO, removal from further exposure, and surveillance for progressive massive fibrosis and lung cancer — silica is an established lung carcinogen.[2]

Would you like to explore TB screening and latent infection treatment in patients with silicosis?

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Question 89

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?

A. Atrial fibrillation
B. Constrictive pericarditis
C. Takotsubo cardiomyopathy
D. Restrictive cardiomyopathy

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The correct answer is **C. Takotsubo cardiomyopathy**.

This presentation is classic for **Takotsubo syndrome (stress cardiomyopathy)**: a woman presenting with **acute chest pain following intense emotional stress** (bereavement), with signs of **acute heart failure** (S3 gallop, bilateral rales), and echocardiographic evidence of **left ventricular dysfunction** (enlarged LV and LA).[1][2]

Key features supporting the diagnosis:

- **Emotional trigger**: Bereavement is specifically cited as a classic precipitant of Takotsubo syndrome. The condition is driven by catecholamine-mediated cardiotoxicity in the setting of intense sympathetic activation.[1][2][3][4]
- **Acute heart failure findings**: S3 and bilateral rales reflect the transient LV systolic dysfunction characteristic of the syndrome.[1][5]
- **Enlarged LV/LA on echocardiography**: Consistent with acute LV dysfunction and elevated filling pressures seen in Takotsubo.[5][6]

- **Normal ECG**: While ECG changes (ST elevation, T-wave inversion, QTc prolongation) are common, the InterTAK diagnostic criteria explicitly acknowledge that **rare cases exist without any ECG changes**.[5]

Why the other options are incorrect:

- **A. Atrial fibrillation** — The heart rate is described as "regular," which excludes AF. AF also would not explain acute LV dysfunction after emotional stress.
- **B. Constrictive pericarditis** — This is a chronic condition with pericardial thickening causing impaired diastolic filling, not an acute stress-triggered presentation.
- **D. Restrictive cardiomyopathy** — This is a chronic condition with impaired diastolic function due to myocardial infiltration (e.g., amyloidosis), not triggered acutely by emotional stress.

Would you like to explore the acute management strategy for Takotsubo cardiomyopathy?

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Question 90

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?

A. Undergo colonoscopy
B. Undergo upper GI endoscopy
C. Proton pump inhibitors with anti-H.pylori regimen
D. Surgery for peptic ulcer disease

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The answer is **B. Upper GI endoscopy**.

This patient presents with classic signs of **acute upper gastrointestinal bleeding (UGIB)**: hematemesis (bloody vomit with clots), melena (black tarry stool), and a history of chronic alcoholism — all pointing to a source proximal to the ligament of Treitz. After initial resuscitation with oxygen, IV fluids, and NG tube placement, the most appropriate next step is **upper endoscopy (EGD)**, which serves as both a diagnostic and therapeutic intervention.[1][2]

Why the other options are incorrect:

- **A. Colonoscopy** — Colonoscopy evaluates the lower GI tract. The combination of hematemesis and melena localizes the bleeding source to the upper GI tract, making colonoscopy inappropriate.
- **C. PPI + anti-H. pylori regimen** — While PPIs are part of UGIB management, empiric H. pylori eradication without first identifying the bleeding source and obtaining biopsies is premature. The etiology must be established endoscopically before initiating targeted therapy.[3][4]

- **D. Surgery for PUD** — Surgery is reserved for cases where endoscopic hemostasis fails or bleeding recurs despite repeat endoscopic therapy. Proceeding directly to surgery without first attempting endoscopic evaluation and treatment is not standard of care.[1]

The ACG recommends that patients hospitalized with overt UGIB undergo **endoscopy within 24 hours of presentation**.[5] Upper endoscopy allows identification of the bleeding source — whether esophageal varices, peptic ulcer disease, Mallory-Weiss tear, or gastritis (all common in alcoholics) — and enables concurrent endoscopic hemostatic treatment such as band ligation, injection therapy, or clip placement.[1][6]

Would you like to explore post-endoscopy management of peptic ulcer bleeding, including PPI dosing and H. pylori eradication?

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Question 91

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?

A. Antigen-specific IgE binding to mast cells
B. Tissue-specific antibodies
C. Antigen-antibody complexes
D. Presensitized CD8+ cytotoxic T-cells

https://openevidence.com/ask/f86425ef-7e46-481a-948f-c861996d80e8

The correct answer is **C. Antigen-antibody complexes**.

This presentation — hematuria, proteinuria, and edema following pharyngitis by ~2 weeks, with an elevated ASO titer — is classic for **post-streptococcal glomerulonephritis (PSGN)**, the prototype of **immune complex–mediated (Type III hypersensitivity) glomerulonephritis**.[1][2]

The pathogenesis centers on the **formation and glomerular deposition of antigen-antibody complexes** directed against streptococcal antigens (notably nephritis-associated plasmin receptor and streptococcal pyrogenic exotoxin B).[2][3] These immune complexes deposit in glomeruli — either from the circulation or formed in situ on the glomerular basement membrane — and **activate complement** (predominantly the alternative pathway), triggering inflammation that produces the nephritic syndrome.[4][5]

Why not the other options:

- **A (Antigen-specific IgE binding to mast cells)** — This describes a **Type I (immediate) hypersensitivity** reaction (e.g., anaphylaxis, allergic rhinitis), not immune complex disease.
- **B (Tissue-specific antibodies)** — This describes **Type II (cytotoxic) hypersensitivity**, where antibodies target antigens on specific cells or tissues (e.g., Goodpasture syndrome with anti-GBM antibodies, autoimmune hemolytic anemia).

- **D (Presensitized CD8+ cytotoxic T-cells)** — This describes **Type IV (delayed-type) hypersensitivity** (e.g., contact dermatitis, transplant rejection), which is cell-mediated rather than antibody/immune complex–mediated.

Would you like to explore how to distinguish post-streptococcal glomerulonephritis from IgA nephropathy, which can also present with hematuria following an upper respiratory infection?

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Question 92

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?

A. Ataxia
B. Conjunctival injection
C. Miosis
D. Nystagmus

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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 the classic **opioid overdose toxidrome**. The triad of **apnea/hypopnea, stupor, and miosis (pinpoint pupils)** defines opioid intoxication.[1][2] A respiratory rate ≤12 breaths/min in a patient not in physiologic sleep strongly suggests acute opioid intoxication, particularly when accompanied by miosis or stupor.[1]

Why the other options are incorrect:

- **A. Ataxia** — Associated with cerebellar dysfunction (e.g., alcohol intoxication, phenytoin toxicity), not the sedation-dominant picture seen here with profound respiratory depression.
- **B. Conjunctival injection** — A hallmark of **cannabis** intoxication. Cannabis does not cause significant respiratory depression or altered mental status to this degree.
- **D. Nystagmus** — Characteristic of **PCP (phencyclidine)** intoxication or alcohol/sedative toxicity. PCP classically presents with agitation, hypertension, and vertical nystagmus — not the depressed vital signs seen here.

The **respiratory rate of 5/min** is the critical clue. As Boyer notes in the NEJM, the **sine qua non of opioid intoxication is respiratory depression**, and a respiratory rate ≤12 breaths/min has approximately 80% sensitivity for predicting response to naloxone.[1][3]

Would you like to explore naloxone dosing strategies for acute opioid overdose management?

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Question 93

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?

A. Diphenhydramine
B. Lorazepam
C. Olanzapine
D. Physical restraints

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The correct answer is **C. Olanzapine**.

This patient presents with classic **hyperactive delirium** in the setting of urosepsis — hallucinations (talking to someone not present), agitation, aggression (striking at a nurse), and wandering behavior. When delirium-related behavior **poses a substantial risk of harm to the patient or staff**, short-term use of a low-dose **atypical antipsychotic** such as olanzapine is the most appropriate pharmacologic intervention among the options listed.[1][2][3]

Why the other options are inferior or harmful:

- **A. Diphenhydramine** — A first-generation antihistamine with significant **anticholinergic properties** that is itself deliriogenic. It is listed on the AGS Beers Criteria as a medication to avoid in older adults and has been associated with increased delirium risk in hospitalized elderly patients.[4][5]
- **B. Lorazepam** — AGS guidelines **strongly recommend against benzodiazepines as first-line treatment** for delirium-associated agitation (except when specifically indicated, such as alcohol or benzodiazepine withdrawal). Benzodiazepines can worsen delirium, increase fall risk, and cause respiratory depression in older adults. Among agitated elderly ED

patients, midazolam was associated with a 5-fold increase in adverse events compared with haloperidol.[2][6][7][8]

- **D. Physical restraints** — Physical restraints are **associated with increased injury** in delirious patients and should be minimized or eliminated on general medical and surgical wards. They can paradoxically worsen agitation.[3]

Important caveats: Nonpharmacologic interventions (de-escalation, reorientation, sitters, environmental modification) remain the cornerstone of delirium management and should be employed alongside any pharmacologic intervention.[1][2][3] Antipsychotics should be used at the **lowest effective dose for the shortest duration**, and underlying precipitants (electrolyte abnormalities, urinary retention, pain, medication effects) should be identified and corrected.[1] It should also be noted that overall evidence for antipsychotics shortening delirium duration or improving outcomes remains limited; their role is primarily to manage dangerous behavioral disturbances acutely.[2][9]

Would you like to explore specific dosing and monitoring protocols for antipsychotics in elderly delirium?

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Question 94

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?

A. Increase in serum ACTH
B. Decrease in urinary 17-hydroxycorticosteroids
C. Decrease in serum 11-deoxycortisol
D. Increase in serum cortisol

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The answer is **A. Increase in serum ACTH**.

Metyrapone inhibits 11β-hydroxylase, the enzyme that converts 11-deoxycortisol to cortisol.[1] By blocking this final step, cortisol production falls, which **removes negative feedback on the pituitary** and results in a **compensatory rise in ACTH** secretion.[1][2] The increased ACTH drive stimulates adrenal steroidogenesis upstream of the block, causing **11-deoxycortisol to accumulate** (rise, not fall) and **urinary 17-hydroxycorticosteroids to increase** (not decrease).[1][2]

A normal (intact HPA axis) response — which this patient demonstrated by ruling out adrenal insufficiency — is indicated by a rise in 11-deoxycortisol to >70 µg/L and an increase in ACTH.[1][3] In contrast, patients with adrenal insufficiency show a subnormal rise in both values.[4]

Evaluating each option:

- **A. Increase in serum ACTH** — Correct. The fall in cortisol releases negative feedback, driving ACTH up.
- **B. Decrease in urinary 17-OHCS** — Incorrect. 17-OHCS include metabolites of 11-deoxycortisol, which accumulates; urinary 17-OHCS therefore **increase**.[1][2]
- **C. Decrease in serum 11-deoxycortisol** — Incorrect. 11-deoxycortisol is the immediate precursor blocked from conversion to cortisol, so it **rises markedly**.[1][4]

- **D. Increase in serum cortisol** — Incorrect. Metyrapone directly blocks cortisol synthesis, so cortisol **decreases**.[1][2]

Would you like to explore how the metyrapone test compares to cosyntropin stimulation for diagnosing secondary adrenal insufficiency?

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Question 95

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?

A. Observer-expectancy bias
B. Length-time bias
C. Surveillance bias
D. Lead-time bias

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The answer is **D. Lead-time bias**.[1][2][3]

Lead-time bias occurs when survival is measured from the time of diagnosis and a screening test detects disease earlier in its natural history than symptom-based diagnosis would. The screened group appears to live longer, but the apparent survival gain may be entirely artificial — the "clock" simply starts ticking earlier. As Black and Welch describe in the *New England Journal of Medicine*:

> "If survival is measured from the time of diagnosis, as is usual, then the comparison between patients who are given diagnoses earlier on the basis of the test and those given diagnoses on the basis of clinical findings is a biased one, regardless of the real effect of the earlier diagnosis. In the simple case in which earlier diagnosis has no real effect on the length of survival, the new test will appear to prolong survival."
>
> —William C. Black et al., Dartmouth Medical School and other institutions. Advances in Diagnostic Imaging and Overestimations of Disease Prevalence and the Benefits of Therapy. N Engl J Med. April 29, 1993.
>
> Used under license from The New England Journal of Medicine.

In this scenario, the study endpoint is **survival time from diagnosis**. The MRI-screened group was diagnosed during the asymptomatic phase, meaning their diagnosis date was moved earlier

in the disease course compared with the symptom-detected group. Both groups may die at the same point in time, yet the screened group will appear to survive longer by the amount of lead time gained — here, 6 weeks. For an aggressive tumor like GBM (median survival ~15 months), a modest 6-week difference is readily explained by lead time alone.[2][3]

Why not the other options:

- **A. Observer-expectancy bias** — arises when investigators' expectations influence how outcomes are measured or interpreted; not related to the endpoint of survival from diagnosis.
- **B. Length-time bias** — occurs when screening preferentially detects slower-growing, more indolent tumors, inflating apparent survival. While a real concern in screening studies, the question specifically asks about the bias arising from the **endpoint selected** (survival time), which is the defining feature of lead-time bias.[2][4]
- **C. Surveillance bias (detection bias)** — refers to increased detection of disease in a more closely monitored group, inflating incidence. It does not explain a spurious increase in measured survival time from the chosen endpoint.

The proper way to evaluate a screening program is through **mortality reduction** in a randomized controlled trial rather than survival measured from diagnosis, which is inherently susceptible to lead-time bias.[2][5]

Would you like to explore how length-time bias differs from lead-time bias in cancer screening studies?

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Question 96

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?

A. CT scan of the chest
B. Bronchoscopy
C. Emergency thoracotomy
D. Needle decompression

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The answer is **D. Needle decompression**.

This patient presents with the classic findings of **tension pneumothorax**: hypotension, tachycardia, hypoxia, **jugular venous distention**, **decreased breath sounds**, and **hyperresonance on percussion** on the left side — in the setting of a penetrating chest wound at the left 5th intercostal space.[1][2] Tension pneumothorax is a **clinical diagnosis** that requires immediate intervention without waiting for confirmatory imaging.[3]

Why needle decompression is correct:

- Per ATLS and WSES-AAST guidelines, tension pneumothorax requires **emergent decompression** — needle thoracostomy at the 2nd intercostal space, midclavicular line (or 5th intercostal space, midaxillary line), followed by definitive tube thoracostomy.[1][3]
- Tension physiology occurs when trapped air progressively displaces mediastinal structures, obstructing venous return and causing hemodynamic collapse. The clinical triad of

hypotension, JVD, and absent/decreased breath sounds with hyperresonance is pathognomonic.[1][4]

Why the other options are incorrect:

- **A (CT chest):** Delays definitive treatment in a hemodynamically unstable patient with an immediately life-threatening condition. Imaging is never pursued before decompression when tension pneumothorax is clinically evident.[3]
- **B (Bronchoscopy):** Not part of the acute management of tension pneumothorax; indicated later if tracheobronchial injury is suspected (e.g., persistent air leak after tube thoracostomy).
- **C (Emergency thoracotomy):** Reserved for traumatic cardiac arrest or massive hemothorax with ongoing hemorrhage — not for tension pneumothorax, which is managed with pleural decompression first.[1]

Would you like to explore the indications for emergency thoracotomy in penetrating chest trauma?

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Question 97

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?

A. Ankylosing spondylitis
B. Gout
C. Osteoarthritis
D. Fibromyalgia

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The correct answer is **C. Osteoarthritis**.

This presentation is classic for **osteoarthritis (OA)**, with several hallmark findings converging:

- **Heberden's nodes** — the non-tender bony nodules at the DIP joints are highly characteristic of OA and strongly associated with underlying radiographic disease.[1][2]
- **First carpometacarpal (CMC) joint tenderness** — the base of the thumb is one of the most commonly affected sites in hand OA, often presenting with pain on palpation and during pinch/grip activities.[1][3][4]
- **Bilateral knee enlargement with crepitus** — bony enlargement (55% sensitivity, 95% specificity) and crepitus (89% sensitivity) are cardinal signs of knee OA on physical examination.[5]
- **Professional athlete history** — high-impact sports participation is a well-established risk factor for OA development, with a pooled risk ratio of 1.37 (95% CI 1.14–1.64) across studies. Joint trauma and repetitive loading contribute to earlier-onset degenerative disease.[6][7][8]

Morning stiffness of ~50 minutes is somewhat longer than typical for OA (usually <30 minutes), but the key clinical threshold distinguishing OA from inflammatory arthritis is generally **>60 minutes**, which favors an inflammatory process such as rheumatoid arthritis.[5][9][10] This patient's stiffness falls below that cutoff.

Why not the other choices:

- **Ankylosing spondylitis** — primarily affects the axial skeleton and sacroiliac joints; does not cause DIP nodules or this peripheral joint distribution.
- **Gout** — while chronic tophaceous gout can be polyarticular, the presentation here lacks episodic inflammatory flares, warmth, or soft-tissue swelling. The bony (not soft/tophaceous) character of the DIP nodules and the classic OA joint distribution pattern make gout far less likely.[11][12]
- **Fibromyalgia** — presents with diffuse musculoskeletal pain and tenderness without objective joint findings such as bony enlargement, crepitus, or nodules.

The absence of **joint swelling, warmth, constitutional symptoms**, and extra-articular features further supports a non-inflammatory, degenerative process.[9][11]

Would you like to explore the current evidence-based treatment approach for hand and knee osteoarthritis?

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Question 98

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?

A. Neisseria gonorrhoeae infection
B. Testicular tumor
C. Chlamydia trachomatis infection
D. Varicocele

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C. Chlamydia trachomatis infection. The picture is acute epididymitis (subacute unilateral scrotal pain, dysuria/frequency, relief with elevation, hyperemia of the affected side on Doppler) accompanied by subclinical urethritis — PMNs on urethral Gram stain without gram-negative intracellular diplococci defines **nongonococcal urethritis**, and *C. trachomatis* is the most common identified cause of both NGU and epididymitis in sexually active men <35 years.[1][2]

Why the smear points to chlamydia over gonorrhea

- Presumed gonococcal infection requires WBCs containing **gram-negative intracellular diplococci**; their absence with inflammation on microscopy defines NGU, of which *C. trachomatis* accounts for 15–40% of cases.[2]
- Chlamydial urethritis is typically **minimally symptomatic or discharge-free**, matching the absent meatal discharge here; gonococcal urethritis usually produces frank purulent discharge.
- The Gram stain is not definitive — **NAAT of first-void urine for both *C. trachomatis* and *N. gonorrhoeae* remains mandatory**, since a negative smear (especially without visible

discharge) does not exclude gonorrhea. *M. genitalium* (15–25% of NGU) is the other leading pathogen not offered as an option.[2]

Why the other choices don't fit

- **Testicular tumor** — presents as a painless or minimally tender mass with a discrete intratesticular lesion on ultrasound, not diffuse hyperemia with pyuria/urethral inflammation.
- **Varicocele** — a dull left-predominant "bag of worms" of dilated pampiniform veins that worsens with standing/Valsalva; it does not cause urethral inflammation or hyperemia.
- **Gonorrhea** — possible but far less likely given the negative smear and absence of discharge.

Clinical caveats

- **Torsion must still be considered** in any acute scrotum. Prehn sign has insufficient sensitivity to exclude it, and reactive hyperemia after torsion–detorsion is sonographically indistinguishable from epididymo-orchitis; clinical correlation and urologic consultation are needed when suspicion persists.[3][4]
- Testicular involvement (epididymo-orchitis) occurs in 20–40% of cases by retrograde spread, consistent with the testicular tenderness and intratesticular hyperemia described.[4]
- **Empiric therapy** for STI-associated epididymitis in this age group is **ceftriaxone 500 mg IM × 1 plus doxycycline 100 mg PO BID × 10 days**, with supportive scrotal elevation and NSAIDs; test for other STIs, treat partners from the prior 60 days, and reassess if no improvement in 48–72 hours.[1][3]

Would you like to explore management of epididymitis that fails to improve on empiric therapy?

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Question 99

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?

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

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The correct answer is **D. Non-enveloped with linear, double-stranded DNA**.

This presentation — a young boy with **dysuria, urinary frequency, and gross hematuria** (cloudy, red urine) — is classic for **adenovirus-associated acute hemorrhagic cystitis**. Adenovirus types 11 and 21 are the serotypes most commonly implicated, with a strong male predominance (approximately 3:1).[1] This occurs in immunocompetent children and is self-limited, distinguishing it from BK virus-associated hemorrhagic cystitis, which typically occurs in immunocompromised or transplant patients.[2][3]

Adenovirus is a **non-enveloped, icosahedral virus** with a **linear double-stranded DNA genome** of approximately 34–37 kb.[4][5][6] These features match answer choice D.

The other options correspond to different virus families:

- **A (non-enveloped, linear ssDNA):** Parvovirus (e.g., parvovirus B19)
- **B (non-enveloped, linear ssRNA):** Picornaviruses (e.g., enteroviruses)
- **C (enveloped, linear ssRNA):** Paramyxoviruses, orthomyxoviruses, or filoviruses

Would you like to explore the management and natural history of adenovirus hemorrhagic cystitis in immunocompetent children?

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Question 100

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?

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

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The answer is **D. Seek a court order for neoadjuvant chemotherapy**.[1][2][3]

This scenario involves parental refusal of **life-saving, curative-intent treatment** for an 18-month-old child who cannot participate in medical decision-making. While parental authority in pediatric medical decisions is generally broad, **it is not absolute**. The AAP states that when parents decline a recommended intervention and the refusal incurs a risk of harm to the child, physicians may be **legally obligated to seek state involvement and a court order** authorizing treatment.[1][2] The ACEP similarly states that when parents make decisions placing children at significant risk of serious harm, governmental intervention (e.g., child welfare agencies, courts) may be necessary.[2]

The ethical and legal justification for a court order here rests on several critical factors:

- **Intermediate-risk neuroblastoma has a highly favorable prognosis with standard treatment** — neoadjuvant chemotherapy followed by surgical resection offers excellent

survival rates. Refusing treatment exposes this child to a **substantial risk of death from an otherwise treatable disease**.[4]

- Under the doctrine of **parens patriae**, the state has authority to intervene to protect children when parental decisions would result in serious harm.[3]
- The scenario specifies that a **thorough discussion** of risks, benefits, and prognosis has already occurred, and the parents remain steadfast in refusal — shared decision-making has been exhausted.[1]
- Parental refusal of clearly beneficial treatment that places a child at risk of death constitutes **medical neglect**, triggering a physician's obligation to act.[2][5]

Why the other options are incorrect:

- **A (Supportive care at home)** — Acquiescing to comfort-only care for a child with a curable malignancy would fail the physician's duty to protect the child's welfare and could constitute complicity in medical neglect.
- **B (Refer to another oncologist)** — Referral does not address the fundamental ethical and legal issue; the child needs treatment regardless of which physician provides it. This simply delays necessary intervention.
- **C (Recommend 2 weeks to think)** — While allowing time for reflection can be a reasonable intermediate step in some disputes, the question states the parents have already had a thorough discussion and remain steadfast. Given the time-sensitive nature of the malignancy, further delay is not appropriate when the risk is imminent.[3][6]

In practice, seeking a court order typically involves engaging hospital legal counsel, ethics consultation, social work, and child protective services as part of an institutional process.[6]

Would you like to explore the stepwise ethical framework for managing treatment refusal disputes in pediatric oncology?

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Question 101

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?

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

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The answer is **B: the mischarged tRNA with valine will be incorporated at the codons specifying lysine**.[1][2][3]

The ribosome's decoding center selects aminoacyl-tRNAs based on **codon-anticodon complementarity**, not on the identity of the attached amino acid. The Lys-tRNA carries an anticodon complementary to lysine codons (AAA/AAG). Even though it has been mischarged with valine, the ribosome will recognize the correct codon-anticodon base pairing and accept the tRNA, resulting in **valine being incorporated into the polypeptide** at positions encoded by lysine codons.[1][2][4]

This principle was established by the landmark **Chapeville experiment (1962)**, in which cysteine attached to Cys-tRNA was chemically converted to alanine using Raney nickel. The ribosome incorporated alanine at cysteine codons, confirming that it is the anticodon — not the amino acid — that determines positional placement during translation.

Why the other options are incorrect:

- **A (ribosome removes the valine):** Ribosomal proofreading operates through kinetic discrimination of the codon-anticodon duplex geometry in the decoding center (involving

16S rRNA residues G530, A1492, A1493), not by inspecting the amino acid. A mischarged tRNA with a correct anticodon passes both initial selection and proofreading.[3][5]

- **C (proteasome degrades the tRNA):** The proteasome degrades ubiquitinated proteins, not tRNAs. This is mechanistically implausible.
- **D (lysyl-tRNA synthetase removes it):** Aminoacyl-tRNA synthetases possess editing domains that can hydrolyze mischarged amino acids, but this occurs primarily during or immediately after the aminoacylation reaction. Once the mischarged tRNA has been released and delivered to the ribosome by EF-Tu, the synthetase does not retrieve it from the translational machinery.[6]

Would you like to explore post-peptidyl transfer quality control mechanisms on the ribosome?

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Question 102

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?

A. Propofol
B. Ketamine
C. Fentanyl
D. Midazolam

https://openevidence.com/ask/d2c15008-c1bc-428f-a18d-59d9ee1b4997

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] It is the only agent among the answer choices that acts through the NMDA receptor. Both the NCCN Adult Cancer Pain guidelines and the ASPN Best Practices guidelines recommend considering ketamine (oral or IV) for **refractory cancer pain** not responding to opioids or other adjuvant analgesics.[1][2]

Why the other options are incorrect:

- **A. Propofol** — a GABA-A receptor agonist used for sedation/anesthesia; no NMDA receptor activity.
- **C. Fentanyl** — a potent mu-opioid receptor agonist; switching to fentanyl would not address opioid-related side effects or act on NMDA receptors.
- **D. Midazolam** — a benzodiazepine (GABA-A receptor modulator) used for anxiolysis and sedation; no NMDA receptor activity.

Mechanism of ketamine's opioid-sparing effect: NMDA receptors play a central role in the development of opioid tolerance and central sensitization. By blocking these receptors, ketamine reduces the "wind-up" phenomenon — progressive amplification of dorsal horn neuron responses — and reverses opioid-induced hyperalgesia.[3] Animal studies have demonstrated

that ketamine prevents fentanyl-induced hyperalgesia and subsequent acute morphine tolerance.[2] A systematic review of 35 RCTs involving 2,279 cancer pain patients found that ketamine significantly reduced pain intensity and morphine dosage requirements.[4]

Would you like to explore dosing protocols and monitoring for subanesthetic ketamine in cancer pain?

References

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Question 103

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?

A. Citalopram
B. Lithium
C. Propranolol
D. Quetiapine

https://openevidence.com/ask/3bc64892-2142-424b-b01a-3556af3e8128

The correct answer is **A. Citalopram**.

This patient presents with classic **panic disorder with developing agoraphobia**: recurrent, discrete episodes of intense fear with autonomic symptoms (chest discomfort, dyspnea, tremulousness, diaphoresis), anticipatory anxiety about future attacks, and progressive avoidance behavior (leaving the house less).[1] The episodes are temporally associated with psychosocial stressors (exams, projects) but lack a clear, consistent trigger, consistent with the unpredictable nature of panic attacks.

SSRIs are first-line pharmacotherapy for the long-term management of panic disorder, with or without agoraphobia.[1][2] A JAMA review states:

> "First-line treatments for anxiety disorders include cognitive behavioral therapy, SSRIs such as sertraline, and SNRIs such as venlafaxine extended release."
>
> —Kristin L. Szuhany, PhD et al., Department of Psychiatry, New York University Grossman School of Medicine, New York. Anxiety Disorders. JAMA. December 27, 2022.

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A network meta-analysis of 87 panic disorder trials (n = 12,800) found that SSRIs provided the best balance of **high remission rates with low adverse events** compared with other drug classes.[3] **Citalopram** is the only SSRI among the answer choices.

Why the other options are incorrect:

- **Lithium (B):** A mood stabilizer used for bipolar disorder; it has no role in the treatment of panic disorder.
- **Propranolol (C):** A beta-blocker sometimes used for situational/performance anxiety (e.g., stage fright), but it does not treat the underlying panic disorder and is not recommended as first-line therapy.[4]
- **Quetiapine (D):** An atypical antipsychotic with some evidence in generalized anxiety disorder but associated with significant metabolic side effects and high discontinuation rates; it is not recommended for panic disorder. Guidelines note limited effectiveness and several adverse effects of antipsychotics for anxiety disorders.[2][5]

Guidelines also recommend continuing antidepressant therapy for **at least 6 to 12 months** after symptom response to minimize relapse risk, as discontinuation before one year leads to relapse in up to 50% of patients.[1][2]

Would you like to explore SSRI dosing and titration strategies specific to panic disorder?

References

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Question 104

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?

A. IL-4
B. TNF-alpha
C. IFN-gamma
D. Histamine

https://openevidence.com/ask/4f3ee65b-d2ba-4e9c-afdf-40235cb54d88

The answer is **C. IFN-gamma**.

IFN-γ is the principal Th1-derived cytokine responsible for all three actions described in the question:

- **Phagosome-lysosome fusion:** M. *tuberculosis* survives intracellularly by arresting phagosome maturation. IFN-γ activation of macrophages overcomes this block, upregulating the LRG p47 GTPase family and enabling delivery of the bacterium to an acidic, hydrolytically competent lysosome.[1][2]
- **Nitric oxide (NO) production:** IFN-γ induces **inducible nitric oxide synthase (iNOS/NOS2)**, driving production of reactive nitrogen intermediates that are directly mycobactericidal.[1][3][4]
- **Granuloma (tubercle) formation:** IFN-γ-activated macrophages are central to the organized granulomatous response characteristic of TB. Deficiency in IFN-γ or its receptor results in failure to form structured granulomas and markedly increased susceptibility to disseminated disease.[5][6]

The other options are incorrect: **IL-4** is a Th2 cytokine that actually inhibits macrophage activation and autophagy-dependent mycobacterial killing.[6] **TNF-α** contributes to granuloma maintenance but is not the Th1-secreted factor that drives phagosome-lysosome fusion and NO

production in this context. **Histamine** is a mast cell/basophil mediator with no role in the antimycobacterial Th1 response.

Would you like to explore how M. tuberculosis evades IFN-γ–mediated macrophage killing mechanisms?

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Question 105

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?

A. Interviewer bias
B. Latency period
C. Recall bias
D. Survival bias

https://openevidence.com/ask/5865ed6c-8ef4-496e-959c-99d8c0eb9cb7

The answer is **C. Recall bias**.

This study is a **retrospective case-control design** in which mothers were asked to recall prenatal folic acid use after the outcome (ASD diagnosis) was already known. Recall bias is the most likely source of distortion here. Mothers of children diagnosed with ASD are more likely to have searched their memories for factors that might explain their child's condition, potentially leading to differential reporting of exposures compared with mothers of healthy children.[1][2]

Several features of this study make it particularly susceptible:

- **Retrospective exposure ascertainment**: Folic acid intake was assessed via standardized questionnaires administered after ASD diagnosis, meaning the outcome could influence how mothers recalled their prenatal behaviors.[3][4]
- **Differential motivation to recall**: Cases tend to scrutinize past exposures more thoroughly than controls, who have no such motivation — a well-documented phenomenon in case-control studies of prenatal exposures. Mothers who gave birth to children with health problems may be more likely to recall details of their pregnancies compared with mothers of healthy children.[5][6]

- **Direction of bias**: The protective OR of 0.3 could be inflated by cases (ASD mothers) underreporting folic acid use or controls overreporting it, consistent with how differential recall can distort effect estimates in either direction.[7][8]

Why not the other choices:

- **A. Interviewer bias** — While possible in case-control studies, the use of standardized questionnaires mitigates this, and there is no indication the interviewers knew case/control status.
- **B. Latency period** — This refers to the time between exposure and disease onset and is not a type of bias; it is a temporal consideration relevant to cohort studies.
- **D. Survival bias** — This would apply if the study selectively included only surviving participants in a way that distorted the exposure-outcome relationship, which is not the primary concern here.

Would you like to explore strategies for minimizing recall bias in prenatal exposure case-control studies?

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Question 106

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?

A. Acute kidney failure
B. Chronic kidney failure
C. Obstructive uropathy
D. Renal cell carcinoma

https://openevidence.com/ask/68748192-9501-471d-ba33-1cba7501f655

The correct answer is **B. Chronic kidney failure**.

CKD is defined as decreased GFR or kidney damage persisting for ≥3 months.[1][2] This patient's renal function was already impaired 4 months ago (BUN 45, Cr 2.0) and has progressively

worsened (BUN 59, Cr 2.3), clearly establishing chronicity beyond the 3-month threshold. Several features of the presentation are classic CKD complications:

- **Anemia (Hgb 8 g/dL)** — a hallmark of CKD, primarily driven by relative erythropoietin deficiency from declining kidney function, with contributions from iron dysregulation and shortened red cell survival. Anemia prevalence increases as GFR declines and affects up to two-thirds of patients with eGFR <15 mL/min/1.73 m².[3][4][5]
- **Hyperkalemia (K+ 5.9 mEq/L)** and **metabolic acidosis (HCO3- 17 mEq/L)** — both expected as nephron loss reduces potassium excretion and acid buffering capacity.
- **Constitutional symptoms** (weakness, weight loss) are consistent with progressive CKD.

Why the other options are less likely:

- **A. Acute kidney failure** — AKI is defined by a rapid rise in serum creatinine within **2–7 days**. This patient's renal dysfunction has been documented over at least 4 months with gradual worsening, making CKD the primary diagnosis.[6][7]
- **C. Obstructive uropathy** — The patient **denies urinary symptoms**. While chronic obstruction can be clinically silent, the progressive biochemical pattern with anemia and metabolic derangements is more consistent with intrinsic CKD than obstruction.
- **D. Renal cell carcinoma** — There is no hematuria, flank mass, or other features suggestive of RCC. While weight loss could raise concern, the constellation of progressive renal dysfunction, anemia, hyperkalemia, and acidosis is best explained by CKD.

Would additional context be helpful regarding the workup to determine the underlying etiology of this patient's CKD (e.g., diabetes, hypertension, glomerular disease)?

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Question 107

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?

A. Glomerular crescents with macrophages
B. Matrix expansion with mesangial proliferation
C. Cortical thinning with tubular atrophy
D. Thickened glomerular capillary loops

https://openevidence.com/ask/644645ff-f4f1-482f-b1a5-d3fbfd8758a5

The answer is **C. Cortical thinning with tubular atrophy**.

This vignette describes **vesicoureteral reflux (VUR)** — a 2-year-old girl with recurrent UTIs, bilateral hydronephrosis on ultrasound, and retrograde contrast flow into the ureters on voiding cystourethrography (the gold standard for VUR diagnosis).[1][2] Recurrent UTIs in the setting of VUR predispose to ascending pyelonephritis and subsequent **reflux nephropathy**, the histopathologic hallmark of which is **chronic tubulointerstitial inflammation, tubular atrophy, interstitial fibrosis, and cortical scarring**.[3][4][5]

Reflux nephropathy is defined by **chronic tubulo-interstitial inflammation and fibrosis** and represents a frequent cause of end-stage renal failure in children.[3] Histologically, the established lesion shows **interstitial fibrosis, chronic inflammatory infiltrates, thyroidization of tubules** (atrophic tubules filled with eoite casts), and **cortical thinning** due to parenchymal loss.[4] These features constitute the classic picture of chronic pyelonephritis.

Why the other options are incorrect:

- **A. Glomerular crescents with macrophages** — characteristic of **rapidly progressive (crescentic) glomerulonephritis**, not reflux nephropathy.
- **B. Matrix expansion with mesangial proliferation** — seen in conditions like **diabetic nephropathy** or **IgA nephropathy**, not chronic pyelonephritis.

- **D. Thickened glomerular capillary loops** — typical of **membranous nephropathy**, a primary glomerular disease unrelated to VUR.

Would you like to explore the management approach for vesicoureteral reflux in children, including indications for prophylaxis versus surgical correction?

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Question 108

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 guragu e. 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?

A. Calcium oxalate crystals
B. Hyaline casts
C. Urine ketones
D. Urate crystals

https://openevidence.com/ask/364a7d8d-3238-420f-b025-dedaf407bc2a

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The answer is **A. Calcium oxalate crystals**.

This clinical scenario is classic for **ethylene glycol (antifreeze) poisoning**. The patient was found unresponsive with a half-empty container of antifreeze, with slurred speech, tachycardia, tachypnea, abdominal tenderness, and **acute kidney injury** (Cr 1.9 mg/dL, BUN 29 mg/dL) — all consistent with ethylene glycol ingestion.

Ethylene glycol is metabolized by alcohol dehydrogenase to glycoaldehyde, then to glycolic acid, glyoxylic acid, and ultimately **oxalic acid**. Oxalic acid combines with calcium to form **calcium oxalate crystals**, which deposit in the kidneys and other tissues and are excreted in the urine.[1] [2] Dihydrate crystals (envelope-shaped) appear early and monohydrate crystals (needle-shaped) appear later.[1] Detection of calcium oxalate crystalluria can serve as a critical real-time diagnostic clue when serum ethylene glycol levels are not readily available.[3]

Why not the other choices:

- **B. Hyaline casts** — nonspecific, seen in concentrated urine, dehydration, or after exercise; not characteristic of ethylene glycol poisoning.
- **C. Urine ketones** — associated with diabetic ketoacidosis, starvation, or **isopropanol** ingestion (which produces acetonemia and ketonuria), not ethylene glycol.[1]
- **D. Urate crystals** — associated with hyperuricemia, gout, or tumor lysis syndrome, not ethylene glycol metabolism.

Would you like to explore the treatment protocol for ethylene glycol poisoning, including fomepizole dosing and hemodialysis indications?

References

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Question 109

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?

A. Superior mesenteric artery
B. Inferior mesenteric artery
C. Celiac artery
D. Splenic artery

https://openevidence.com/ask/13842bb8-5f34-41d3-a598-0fb885302beb

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The answer is **B. Inferior mesenteric artery**.

This patient has a **horseshoe kidney**, the most common renal fusion anomaly, occurring in approximately **10% of patients with Turner syndrome**.[1][2] In ~90% of cases, the lower poles are fused by a parenchymal or fibrous isthmus.[3]

During embryological development, the metanephric kidneys normally ascend from the pelvis to the lumbar region. In a horseshoe kidney, **the fused isthmus becomes trapped behind the inferior mesenteric artery (IMA)**, which prevents the kidney from completing its normal ascent and leaves it in a lower-than-normal position.[3] The fusion itself occurs before the kidneys ascend between the umbilical arteries.[4]

The other arteries listed do not obstruct the ascending horseshoe kidney:

- **Superior mesenteric artery** — lies more superiorly and is not the structure that blocks ascent
- **Celiac artery** — arises from the aorta at T12, well above the path of renal ascent
- **Splenic artery** — a branch of the celiac trunk, not in the path of kidney migration

Would you like to explore the clinical complications and recommended surveillance for horseshoe kidney in Turner syndrome?

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Question 110

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?

A. LOD Score < 1
B. LOD Score < 2
C. LOD Score > 3
D. LOD Score = 0

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The correct answer is **C. LOD Score > 3**.

A **LOD (logarithm of the odds) score ≥ 3** is the traditional threshold for declaring **significant evidence of genetic linkage** between two loci.[1][2] This score represents odds of **1000:1 in favor of linkage** ($10^3 = 1000$), equivalent to a p-value of approximately 0.0001.[1] More stringent criteria proposed by Lander and Kruglyak raise this threshold to 3.3 for genome-wide significance, though a LOD of 3 remains the classic benchmark.[1][3]

Key interpretation of the other answer choices:

- **LOD = 0** indicates equal probability of linkage versus no linkage (no evidence either way).[1]
- **LOD < −2** is generally accepted as evidence **against** linkage.[2]
- **LOD scores of ~1.9–2** are considered only **suggestive** of linkage and are unreliable for establishing true linkage.[3][4]

Since both the ΔF508 mutation and the novel mutation reside in the CFTR gene, they would be expected to cosegregate during meiosis with minimal recombination, yielding a high LOD score consistent with close physical linkage.

Would you like to explore how recombination fraction estimates complement LOD scores in determining genetic distance?

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Question 111

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?

A. Prevents viral transcription
B. Inhibits viral assembly
C. Inhibits viral entry
D. Prevents T-cell binding

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The answer is **B. Inhibits viral assembly**.

Darunavir is an **HIV-1 protease inhibitor** that selectively inhibits the cleavage of HIV-encoded **Gag-Pol polyproteins** in infected cells, thereby **preventing the formation of mature, infectious virus particles**.[1][2] Since DN501 shares the same mechanism of action, it also inhibits viral assembly.

HIV protease cleaves precursor polyproteins during the final stages of the viral life cycle. As described in the NEJM:

> "After separation, viral precursor proteins are cleaved by a third HIV-specific enzyme, HIV protease, to promote full maturation and infectiousness of the viral particles."
>
> —Roy M. Gulick, M.D., M.P.H., Weill Cornell Medicine. Antiretroviral Therapy. N Engl J Med. July 23, 2026.
>
> Used under license from The New England Journal of Medicine.

Inhibition of this enzyme produces **immature, noninfectious virions**, effectively halting further rounds of infection.[4][5] This is distinct from the other answer choices:

- **A (Prevents viral transcription)** — describes the action of integrase inhibitors or transcription inhibitors, not protease inhibitors.
- **C (Inhibits viral entry)** — describes entry inhibitors such as enfuvirtide (fusion inhibitor) or maraviroc (CCR5 antagonist).[3]

- **D (Prevents T-cell binding)** — describes CD4 attachment inhibitors such as fostemsavir.

The question also notes an increased incidence of **hyperglycemia**, which is a recognized metabolic side effect of the protease inhibitor class as a whole.[6]

Would you like to explore the metabolic side effects associated with HIV protease inhibitors in more detail?

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Question 112

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?

A. G1 phase arrest
B. Prophase I arrest
C. Initiation of S phase
D. Completion of G2 phase

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The answer is **C. Initiation of S phase**.

CDK4 activation leads to phosphorylation of the Rb protein, which inactivates its growth-suppressive function and drives cells from G1 into S phase.[1][2] The mechanism proceeds as follows:

- **Unphosphorylated Rb** represses E2F transcription factors, which are required for transcription of genes essential for DNA replication and S phase entry.[3]
- **CDK4 (in complex with cyclin D) phosphorylates Rb**, initiating its inactivation. This progressive phosphorylation releases E2F from Rb-mediated repression.[2][4]
- **Freed E2F** drives transcription of S phase genes, including cyclin E, which activates CDK2 to complete Rb hyperphosphorylation and trigger DNA replication.[5][6]

Drug X, by activating CDK4, accelerates this cascade and promotes the **G1-to-S phase transition**.[7][8]

The other options are incorrect:

- **A (G1 phase arrest)** — CDK4 activation promotes G1 progression, not arrest. CDK4 *inhibitors* (e.g., palbociclib) cause G1 arrest.[7]

- **B (Prophase I arrest)** — Prophase I is a stage of meiosis; endometrial cells are somatic cells undergoing mitotic division, and CDK4 does not regulate meiotic checkpoints.
- **D (Completion of G2 phase)** — CDK4 acts specifically at the **G1/S boundary**; G2/M progression is governed by cyclin B-CDK1 complexes.

Would you like to explore how CDK4/6 inhibitors like palbociclib exploit this pathway for cancer treatment?

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Question 113

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?

A. Acalculous cholecystitis
B. Calculous cholescystitis
C. Choledocholithiasis
D. Emphysematous cholecystitis

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The answer is **A. Acalculous cholecystitis**.

This patient's presentation — **fever, tachycardia, RUQ tenderness, gallbladder wall thickening, and pericholecystic fluid without gallstones** — is classic for **acute acalculous cholecystitis (AAC)**. Her debilitated state on home hospice is a key risk factor, as AAC occurs in critically ill or debilitated patients due to **bile stasis and/or gallbladder wall ischemia**.[1]

AAC accounts for approximately **5–10% of all acute cholecystitis cases** and is associated with critical illness, prolonged fasting, diabetes, total parenteral nutrition, and other states of physiologic stress.[1][2] The pathogenesis involves bile stasis from fasting or ileus (causing bile inspissation toxic to the gallbladder epithelium) and microvascular ischemia of the gallbladder wall.[1] Ultrasound diagnostic criteria for AAC include **gallbladder wall thickening (>3.5–4 mm), pericholecystic fluid, and distension** — all in the absence of gallstones.[2]

Why the other choices are incorrect:

- **B. Calculous cholecystitis** — This is the most common form of acute cholecystitis (~90–95%), but it requires gallstones or sludge obstructing the cystic duct. The ultrasound here explicitly shows **no gallstones**.[1]

- **C. Choledocholithiasis** — Stones in the common bile duct typically present with **jaundice, elevated bilirubin, and transaminase/alkaline phosphatase elevations**, not a primary gallbladder wall abnormality on ultrasound.[3]
- **D. Emphysematous cholecystitis** — A rare, severe variant characterized by **intramural gas** in the gallbladder wall, typically in elderly diabetic men. No gas was described on this ultrasound.[2]

Would you like to explore the management of acalculous cholecystitis in patients who are poor surgical candidates?

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Question 114

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?

A. Stratum corneum
B. Stratum granulosum
C. Stratum basale
D. Dermis

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The answer is **D. Dermis**.

Urticarial wheals result from **degranulation of dermal mast cells**, with histamine as the major mediator. The primary cause of urticaria is the **release of histamine in the dermis** from mast cells through IgE-mediated type I hypersensitivity.[1] In this case, peanut allergen cross-links IgE on dermal mast cells, triggering degranulation.

Histologically, wheals are characterized by **edema of the upper and mid-dermis**, with **dilatation and augmented permeability of postcapillary venules** and a mixed inflammatory **perivascular infiltrate** consisting of lymphocytes, eosinophils, neutrophils, and mast cells.[2][3] Classic findings on biopsy include dermal edema and capillary dilatation with perivascular infiltrates mostly involving the superficial dermis.[3]

The epidermal layers (stratum corneum, stratum granulosum, stratum basale) are **not the site of histologic changes** in urticaria. The pathology is entirely dermal — the epidermis remains uninvolved. This distinguishes urticaria from conditions like eczema or contact dermatitis, which do show epidermal changes (spongiosis, acanthosis).

Would you like to explore the mechanism of IgE-mediated mast cell degranulation in type I hypersensitivity?

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Question 115

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?

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

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The answer is **A. Dysfunction in a transmembrane regulator**.

This presentation is classic for **cystic fibrosis (CF)**, caused by mutations in the **CFTR (cystic fibrosis transmembrane conductance regulator)** gene, which encodes a chloride and bicarbonate channel in the apical membrane of epithelial cells.[1] Loss of CFTR function leads to dehydrated, thickened secretions across multiple organ systems, producing the triad seen here: **recurrent pulmonary infections**, **steatorrhea with failure to thrive**, and **nasal polyposis**.[1][2][3]

Why this presentation fits CF:

- **Recurrent pneumonia and thick purulent cough** — CFTR dysfunction causes decreased chloride and bicarbonate secretion and persistent sodium absorption in airway epithelium, resulting in thickened mucus, impaired mucociliary clearance, mucus plugging, and chronic bacterial infection (typically *S. aureus* early, then *P. aeruginosa*). By age 3, nearly one-third of children with CF already have bronchiectasis on CT.[3][4][5]

- **Loose, foul-smelling stools and poor weight gain** — Approximately **80% of patients** with severe CFTR variants have pancreatic insufficiency, with mucus obstruction of pancreatic ducts causing autodigestion, fat malabsorption, and steatorrhea.[1][3]
- **Nasal polyp** — Nasal polyposis affects **25–40% of children with CF** (compared to ~4% in the general population), making it a hallmark finding that should always raise suspicion for CF in a child.[6][7]

Why not the other choices:

- **B (Maple syrup urine disease)** — Caused by defective branched-chain amino acid metabolism; presents with encephalopathy and a distinctive sweet urine odor in neonates, not recurrent pneumonia or steatorrhea.
- **C (Primary ciliary dyskinesia)** — Can cause recurrent sinopulmonary infections and bronchiectasis, but classically associated with **situs inversus** (Kartagener syndrome), neonatal respiratory distress, and chronic otitis media — not pancreatic insufficiency or nasal polyps in this pattern.
- **D (Lymphocytic deficiency)** — Suggests a primary immunodeficiency; would present with opportunistic infections rather than this specific combination of sinopulmonary disease, malabsorption, and nasal polyps.

The next diagnostic step would be a **sweat chloride test** (pilocarpine iontophoresis), with values **>60 mmol/L** confirming CF, followed by CFTR genotyping.[2][8]

Would you like to explore current CFTR modulator therapies and their eligibility criteria by genotype?

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Question 116

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?

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

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A. Endometrial sloughing and uterine contractions mediated by prostaglandin — this is primary dysmenorrhea.

The history is classic: cyclic, cramping suprapubic pain beginning a few hours before flow and lasting ~2 days, radiating to back and thighs, in an adolescent ~3 years post-menarche with regular ovulatory cycles, a normal examination, and partial relief with an NSAID.[1][2][3] Prostaglandins (especially PGF2α) and leukotrienes released from the sloughing endometrium as progesterone withdraws stimulate dysrhythmic myometrial contractions, reduce uterine blood flow, and produce ischemic pain.[4][5][6] Response to a COX inhibitor supports the mechanism.[7][8] Most adolescents with dysmenorrhea have the primary form.[9]

Why the others are less likely

- **B. Pelvic inflammatory disease** — she is at risk (two partners, inconsistent condom use), but PID causes non-cyclic pain with cervical motion/adnexal tenderness, discharge, and often fever; her exam and vitals are normal, and the pain is strictly menstrual. Risk behavior still warrants gonorrhea/chlamydia screening and contraception counseling, but it does not explain these symptoms.[3]
- **C. Ovarian cyst** — would cause pain unrelated to menses or mid-cycle (mittelschmerz), typically with an adnexal mass or acute unilateral pain.

- **D. Leiomyoma** — essentially unheard of at 15; fibroids are a cause of secondary dysmenorrhea with heavy menses and an enlarged/irregular uterus in older reproductive-age women.[5]

Management implication: empiric therapy is appropriate without further imaging — scheduled NSAIDs started at or just before onset of flow (loading dose then regular dosing), with hormonal contraception added if inadequate relief; failure to improve after 3–6 months should prompt evaluation for secondary causes, with endometriosis the leading one in adolescents.[9][10]

Would you like to explore the specific NSAID and hormonal regimens recommended for adolescent dysmenorrhea?

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Question 117

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:

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

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The answer is **B. Retrograde migration up peripheral nerve axons**.

The clinical presentation — **agitation, photophobia, dysphagia** (hydrophobia), flu-like prodrome, progression to coma and death, and **bat exposure during spelunking** in Mexico — is classic for **rabies encephalitis**. Autopsy findings of viral encephalitis with characteristic Negri bodies confirm the diagnosis.

Mechanism of CNS spread: Rabies virus (RABV) is inoculated into peripheral tissue (muscle/subcutaneous) via a bite or scratch from a rabid animal (bats being the primary reservoir in the Americas). The virus enters peripheral nerve terminals — particularly at neuromuscular junctions by binding **nicotinic acetylcholine receptors** — and undergoes **retrograde axonal transport** along microtubules, mediated by dynein motor complexes, at a rate of approximately 8–20 mm/day.[1][2][3] Once it reaches the spinal cord and brainstem, massive replication occurs and the virus disseminates throughout the CNS via trans-synaptic spread.[4][5]

Why the other options are incorrect:

- **A (Hematogenous dissemination to the meninges):** This mechanism applies to certain bacterial meningitides and some viruses (e.g., enteroviruses), but RABV is strictly neurotropic and does not use bloodstream dissemination.[6][7]
- **C (Reactivation from dorsal root ganglia):** This describes varicella-zoster virus (VZV) reactivation causing herpes zoster. RABV does not establish latency.[8]

- **D (Infection of oligodendrocytes and astrocytes):** This describes the pathogenesis of JC virus (progressive multifocal leukoencephalopathy). RABV primarily infects neurons, not glial cells.[1][4]

Would you like to explore the evidence on experimental treatment approaches for symptomatic rabies, such as the Milwaukee protocol?

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Question 118

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?

A. Tinea versicolor
B. Albinism
C. Vitiligo
D. Melanoma

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The answer is **C. Vitiligo**.

The pathologic hallmark of **vitiligo** is the **loss of epidermal melanocytes**, which is the key finding described in this biopsy.[1][2] Vitiligo is an acquired autoimmune depigmenting disorder in which CD8+ T cells target and destroy melanocytes, resulting in their complete absence from the epidermis.[3][4]

This finding distinguishes vitiligo from the other answer choices:

- **Albinism** — Melanocytes are **present** but have defective or absent tyrosinase, resulting in little or no melanin production. The biopsy would show melanocytes with absent or reduced pigment, not absent melanocytes.[5]
- **Tinea versicolor** — Caused by *Malassezia* fungus; melanocytes are present but melanin transfer and production are disrupted. Biopsy shows hyphae and spores ("spaghetti and meatballs"), not melanocyte loss.
- **Melanoma** — Characterized by malignant **proliferation** of melanocytes, the opposite of what is described here.

The patient's age is also consistent: nearly half of vitiligo cases present before age 20.[1]

Would you like to explore the current treatment approach for vitiligo, including newer JAK inhibitor therapies?

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Question 119

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?"

A. Trimethoprim-sulfamethoxazole
B. Eplerenone
C. Amphotericin B
D. Heparin

https://openevidence.com/ask/2fd3d9cb-14c5-4db6-84c9-63e371f34566

The answer is **C. Amphotericin B**.

This patient presents with a constellation of findings that point to **distal (Type 1) renal tubular acidosis (RTA)** secondary to amphotericin B nephrotoxicity:

- **Non-anion gap metabolic acidosis**: AG = 136 − (115 + 14) = **7** (normal), with hyperchloremia (Cl^- 115) and low bicarbonate (14 mEq/L)
- **Inappropriately alkaline urine (pH 7.0)** despite systemic acidosis — the hallmark of distal RTA, reflecting failure to secrete H^+ in the collecting duct (urine pH should be <5.5 in acidosis)
- **Hypokalemia** (K^+ 3.2) and **hypomagnesemia** (Mg^{2+} 1.4) from tubular wasting
- **Decreased urination** reflecting reduced GFR from amphotericin-induced nephrotoxicity

Why amphotericin B?

Amphotericin B inserts into renal tubular cell membranes, disrupting membrane permeability. This causes **direct injury to type A intercalated cells** of the collecting duct, impairing hydrogen ion secretion and producing distal RTA.[1][2] The FDA label lists **hypokalemia, renal tubular acidosis, and azotemia** as recognized renal adverse effects.[3] The IDSA aspergillosis guidelines note nephrotoxicity including **urinary potassium/magnesium wasting and renal tubular acidosis**.[4] In a prospective study of amphotericin B deoxycholate, hypokalemia occurred in 60% and hypomagnesemia in 82% of patients.[5]

Why not the other options?

- **Trimethoprim-sulfamethoxazole (A)**: Trimethoprim blocks ENaC in the collecting duct, causing **hyperkalemia** — the opposite of this patient's findings.
- **Eplerenone (B)**: A mineralocorticoid receptor antagonist that causes **hyperkalemia** and Type 4 RTA.
- **Heparin (D)**: Can cause **hypoaldosteronism**, leading to Type 4 RTA with **hyperkalemia** and acidic urine (pH <5.5).

All three incorrect options would produce hyperkalemia, whereas this patient has hypokalemia — a key distinguishing feature of distal (Type 1) RTA caused by amphotericin B.[6]

Would you like to explore strategies for preventing amphotericin B nephrotoxicity?

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Question 120

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?

A. Pulmonic stenosis
B. Coarctation of the aorta
C. Aortic stenosis
D. Transposition of great vessels

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The answer is **B. Coarctation of the aorta**.

This presentation is classic for **coarctation of the aorta (CoA)**, with every finding pointing to this diagnosis:

- **Upper-to-lower extremity blood pressure gradient (140/90 vs. 110/70 mmHg):** Upper extremity hypertension with lower extremity hypotension is the hemodynamic hallmark of CoA. A systolic BP difference **>20 mmHg** between upper and lower extremities is considered significant. Here the gradient is 30 mmHg.[1][2]
- **Brachiofemoral pulse delay:** A **pulse delay between the arm and femoral arteries** is a characteristic physical finding due to the aortic narrowing, with distal perfusion maintained via collateral vessels.[3]
- **Ejection systolic murmur in the interscapular area:** A murmur or bruit heard in the **left interscapular region** is produced by turbulent flow across the coarctation site, which is typically just distal to the left subclavian artery.[3]
- **Rib notching on chest X-ray:** This results from **dilated intercostal collateral arteries** that develop to bypass the obstruction, eroding the inferior borders of the ribs — a pathognomonic radiographic sign of CoA.[4]
- **S4 gallop:** Reflects **left ventricular hypertrophy** from chronic pressure overload proximal to the coarctation.

- **Leg pain with exertion:** Due to **lower extremity hypoperfusion** (claudication), a recognized symptom in older children and adults with CoA.[5]

The other choices are excluded:

- **Pulmonic stenosis** — would not cause upper-lower extremity BP gradient or rib notching.
- **Aortic stenosis** — causes an ejection murmur at the right upper sternal border (not interscapular), and does not produce a BP differential between limbs.
- **Transposition of great vessels** — presents with cyanosis in the neonatal period, not hypertension with limb BP discrepancy.

Would you like to explore the current approach to surgical versus endovascular repair of coarctation in children?

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Question 121

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?

A. Active hepatitis A infection
B. Previous hepatitis A infection
C. Chronic hepatitis B infection
D. Chronic hepatitis C infection

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The answer is **A. Active hepatitis A infection**.

Anti-HAV IgM positive with anti-HAV IgG negative is the key finding. Anti-HAV IgM is diagnostic of **acute hepatitis A infection**, becoming detectable 5–10 days before symptom onset and typically persisting for up to 6 months.[1][2][3] Anti-HAV IgG appears later in the course of infection (around the time of symptom onset) and persists lifelong.[3][4] The absence of IgG with presence of IgM indicates **very early acute infection**, likely in the pre-symptomatic phase. Recent travel to Guatemala — an HAV-endemic region — is a relevant epidemiologic risk factor.

Why other options are incorrect:

- **B. Previous hepatitis A infection** — A resolved/past infection would show **IgG positive and IgM negative**, the opposite of this patient's pattern.[1][2]

- **C. Chronic hepatitis B infection** — Chronic HBV requires **persistent HBsAg positivity**, which is absent here. The pattern of **anti-HBs positive with anti-HBc negative** is characteristic of **prior hepatitis B vaccination**, not natural infection. Recovered natural HBV infection produces both anti-HBs and anti-HBc positivity.[5][6]
- **D. Chronic hepatitis C infection** — **Anti-HCV is negative**, effectively excluding chronic HCV.[6]

The hepatitis B serologies are a notable secondary finding: **isolated anti-HBs positivity** (without anti-HBc) indicates this patient was previously vaccinated against hepatitis B, even though immunization records are unavailable.[5][6]

Would you like to explore the current recommendations for hepatitis A vaccination in travelers to endemic areas?

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Question 122

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?

A. Nucleotide excision repair
B. Non-homologous end joining
C. Homologous recombination
D. Mismatch repair

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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 irritation** — is classic for **xeroderma pigmentosum (XP)**. About 60% of XP patients present with increased sun sensitivity such as severe sunburn in the first weeks to months of life, and ocular findings (photophobia, keratitis, conjunctival injection) are nearly as common as cutaneous findings.[1][2][3]

XP is an autosomal recessive disorder caused by defective **nucleotide excision repair (NER)**, which is responsible for removing **bulky, helix-distorting DNA lesions** — most notably UV-induced **pyrimidine dimers** (cyclobutane pyrimidine dimers and 6-4 photoproducts).[1][4][5] Seven of the eight XP complementation groups (XPA through XPG) involve genes directly in the NER pathway; the eighth (XPV) involves DNA polymerase eta, a translesion synthesis polymerase.[6][7]

> "Nucleotide excision repair was the first DNA-repair process to be identified as involved in a disease — specifically, xeroderma pigmentosum. Cells from affected patients have decreased repair of UV light–induced DNA dimers, accounting for the apparent sun sensitivity and predisposition to skin cancer in this patient population."
>
> —Guido Keijzers, Ph.D. et al., University of Copenhagen. Monogenic Diseases of DNA Repair. N Engl J Med. November 09, 2017.

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Why the other options are incorrect:

- **B. Non-homologous end joining (NHEJ)** — repairs double-strand DNA breaks (e.g., from ionizing radiation). Defects cause radiosensitivity syndromes (e.g., LIG4 syndrome), not photosensitivity.
- **C. Homologous recombination** — also repairs double-strand breaks using a sister chromatid template. Defects are associated with BRCA-related cancers, Fanconi anemia, and ataxia-telangiectasia, not UV hypersensitivity.
- **D. Mismatch repair (MMR)** — corrects base-base mismatches and insertion/deletion loops arising during replication. Defects cause **Lynch syndrome** (hereditary nonpolyposis colorectal cancer), not UV-induced sunburns.[4]

The key distinguishing feature is that **UV radiation specifically generates bulky pyrimidine dimers**, and **NER is the primary pathway for their removal**.[5][8] Sunscreen does not fully block UV penetration, explaining the mother's observation that it has not prevented sunburns in this child.

Would you like to explore the recommended surveillance and management strategies for xeroderma pigmentosum?

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Question 123

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?

A. Bence-Jones protein
B. Calcitonin
C. CA 15-3
D. Neuron-specific enolase

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The answer is **D. Neuron-specific enolase (NSE)**.

NSE is the most well-established serum tumor marker for 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.[1][2] Serum NSE is elevated in approximately **60–80% of SCLC patients**, with higher rates in extensive-stage disease (83–91%) compared to limited-stage disease (39–59%).[3][4][5] NSE correlates with tumor burden, number of metastatic sites, and response to treatment, making it useful for staging, monitoring therapy, and predicting relapse.[2][4][6]

Why the other options are incorrect:

- **A. Bence-Jones protein** — Light chain immunoglobulins found in the urine of patients with **multiple myeloma** and other plasma cell dyscrasias; not associated with lung cancer.

- **B. Calcitonin** — A marker for **medullary thyroid carcinoma**, which arises from parafollicular C cells. While SCLC can produce ectopic hormones (e.g., ACTH, ADH), calcitonin is not the characteristic marker.
- **C. CA 15-3** — A tumor marker primarily associated with **breast cancer** monitoring; not relevant to SCLC.

ProGRP (pro-gastrin-releasing peptide) is another important SCLC marker with possibly even better specificity than NSE, but it was not among the answer choices.[7][8][9]

Would you like to explore the paraneoplastic syndromes commonly associated with small cell lung cancer?

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Question 124

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?

A. Increase the FiO2
B. Increase the tidal volume
C. Increase PEEP
D. Increase the respiratory rate

https://openevidence.com/ask/d3675f41-6585-4747-a098-5db155508e23

The correct answer is **C. Increase PEEP**.

This patient has **severe postoperative hypoxemia** (PaO2 54 mmHg on FiO2 50%, P/F ratio of 108) with bilateral rales after emergent abdominal surgery. The current **PEEP of 2.5 cm H2O is subtherapeutically low**. PEEP recruits collapsed alveoli, increases functional residual capacity, reduces intrapulmonary shunt, and improves ventilation-perfusion matching — directly addressing the likely mechanism of hypoxemia in this postoperative setting.[1][2] In laparotomy patients, increasing PEEP from 0 to 5 cm H2O significantly reduced pulmonary shunt from 12% to 6%.[3] Nitrous oxide use during the case may have further promoted absorption atelectasis.[4][5]

Why the other options are incorrect:

- **A. Increase FiO2** — Hypoxemia driven by intrapulmonary shunt (atelectasis, alveolar collapse) responds poorly to increasing FiO2 alone. While temporarily raising FiO2 is reasonable as a bridge, the fundamental problem is derecruitment, which requires PEEP to correct.[1][2]
- **B. Increase tidal volume** — The tidal volume of **1000 mL is already excessive** for a 70-year-old woman (likely >12 mL/kg predicted body weight). Increasing it further risks ventilator-induced lung injury and barotrauma. Lung-protective ventilation targets **6–8 mL/kg** predicted body weight; the tidal volume should actually be reduced.
- **D. Increase respiratory rate** — Respiratory rate primarily affects minute ventilation and CO2 clearance. The pCO2 is already low at 31 mmHg; increasing the rate would worsen the respiratory alkalosis without meaningfully improving oxygenation.

An additional concern in this case is the markedly elevated tidal volume, which should be reduced to lung-protective levels (~6–8 mL/kg predicted body weight) alongside the PEEP increase, with monitoring of plateau pressures, oxygenation, and hemodynamics during titration.[6]

Would you like to explore evidence-based strategies for PEEP titration in postoperative hypoxemia?

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Question 125

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?

A. Voriconazole
B. Amphotericin B and itraconazole
C. Erythromycin
D. Azithromycin and ethambutol

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The correct answer is **D. Azithromycin and ethambutol**.

This presentation is consistent with **disseminated Mycobacterium avium complex (MAC)** infection. Several features point to MAC rather than M. tuberculosis:

- **CD4 count of 49/mm³** — MAC typically occurs at CD4 <50 cells/mm³[1][2]
- **Acid-fast organisms in blood cultures** — MAC commonly causes mycobacteremia, with blood cultures positive in >90% of diagnosed cases; disseminated TB less commonly presents this way[3]
- **Hepatosplenomegaly** — reticuloendothelial organ involvement (liver, spleen, bone marrow) is the hallmark of disseminated MAC[2]
- **Negative PPD (4 mm)** — below the 5 mm threshold for HIV-positive patients, arguing against TB
- **Constitutional symptoms** (fever, weight loss, malaise, abdominal pain) are typical of disseminated MAC[2]

Per NIH/IDSA guidelines, the preferred treatment for disseminated MAC is a **macrolide (clarithromycin or azithromycin) plus ethambutol**, with or without rifabutin.[1][2][4] Macrolide monotherapy leads to resistance emergence within 12–16 weeks and is not recommended.[1][5] Treatment should continue for a **minimum of 12 months**, with discontinuation considered only after sustained immune reconstitution (CD4 >100 for ≥6 months on ART).[4]

The other options are incorrect: voriconazole (A) and amphotericin B with itraconazole (B) are antifungals, not anti-mycobacterial agents. Erythromycin (C) lacks clinically meaningful activity against MAC.

Would you like to explore current guidelines for MAC prophylaxis initiation and discontinuation in the setting of ART?

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Question 126

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?

A. Cognitive behavioral therapy (CBT)
B. The patient does not require any intervention
C. Electroconvulsive therapy (ECT)
D. Refer to outpatient group therapy

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A. Cognitive behavioral therapy (CBT).

This presentation fits **delusional disorder, persecutory type** — a fixed, systematized belief of being conspired against/tracked, with **no hallucinations, no disorganization, and preserved functioning outside the delusional theme** (steady employment, independent living, longstanding community residence).[1] DSM-5 requires ≥1 month of delusions, that criterion A for schizophrenia has never been met, and that behavior is not otherwise bizarre or odd apart from the delusion's ramifications.[1] Of the listed options, CBT — specifically CBT for psychosis — is the appropriate initial intervention, with meta-analytic evidence of benefit for delusions (g = 0.37 vs. any control).[2][3]

Why the other options are wrong

- **B. No intervention** — She has a psychiatric disorder with real-world consequences. Setting bear traps creates a hazard to neighbors and to herself, and persecutory-type delusions carry recognized risk of anger and violence toward perceived persecutors. Risk assessment and treatment are warranted.[1]

- **C. ECT** — Reserved for treatment-refractory illness, catatonia, or severe mood disorder with psychosis; not an initial treatment for uncomplicated delusional disorder.
- **D. Outpatient group therapy** — Poorly suited to a suspicious, socially withdrawn, paranoid patient; group exposure typically worsens guardedness and undermines engagement. Individual work building a therapeutic alliance comes first.

Practical caveats beyond the exam answer

- **Antipsychotics remain the mainstay of treatment for delusional disorder in real practice**, though the evidence base is weak and consists largely of case series and observational data, with good response in roughly one-third of patients. In a Swedish national cohort of 9,076 patients, antipsychotic use was associated with a 46% lower risk of psychosis-related hospitalization (HR 0.54, 95% CI 0.38–0.77). Cochrane found only limited, weak evidence for cognitive therapy in this specific disorder — so CBT is the best choice among those offered, not necessarily the best treatment available.[4][5][6][7]
- **Rule out organic and substance causes** before settling on the diagnosis (Criterion E) — stimulant or cannabis use, delirium, thyroid disease, neurologic disease, and medication effects.[1]
- **Do not directly confront or endorse the delusion.** Engage around the distress and the functional consequences (safety of the traps, legal exposure) rather than the veracity of the belief; insight is characteristically absent even when the patient can state that others find the belief irrational.[1]
- Monitor for emergence of hallucinations, disorganization, or negative symptoms, which would reclassify this as schizophrenia spectrum illness.[1][8]

Would you like to explore engagement strategies for patients with delusional disorder who lack insight and refuse medication?

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Question 127

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?

A. Methylphenidate
B. Sodium oxybate
C. Imipramine
D. Increase daytime naps

https://openevidence.com/ask/bcc399cd-c07f-4371-8d33-5f0f641c4357

The answer is **A. Methylphenidate**.

This patient presents with **excessive daytime sleepiness (EDS) despite adequate nighttime sleep**, no features of obstructive sleep apnea (no snoring, no witnessed apneas), and **a mean sleep latency of 6 minutes on MSLT** (≤8 minutes indicates pathologic sleepiness).[1] This constellation is consistent with a **central disorder of hypersomnolence** — either narcolepsy type 2 or idiopathic hypersomnia. Distinguishing between these two entities requires assessment for sleep-onset REM periods (SOREMPs) on MSLT, which is not specified in the stem, but the treatment approach for EDS is similar.

Why methylphenidate: CNS stimulants such as **methylphenidate and amphetamines** are established pharmacologic treatments for EDS in central hypersomnolence disorders.[1][2] Wake-promoting agents (modafinil/armodafinil) are often considered first-line in practice due to a more favorable side-effect profile, but methylphenidate is the only stimulant option among the choices and is an appropriate treatment for EDS.[3][4]

Why not the other options:

- **Sodium oxybate (B):** Effective for both EDS and cataplexy, and FDA-approved for narcolepsy and idiopathic hypersomnia. However, it is a CNS depressant that consolidates nighttime sleep and is particularly advantageous when **cataplexy** or **disrupted nighttime sleep** is present — neither of which applies here. Among these choices, a stimulant is the more straightforward first-line approach for isolated EDS.[1][5][6]
- **Imipramine (C):** A tricyclic antidepressant used off-label primarily for **cataplexy** (via REM sleep suppression), not for EDS. This patient has no cataplexy.[2][7]
- **Increased daytime naps (D):** Scheduled brief naps can be a useful **behavioral adjunct** but are insufficient as primary treatment for a central hypersomnolence disorder.[3][8]

Would you like to explore how MSLT findings (particularly SOREMPs) distinguish narcolepsy type 2 from idiopathic hypersomnia?

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Question 128

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?

A. Surgical debridement
B. Negative pressure wound management
C. Sternal wiring
D. Sternal fixation

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The most appropriate next step is **A. Surgical debridement**.[1][2]

This patient presents with a **post-sternotomy wound infection** 3 weeks after CABG, characterized by wound dehiscence, necrotic tissue, purulent discharge, and CT findings of perisurgical fluid collection with fat stranding. Multiple risk factors are present, including **diabetes mellitus** and the cardiac surgery itself.

The **ACCF/AHA guidelines** recommend that a deep sternal wound infection be treated with **aggressive surgical debridement** in the absence of complicating circumstances, followed by primary or secondary closure with muscle or omental flap.[1] The **AATS guidelines** similarly state that treatment principles include **debridement of all devitalized and necrotic tissue, drainage of all infected spaces**, antibiotic therapy, and techniques to achieve sternal closure.[2] Early debridement has been associated with fewer hospital admissions and shorter total hospital stays compared to delayed intervention.[3]

Why the other options are incorrect:

- **B. Negative pressure wound management (NPWT)** — NPWT serves as a **bridge to closure after debridement**, not as a first-line stand-alone therapy. It is initiated when delayed sternal closure is anticipated following debridement of the infected wound.[2]

- **C. Sternal wiring / D. Sternal fixation** — These are **reconstruction steps** performed only after adequate debridement and infection control have been achieved. Closing or stabilizing a sternum over necrotic, infected tissue would trap the infection and worsen outcomes.[2][4]

The presence of necrotic tissue and pus mandates that the **source control step — surgical debridement — must precede** any reconstructive or adjunctive wound therapy.

Would you like to explore antibiotic selection and duration for post-sternotomy wound infections?

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Question 129

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?

A. Macrocytic red blood cells
B. Hyperchromic red blood cells
C. Microcytic red blood cells
D. Bite cells

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The answer is **C. Microcytic red blood cells**.

The **Kozak consensus sequence** (GACACCATGG) of the beta-globin gene plays a critical role in translation initiation. The first identified mutation in this sequence, **β+45 G→C**, reduces beta-globin chain translation efficiency by approximately 30%, consistent with **β+-thalassemia**.[1] When compound heterozygous with a severe beta-thalassemia mutation (or coinherited with extra alpha-globin gene copies), this produces a phenotype of **thalassemia intermedia**.[1]

The peripheral blood smear in beta-thalassemia intermedia shows findings similar to beta-thalassemia major: **microcytosis, hypochromia**, anisocytosis, poikilocytosis, and target cells.[2] This results from deficient beta-globin chain production, which impairs hemoglobin synthesis and leads to smaller, paler red blood cells.[3][4]

The other choices are incorrect:

- **A. Macrocytic red blood cells** — Thalassemias produce microcytic, not macrocytic, anemia. Macrocytosis is seen in B12/folate deficiency or myelodysplasia.
- **B. Hyperchromic red blood cells** — Thalassemia causes **hypo**chromia due to reduced hemoglobin content, not hyperchromia.
- **D. Bite cells** — Bite cells are characteristic of **G6PD deficiency**, where Heinz bodies are removed by splenic macrophages, not of thalassemia.

Would you like to explore other 5' UTR mutations in the beta-globin gene and their clinical significance?

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Question 130

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?

A. BCR-ABL gene
B. BRCA gene
C. FA gene
D. HFE gene

https://openevidence.com/ask/27d95500-db70-43ad-9863-ed91e480a254

The correct answer is **D. HFE gene**.

The **HFE gene** (homeostatic iron regulator, chromosome 6p22.2) is the gene screened in hereditary hemochromatosis. Approximately **95% of hereditary hemochromatosis cases** are caused by mutations in HFE, most commonly the **C282Y homozygous mutation** (p.Cys282Tyr), which accounts for ~90% of cases.[1][2] The C282Y mutation disrupts a disulfide bond in the HFE protein, impairing its interaction with β2-microglobulin and transferrin receptor 2, ultimately leading to **hepcidin deficiency** and uncontrolled intestinal iron absorption.[1] A compound heterozygous state (C282Y/H63D) accounts for an additional ~5% of cases.[2]

The other answer choices are associated with different conditions:

- **A. BCR-ABL** — the fusion gene (Philadelphia chromosome) associated with **chronic myelogenous leukemia**
- **B. BRCA** — tumor suppressor genes associated with **hereditary breast and ovarian cancer**
- **C. FA (Fanconi anemia)** — genes associated with **Fanconi anemia**, a bone marrow failure syndrome

In this clinical scenario, first-degree relatives of an affected individual should undergo **HFE genotyping**, which the ACG guidelines recommend as the appropriate screening strategy for family members.[3] Notably, this patient's normal iron studies are consistent with either a non-carrier state or an early/non-penetrant genotype, as clinical penetrance of even C282Y homozygosity is incomplete (50–90%) and is lower in women.[1]

Would you like to explore the recommended screening and monitoring approach for first-degree relatives of hemochromatosis patients?

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Question 131

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?

A. Salmonella enteritidis
B. Listeria monocytogenes
C. Staphylococcus aureus
D. Vibrio cholerae

https://openevidence.com/ask/0082c50b-ef10-4874-b2c2-b20036908bc1

The answer is **C. Staphylococcus aureus**.

The **rapid onset of symptoms within 2–3 hours** after eating unrefrigerated food is the hallmark of **staphylococcal food poisoning**, which results from ingestion of a **preformed, heat-stable enterotoxin** rather than a true enteric infection.[1][2] S. *aureus* typically causes illness **2–7 hours** after ingestion of improperly stored food, with abdominal cramping, diarrhea, and often vomiting.[1] Contamination by food workers handling cooked food, followed by holding at room temperature (as in this unrefrigerated buffet), is the classic epidemiologic scenario.[3][4]

Why the other options are incorrect:

- **A. Salmonella enteritidis** — Incubation period is typically **12–72 hours**, far longer than this patient's 2–3 hour onset.[5]
- **B. Listeria monocytogenes** — Invasive listeriosis has an incubation of **days to weeks**; even noninvasive gastroenteritis typically requires ≥24 hours.[6]
- **D. Vibrio cholerae** — Associated with **contaminated water** in endemic regions, not a barbecue buffet in a typical setting; incubation is usually **12 hours to 5 days**.[7]

Outbreaks from preformed bacterial toxins (S. *aureus*, B. *cereus*, C. *perfringens*) have the **shortest incubation periods** (median 4–10 hours) of all foodborne pathogens, and the combination of an

unrefrigerated buffet, rapid onset, and self-limiting watery diarrhea makes S. *aureus* the most likely cause here.[5][8] The illness is self-limiting, typically resolving within **24–48 hours**, and management is **supportive** with fluid rehydration; antibiotics are not indicated.[2]

Would you like to explore how to differentiate S. aureus food poisoning from Bacillus cereus emetic syndrome?

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Question 132

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?

A. Primary respiratory acidosis
B. Primary respiratory alkalosis
C. Compensatory respiratory acidosis
D. Anion gap metabolic acidosis with respiratory alkalosis

https://openevidence.com/ask/e2c1b49c-8d35-49e0-b3b8-ed06e05cb555

The answer is **A. Primary respiratory acidosis**.

This patient has classic findings of **COPD**: 30-pack-year smoking history, barrel-shaped chest, pursed-lip breathing, diminished breath sounds bilaterally, flattened diaphragm on chest X-ray, and an **FEV1/FVC ratio of 60%** (obstructive physiology). The acute worsening represents a **COPD exacerbation** triggered by a viral upper respiratory infection.[1]

The fundamental acid-base disturbance in COPD is **CO2 retention (hypercapnia)** due to V/Q mismatch and impaired alveolar ventilation. Elevated PaCO2 drives carbonic acid formation ($CO_2 + H_2O \rightarrow H_2CO_3 \rightarrow HCO_3^- + H^+$), producing a **respiratory acidosis**.[2] The 2026 GOLD guidelines note that during COPD exacerbations, ABG may demonstrate **hypoxemia (PaO2 ≤ 60 mmHg) and/or hypercapnia with acidosis (PaCO2 > 45 mmHg, pH < 7.35)**.[1][3] This patient's advanced structural changes (barrel chest, flattened diaphragm) suggest significant hyperinflation and gas trapping consistent with chronic CO2 retention, which would worsen acutely during an exacerbation.[1]

Notably, in chronic hypercapnia, renal compensation raises bicarbonate to buffer pH; during an acute exacerbation superimposed on chronic disease, the acute rise in PaCO2 overwhelms compensation, producing an acute-on-chronic respiratory acidosis — but the **primary** disorder remains respiratory acidosis.[4][5]

Why not the other options:

- **B (Primary respiratory alkalosis)** — Would indicate hyperventilation-driven CO2 washout, as in pulmonary embolism or early sepsis. The obstructive physiology here impairs CO2 elimination rather than enhancing it.
- **C (Compensatory respiratory acidosis)** — Implies CO2 retention is a secondary response to a primary metabolic alkalosis. No clinical features suggest metabolic alkalosis.
- **D (Anion gap metabolic acidosis with respiratory alkalosis)** — This mixed disturbance is characteristic of salicylate toxicity or sepsis with concurrent lactic acidosis. Neither applies here.

Would you like to explore the stepwise management of acute COPD exacerbations, including indications for noninvasive ventilation?

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Question 133

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?

A. 0%
B. 25%
C. 50%
D. 100%

https://openevidence.com/ask/6ea548e8-18fe-460b-ae9d-c7904c68a0d4

The answer is **D. 100%**.

Hemophilia A is an **X-linked recessive** disorder caused by pathogenic variants in the *F8* gene on the X chromosome. A man affected with hemophilia A has the genotype X^h Y — his single X chromosome carries the mutant allele. Because **every daughter receives her father's only X chromosome**, all daughters of an affected male are **obligate carriers** (genotype X^h X), regardless of birth order.[1][2][3]

The key genetic principles:

- **Affected males transmit the *F8* pathogenic variant to all of their daughters and none of their sons**. Sons receive only the Y chromosome from their father and are unaffected.[2][4]
- **Daughters of male hemophilia patients are obligate carriers** — this is independent of the mother's carrier status (assuming the mother is unaffected, as stated).[5][6]
- The fact that the daughters are clinically "unaffected" is expected, since female carriers are heterozygous (X^h X) and typically have sufficient factor VIII activity (~50% of normal) for normal hemostasis, though up to 30% may have some bleeding tendency.[7][8]

Therefore, the probability that the **second daughter** — or any daughter — of this affected male is a carrier is **100%**, not 50%. The 50% probability applies to daughters of a **female carrier**, not daughters of an affected male.

Would you like to explore the clinical implications and management recommendations for obligate female carriers of hemophilia A?

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Question 134

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?

A. Tympanic membrane
B. Malleus
C. Incus
D. Cochlea

https://openevidence.com/ask/7de7fd70-1571-4d2a-a450-b09f2ee99deb

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The answer is **D. Cochlea**.

This presentation is classic **presbycusis (age-related sensorineural hearing loss)**: progressive bilateral hearing loss over a decade, difficulty with speech discrimination in background noise, tinnitus, and episodes of unsteadiness in an elderly patient.[1][2] The tuning fork findings confirm **sensorineural** rather than conductive hearing loss:

- **Weber test midline** (heard equally in both ears): This rules out a unilateral process and is expected in bilateral symmetric sensorineural hearing loss, since neither ear has an air-bone gap advantage.[3]
- **Rinne test positive** (air conduction > bone conduction): This is the normal pattern preserved in sensorineural hearing loss. A conductive loss (from tympanic membrane, malleus, or incus pathology) would produce a **negative Rinne** (bone conduction > air conduction).[3][4]

The **cochlea** is the primary site of pathology in presbycusis. Age-related degeneration affects cochlear sensory hair cells (particularly outer hair cells at the basal, high-frequency end), the stria vascularis, and spiral ganglion neurons.[1][5][6] Loss of outer hair cells impairs cochlear amplification, while neuronal degeneration underlies the characteristic difficulty with speech discrimination in noisy environments.[2][5]

Why not the other options:

- **Tympanic membrane (A), malleus (B), incus (C)** — These are components of the conductive apparatus. Impairment of any of these structures causes **conductive hearing loss**, which would produce a negative Rinne test (BC > AC) and Weber lateralization to the affected ear. The normal otoscopic exam and positive Rinne test exclude these.[4][7]

Would you like to explore current treatment options for presbycusis, including when cochlear implantation should be considered over hearing aids?

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Question 135

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?

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

https://openevidence.com/ask/e2cdc3cf-73d4-4300-9c90-7a5cf52994f0

C. Gram-negative, oxidase-positive bacilli — Pseudomonas aeruginosa.

Why this fits

- **Contact lens–associated keratitis is dominated by P. aeruginosa.** In the US, bacteria cause ~90% of contact lens–related keratitis, and Pseudomonas accounts for >40% of cases. The IDSA/ASM microbiology utilization guideline names P. aeruginosa the most common cause of contact lens–associated keratitis. A 7-year UK cohort of contact lens–related bacterial keratitis found P. aeruginosa in 49.3% of culture-positive cases, most in soft lens wearers. [1][2][3][4]
- **Clinical picture matches:** overnight/extended soft lens wear with poor hygiene, rapid onset (hours), severe pain, a **rapidly progressive deep stromal ulcer** with dense purulent/mucopurulent discharge. Pseudomonas produces proteases and elastase that cause rapid stromal melt.[5][6]
- **Microbiology:** P. aeruginosa is a **gram-negative, aerobic, non–lactose-fermenting bacillus that is oxidase-positive** (a key feature distinguishing it from Enterobacterales), motile by a polar flagellum, grows on MacConkey as colorless colonies, and produces pyocyanin/pyoverdine giving blue-green pigment and a grape-like odor.

- **Therapy is consistent:** topical ciprofloxacin 0.3% is FDA-approved for bacterial corneal ulcer and has strong antipseudomonal activity; a 9-year series of Pseudomonas keratitis isolates showed >85% ciprofloxacin susceptibility, supporting its empiric use.[7][8]

Why the other options are wrong

Option	Organism	Why it doesn't fit	Refs
A. Gram-negative, non–maltose-fermenting diplococci	Neisseria gonorrhoeae	Causes hyperacute purulent conjunctivitis with copious discharge and chemosis (neonates, or sexually active adults with autoinoculation); can penetrate intact cornea, but not the classic contact lens ulcer, and requires systemic ceftriaxone, not topical ciprofloxacin	[1]
B. Gram-negative, lactose-fermenting bacilli	E. coli / Klebsiella	Rare ocular pathogens; oxidase-negative and not associated with soft lens wear	[1]
D. Gram-positive, optochin-sensitive diplococci	Streptococcus pneumoniae	A genuine keratitis pathogen, but typically follows trauma, corneal epithelial defects, or dacryocystitis rather than extended lens wear; also has variable fluoroquinolone susceptibility	[2-3]

Practical note: despite the "textbook" answer, corneal scrapings for Gram stain and culture (not lens or lens-case cultures, which have high false-positive rates) should be obtained before or at initiation of therapy in any large, central, or vision-threatening ulcer, with urgent ophthalmology involvement.[3][8] Fortified topical antibiotics (e.g., tobramycin plus vancomycin) are preferred over fluoroquinolone monotherapy for large or visually significant infiltrates, particularly with hypopyon.[8] Contact lens wear must be discontinued and the lenses/case discarded.

Would you like to explore dosing regimens and when fortified antibiotics should replace fluoroquinolone monotherapy in severe Pseudomonas keratitis?

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Question 136

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?

A. Hemorrhagic diathesis
B. Ocular telangiectasias
C. Autoimmune endocrinopathy
D. Retained primary teeth

https://openevidence.com/ask/a33ecd70-9ea9-4ca9-b4b6-ef322a9198bb

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The answer is **C. Autoimmune endocrinopathy**.

The clinical presentation — a male infant with **watery diarrhea, eczematous dermatitis, failure to thrive, defective regulatory T cells, and a FOXP3 mutation** — is classic for **IPEX syndrome** (Immune dysregulation, Polyendocrinopathy, Enteropathy, X-linked).[1][2] FOXP3 is the master transcription factor required for differentiation and function of CD4+ regulatory T cells; its loss leads to multiorgan autoimmunity.[3][4]

Autoimmune endocrinopathy is a defining feature of IPEX — the "P" in the acronym. **Type 1 diabetes mellitus** is the most common endocrine manifestation, present in approximately 50–60% of patients, typically with neonatal or early infantile onset.[5][6] **Autoimmune thyroid disease** (usually hypothyroidism) is the next most frequent endocrinopathy.[2][3]

The other answer choices correspond to different primary immunodeficiencies:

- **A. Hemorrhagic diathesis** — characteristic of **Wiskott-Aldrich syndrome** (WAS gene; thrombocytopenia with small platelets, eczema, recurrent infections).
- **B. Ocular telangiectasias** — characteristic of **ataxia-telangiectasia** (ATM gene; cerebellar ataxia, oculocutaneous telangiectasias, immunodeficiency).

- **D. Retained primary teeth** — associated with **hyper-IgE (Job) syndrome** (STAT3 mutations; recurrent staphylococcal abscesses, elevated IgE, retained primary teeth, characteristic facies).

Would you like to explore the role of hematopoietic stem cell transplantation as definitive therapy for IPEX syndrome?

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Question 137

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?

A. Abdominal CT scan
B. Endoscopic ultrasonography
C. Abdominal ultrasound
D. Upper gastrointestinal endoscopy

https://openevidence.com/ask/a39403d7-026c-47d3-a8f9-6a164da74ffc

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The correct answer is **A. Abdominal CT scan**.

This patient presents with **steatorrhea** (bulky, foul-smelling, difficult-to-flush stools), **chronic postprandial epigastric pain**, and **significant weight loss** in the setting of heavy alcohol use (6–8 beers daily for 12 years) and a 37-pack-year smoking history — a classic presentation for **chronic pancreatitis with exocrine insufficiency**.[1]

Contrast-enhanced CT is the recommended first-line imaging study for suspected chronic pancreatitis. A JAMA review on chronic pancreatitis diagnosis states that CT should be performed for all patients with suspicion of CP, with an overall sensitivity of 75% (95% CI, 66%–83%) and specificity of 91% (81%–96%).[2] The ACG clinical guideline similarly recommends CT or MRI as first-line, with EUS reserved only if the diagnosis remains in question after cross-sectional imaging.[3] CT effectively identifies **calcifications, ductal dilation, parenchymal atrophy**, and complications, and is also critical for evaluating for **pancreatic malignancy**, which must be considered given the alarm features (weight loss, new pain in a heavy smoker).[4][5]

Why the other options are less appropriate:

- **B. Endoscopic ultrasonography** — EUS has high sensitivity (81%) but is invasive and operator-dependent. Guidelines uniformly reserve EUS for cases where CT and MRI are normal or inconclusive but clinical suspicion persists.[3][4]
- **C. Abdominal ultrasound** — Transabdominal US has the lowest sensitivity (67%) among imaging modalities for chronic pancreatitis and is limited by bowel gas and body habitus. Most guidelines do not recommend it as initial diagnostic imaging.[4][6]
- **D. Upper GI endoscopy** — Would evaluate for peptic ulcer disease or gastric pathology, but the combination of steatorrhea, weight loss, and heavy alcohol/smoking history makes pancreatic pathology far more likely and warrants pancreas-directed imaging first.

Would you like to explore the stepwise approach when initial CT is inconclusive in suspected chronic pancreatitis?

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Question 138

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?

A. Adenosine
B. Inorganic phosphate
C. Prostaglandin E2
D. Transforming growth factor beta

https://openevidence.com/ask/dc5e73dd-3954-421f-ab41-da7873aa2133

The answer is **A. Adenosine**.

During exertion, increased myocardial oxygen consumption leads to a **fall in the partial pressure of oxygen (PO_2) within cardiomyocytes**, which triggers the **breakdown of adenine nucleotides and local generation of adenosine**. This is the basis of the classic "adenosine hypothesis" proposed by Berne in 1963.[1] The locally produced adenosine diffuses to coronary resistance vessels and causes **vasodilation primarily through activation of A_2A receptors** on vascular smooth muscle cells, increasing adenylyl cyclase activity and cAMP levels, which relaxes smooth muscle and augments coronary blood flow.[2][3]

This mechanism is particularly relevant to exercise stress testing — pharmacologic stress agents like adenosine and regadenoson exploit this same pathway. In normal coronary arteries, adenosine produces marked vasodilation and increases myocardial blood flow by 200–350%, whereas stenotic vessels with already-recruited vasodilator reserve cannot augment flow proportionally, creating a perfusion mismatch detectable on imaging.[4][5]

Regarding the other options:

- **Inorganic phosphate** is a byproduct of ATP hydrolysis in skeletal muscle contraction but is not the primary recognized local mediator of coronary vasodilation during exercise.[6]
- **Prostaglandin E_2** does accumulate in the interstitium during exercise and may contribute to skeletal muscle hyperemia, but it is not the principal local metabolic vasodilator of the coronary circulation.[6][7]
- **Transforming growth factor beta (TGF-β)** is involved in tissue remodeling and fibrosis, not acute exercise-induced coronary vasodilation.

Would you like to explore how exercise versus pharmacologic stress testing detects coronary artery disease?

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Question 139

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?

A. Focal segmental glomerulosclerosis
B. Ischemic acute tubular necrosis
C. Nephrotoxic acute tubular necrosis
D. Toxic tubulointerstitial nephritis

https://openevidence.com/ask/976fa0a1-d4a9-4969-9f36-03e8c04a3479

D. Toxic tubulointerstitial nephritis. Years of unsupervised over-the-counter analgesic use (NSAIDs ± acetaminophen combinations) producing an indolent decline in GFR, low-grade tubular-range proteinuria (1+), and a bland urine sediment, with a biopsy showing eosinophilic and diffuse interstitial inflammation, is the classic picture of drug-induced (toxic/hypersensitivity) tubulointerstitial nephritis.[1][2] Frequent interstitial eosinophils specifically point to a drug etiology, and eosinophils permeating the tubular basement membrane ("eosinophilic tubulitis") is highly suggestive of a hypersensitivity/drug-induced process.[1]

Why the features fit

- **Exposure and latency:** NSAID-associated interstitial nephritis typically follows months of continuous use (often 6–18 months) rather than days, and characteristically lacks the classic triad of fever, rash, and peripheral eosinophilia seen with β-lactams.[1][3]
- **Urinalysis:** Bland sediment with modest proteinuria and no casts or dysmorphic RBCs — no granular/muddy-brown casts (ATN) and no nephritic sediment.[4]
- **Histology:** Interstitial edema, diffuse mononuclear/eosinophilic infiltrate, and tubulitis; glomeruli and vessels are typically spared. With chronicity this evolves to interstitial fibrosis and tubular atrophy, matching the progressive creatinine rise over 2 years. Long-

term analgesic use is one of the most common identifiable causes of chronic interstitial nephritis.[1][5]

Why the other options are less likely

- **A. FSGS** would produce heavier, glomerular-range proteinuria and glomerular scarring on biopsy, not an eosinophil-rich interstitial infiltrate; available data do not support an NSAID–FSGS relationship (NSAID-associated glomerular disease is typically minimal change disease, usually accompanied by interstitial nephritis).[1]
- **B. Ischemic ATN** requires a hypoperfusion insult and presents as abrupt AKI with muddy-brown granular casts; histology shows brush-border loss, epithelial sloughing, and cast obstruction with only mild leukocyte infiltration — not diffuse eosinophilic inflammation.[6]
- **C. Nephrotoxic ATN** (contrast, aminoglycosides, cisplatin) likewise shows tubular epithelial necrosis without a prominent interstitial inflammatory infiltrate. NSAIDs can cause hemodynamically mediated acute tubular injury, but that is an acute, sediment-positive event without eosinophilic interstitial inflammation.[1][6]

Management implication: Discontinuation of the offending analgesic is the mainstay; early corticosteroids (within ~7 days of diagnosis) may improve renal recovery in acute interstitial nephritis, but benefit is markedly attenuated once interstitial fibrosis is established.[7] Expediting definitive hip arthroplasty and substituting non-NSAID analgesia addresses the driver of ongoing exposure.

Would you like to explore the evidence on corticosteroid timing and dosing in drug-induced interstitial nephritis?

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Question 140

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?

A. BiPAP
B. Chest tube placement
C. Intubation
D. Needle decompression

https://openevidence.com/ask/5f0cab84-3f91-4901-b9c1-0e747688452b

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The best next step is **A. BiPAP (noninvasive positive pressure ventilation)**. This patient has a **severe COPD exacerbation with persistent hypoxemia (SpO_2 80%) despite maximal initial medical therapy** (bronchodilators, magnesium, systemic corticosteroids, and supplemental oxygen). He remains alert and able to communicate, making him an appropriate candidate for noninvasive ventilation (NIV) before proceeding to intubation.[1][2]

Why BiPAP is preferred here:

- The **2026 GOLD guidelines** recommend NIV as the **first-line ventilatory support** for COPD exacerbations with respiratory failure despite optimal medical therapy, with RCTs demonstrating an **80–85% success rate**. NIV improves oxygenation, reduces work of breathing, and — critically — **decreases intubation rates, mortality, and length of stay**.[1][2][3]
- The ERS/ATS guideline similarly recommends NIV for patients with **severe dyspnea and clinical signs of increased work of breathing** (as seen here with tachypnea at 33/min and poor air movement).[4]

> "Face-mask noninvasive ventilation consistently showed success in preventing intubation and decreasing hospital mortality among these patients. Noninvasive ventilation is therefore strongly recommended as the first-line therapy for this population."
>
> —Laveena Munshi, M.D. et al., University of Toronto and other institutions. Noninvasive Respiratory Support for Adults with Acute Respiratory Failure. N Engl J Med. November 03, 2022.
>
> Used under license from The New England Journal of Medicine.

Why not the other options:

- **C. Intubation** would be appropriate if this patient had **altered mental status, inability to protect the airway, or hemodynamic instability**, or if BiPAP fails to improve his respiratory status. Since he is conscious and communicating, a trial of NIV should precede invasive ventilation.[1][4]
- **B. Chest tube** and **D. Needle decompression** would be indicated for pneumothorax or tension pneumothorax, respectively. This patient has **bilateral wheezes** (not unilateral absent breath sounds), and no findings suggesting pneumothorax (tracheal deviation, subcutaneous emphysema, hyperresonance).

An important caveat: an SpO_2 of 80% despite 100% oxygen is concerning and warrants an **urgent ABG** to assess for severity of hypercapnia and acidosis, and close reassessment after initiating BiPAP. If the patient deteriorates — worsening mental status, fatigue, or failure to improve within 1–2 hours — escalation to intubation should not be delayed.[1][5]

Would you like to explore the criteria for escalating from BiPAP to intubation in COPD exacerbations?

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Question 141

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?

A. Radiation therapy
B. Intravenous dexamethasone therapy
C. Intravenous acyclovir therapy
D. Intravenous ceftriaxone and azithromycin therapy

https://openevidence.com/ask/2dc4828f-617f-4cc0-b043-550c99e9ab07

The answer is **B. Intravenous dexamethasone therapy**.[1][2][3]

This patient presents with classic **malignant spinal cord compression (MSCC)**: upper motor neuron signs (**hyperreflexia, bilateral Babinski**), a **T4 sensory level**, **3/5 lower extremity weakness**, and **bowel/bladder dysfunction** — in the setting of a likely advanced malignancy (60 pack-year smoker with hemoptysis, weight loss, and multiple bilateral pulmonary opacities).[2][4]

Why dexamethasone first, not radiation therapy?

The NCCN CNS guideline algorithm for metastatic spine tumors with spinal cord compression directs that **steroids be initiated immediately** as the first treatment step, before proceeding to definitive therapy (surgery ± RT, or primary RT).[1] Corticosteroids should be administered promptly even before confirmatory imaging when cord compression is strongly suspected on clinical grounds.[5][6] Dexamethasone reduces vasogenic edema, improves neurologic function,

and alleviates pain in the acute setting, buying critical time before definitive treatment can be arranged.[6][7]

A typical regimen is **dexamethasone 10 mg IV**, followed by **4 mg every 6 hours**, with a subsequent taper during radiation therapy.[6] The NCCN footnotes note the minimum dose is 4 mg every 6 hours, with doses ranging from 10–100 mg depending on severity.[1] An **urgent whole-spine MRI** and **multidisciplinary consultation** (radiation oncology, spine surgery) should follow immediately to plan definitive treatment.[1][2][3]

Why not the other options?

- **A (Radiation therapy)** is the definitive treatment for most patients with MSCC but is not the immediate first step — steroids precede and supplement RT.[1][5][8]
- **C (Acyclovir)** would treat herpes zoster. While the pain has a burning quality, bilateral upper motor neuron signs with a discrete sensory level and bowel/bladder dysfunction indicate cord compression, not a dermatomal radiculopathy.
- **D (Ceftriaxone and azithromycin)** would treat community-acquired pneumonia. The bilateral round opacities of varying sizes are consistent with metastases (cannonball lesions), not an infectious consolidation, and would not explain the neurologic findings.

Would you like to explore the evidence comparing surgical decompression versus radiation alone for metastatic spinal cord compression?

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Question 142

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?

A. Alprazolam
B. Cognitive behavioral therapy
C. Fluoxetine
D. Psychodynamic psychotherapy

https://openevidence.com/ask/87ae7917-ab07-458f-86d5-d2f05ec7d053

The answer is **B. Cognitive behavioral therapy (CBT)**.

This patient presents with a classic **specific phobia (situational type — aviophobia)**, characterized by persistent, irrational fear of flying triggered by a specific event (turbulence during a flight), marked avoidance behavior over 15 years, recognition that the fear is excessive, and significant functional impairment in personal and professional life.

CBT with exposure therapy is the first-line treatment for specific phobias.[1][2][3] Exposure-based treatment produces large effect sizes relative to no treatment and outperforms both placebo conditions and alternative psychotherapeutic approaches.[4] A key component involves **graded exposure to the feared stimulus** — either in vivo (e.g., airport visits, simulated flights, actual flights) or through virtual reality — to break the cycle of avoidance and enable new safety learning.[1][2] Meta-analytic data show that CBT achieves very large effect sizes (Hedges $g > 1.0$) for specific phobias, among the largest of any anxiety disorder treated with CBT.[5]

Why the other options are incorrect:

- **Alprazolam (A):** Benzodiazepines may reduce acute anxiety but do not address the underlying phobia and can interfere with extinction learning during exposure. They are not recommended as primary treatment for specific phobias.
- **Fluoxetine (C):** SSRIs are first-line pharmacotherapy for generalized anxiety disorder, social anxiety disorder, and panic disorder, but **pharmacotherapy has limited evidence and a minimal role in treating specific phobias**.[2][3]
- **Psychodynamic psychotherapy (D):** The evidence base for psychodynamic therapy in anxiety disorders is not as strong as for CBT, and it is not considered first-line.[1][3]

Would you like to explore the comparative effectiveness of virtual reality versus in vivo exposure therapy for specific phobias?

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Question 143

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?

A. Desmosomes
B. Gap junctions
C. Hemidesmosomes
D. Tight junctions

https://openevidence.com/ask/93e9903a-cf6d-42d0-94a6-2f78351e9a84

The correct answer is **C. Hemidesmosomes**.

This clinical presentation — an elderly patient with **tense, pruritic bullae** and a biopsy showing **linear IgG deposition at the epidermal basement membrane** — is classic for **bullous pemphigoid (BP)**, the most common autoimmune blistering disease.[1][2] The autoantibodies in BP target two **hemidesmosomal proteins**: **BP180** (type XVII collagen), a transmembrane glycoprotein, and **BP230**, an intracellular plakin family protein.[3] Both are structural components of hemidesmosomes at the dermal-epidermal junction, which anchor basal keratinocytes to the underlying basement membrane.[1][4]

Binding of IgG autoantibodies to these hemidesmosomal antigens — particularly the NC16A domain of BP180 — triggers complement activation, inflammatory cell recruitment, and protease release, ultimately causing subepidermal blistering.[1][5]

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 and a "tombstone" pattern on histology.[6]
- **B. Gap junctions** — Involved in intercellular communication; not targeted in autoimmune blistering diseases.

- **D. Tight junctions** — Form epithelial permeability barriers; not a target in pemphigoid or pemphigus.

Would you like to explore the key clinical and histopathologic differences between bullous pemphigoid and pemphigus vulgaris?

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Question 144

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?

A. Streptococcus pneumoniae
B. Mycoplasma pneumoniae
C. Chlamydophila pneumoniae
D. Haemophilus influenzae

https://openevidence.com/ask/056d3111-603f-4b6f-b109-050630016c64

The answer is **A. Streptococcus pneumoniae**.

This case presents a classic **biphasic illness** consistent with bacterial superinfection following a viral upper respiratory infection. The initial phase (fever, sore throat, generalized aches for 10 days with initial improvement) represents a viral URI, followed by clinical worsening with new productive purulent sputum, high-grade fever, and respiratory distress — the hallmark pattern of secondary bacterial pneumonia.[1][2]

Several features point specifically to S. *pneumoniae*:

- **Lobar consolidation** (right upper lobe infiltrate) is the radiographic hallmark of typical bacterial pneumonia, most commonly pneumococcal.[3]
- **Purulent (green) sputum** and **leukocytosis** (15,000/mm³) indicate a pyogenic bacterial process rather than an atypical pathogen.
- **S. pneumoniae is the most common bacterial cause of community-acquired pneumonia** across all age groups, and the paradigmatic organism in post-viral bacterial superinfection.

The combination of S. pneumoniae with preceding viral respiratory infection is the most frequent viral-bacterial pairing identified in pneumonia studies.[1][4][5][6]

Why not the other choices:

- **Mycoplasma pneumoniae and Chlamydophila pneumoniae** (B, C) cause **atypical pneumonia**, which typically presents with a dry, nonproductive cough, diffuse or interstitial infiltrates (not lobar consolidation), and a more indolent course without marked leukocytosis.[7]
- **Haemophilus influenzae** (D) is a less common cause of CAP in adolescents, particularly in vaccinated populations, and is not the classic post-viral superinfection pathogen.[5]

Would you like to explore empirical antibiotic selection for this patient's community-acquired pneumonia?

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Question 145

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?

A. Enzyme-linked immunosorbent assay (ELISA)
B. Rapid HIV antibody test
C. Polymerase chain reaction
D. Southern blot

https://openevidence.com/ask/9b6d00f9-0caa-473f-a9cd-696139185050

The answer is **C. Polymerase chain reaction (PCR)**.

PCR-based nucleic acid tests (NATs) — which detect **HIV DNA or RNA genetic material** — are the gold standard for diagnosing HIV infection in neonates and infants younger than 18 months.[1][2] The key reason the other options are incorrect:

- **ELISA (A) and Rapid HIV antibody test (B)** detect **antibodies**, not viral genetic material. In neonates, **passively transferred maternal IgG antibodies** cross the placenta and can persist in the infant's bloodstream until approximately 18 months of age, rendering antibody-based assays unreliable (high false-positive rate). These tests cannot distinguish between true infant infection and passive maternal antibody transfer.[1][2][3]
- **Southern blot (D)** is a laboratory technique used to detect specific DNA sequences but is not a standard clinical assay for HIV diagnosis. It is too slow, labor-intensive, and not used in the clinical diagnostic algorithm for HIV.

The question specifically asks which assay detects the **genetic material** of HIV — PCR directly amplifies and detects HIV nucleic acids (DNA or RNA), making it the only answer choice that both detects genetic material and is clinically used for neonatal HIV diagnosis.[2][4][5]

Would you like to explore the recommended testing schedule for HIV-exposed neonates?

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Question 146

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?

A. Doxycycline
B. Ciprofloxacin
C. Erythromycin
D. Antibiotics would not be appropriate at this time

https://openevidence.com/ask/378ec331-7c87-4efa-837c-96cea6007e72

The correct answer is **A. Doxycycline**.

This patient presents with an **acute exacerbation of COPD (AECOPD)** characterized by all three cardinal symptoms: **increased dyspnea, increased sputum volume, and purulent sputum**, along with fever and tachycardia. He has already been started on oxygen and oral prednisone. The question is what additional treatment to consider.

Why antibiotics are indicated

Per the **2026 GOLD guidelines**, antibiotics are indicated in AECOPD when patients have **purulent sputum**, prior positive sputum culture, or require mechanical ventilation (Evidence A).[1][2] The presence of copious greenish-yellow purulent sputum in this patient meets the threshold for antibiotic initiation. A JAMA review similarly recommends oral antibiotics such as **TMP-SMX, doxycycline, or macrolides as first-line treatment** in patients exhibiting increasing sputum volume and purulence.[3]

Why doxycycline over the other options

- **Doxycycline** is a well-established **first-line antibiotic** for AECOPD, listed as such in guidelines from GOLD, the VA, the AAFP, and the ERS/ATS. A real-world cohort study demonstrated that doxycycline supplementing systemic corticosteroids significantly **reduced short-term treatment failure** (aOR 0.53, 95% CI 0.28–0.99).[1][3][4][5][6]
- **Ciprofloxacin (B)** is a fluoroquinolone with **relatively poor pneumococcal activity** and is generally reserved for patients with risk factors for gram-negative or resistant organisms (repeated exacerbations, prior Pseudomonas isolation, frequent antibiotic use). No such risk factors are described in this patient.[1][3]
- **Erythromycin (C)** is an older macrolide with a less favorable side-effect profile (more GI effects, more drug interactions) compared to azithromycin, and is not a standard first-line choice for AECOPD in current guidelines.[4]
- **No antibiotics (D)** is incorrect given the clear indication: purulent sputum with increased dyspnea.[1][7]

Would you like to explore the recommended duration and dosing of antibiotics and corticosteroids for COPD exacerbations?

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Question 147

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?

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

https://openevidence.com/ask/9c723e9f-1eef-4d05-a439-48b5ba0dc80d

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The answer is **B. Impaired CSF flow through the arachnoid granulations**.

This child's history of bacterial meningitis (fever, irritability, neck rigidity treated with antibiotics) followed by morning headaches with nausea/vomiting and MRI showing **both ventricular enlargement and enlarged subarachnoid space** is classic for **communicating hydrocephalus** — one of the most common complications of bacterial meningitis.[1][2]

The critical imaging clue is that **both the ventricles and subarachnoid space are dilated**. This pattern indicates that CSF flows freely from the ventricles into the subarachnoid space but cannot be adequately reabsorbed. Post-meningitic inflammatory exudate and fibrosis scar the **arachnoid granulations**, impairing CSF resorption into the dural venous sinuses.[1][3][4] As noted in a study of community-acquired bacterial meningitis, "almost all patients had communicating hydrocephalus…reflecting the failure of cerebrospinal resorption through arachnoid granulations due to severe infection".[1]

Why the other choices are incorrect:

- **A (Increased CSF production):** Overproduction hydrocephalus is exceedingly rare (e.g., choroid plexus papilloma) and is not a sequela of meningitis.

- **C (Impaired CSF drainage into the subarachnoid space):** This describes **obstructive (non-communicating) hydrocephalus** — the ventricles would enlarge but the subarachnoid space would be compressed or normal, not enlarged.
- **D (Impaired CSF drainage into the fourth ventricle):** This also describes an intraventricular obstruction (e.g., aqueductal stenosis), which would cause selective dilation of the lateral and third ventricles with a normal-sized fourth ventricle and subarachnoid space.

Would you like to explore surgical management options for post-infectious hydrocephalus in children?

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Question 148

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?

A. Anti-cardiolipin
B. Anti-centromere
C. Anti-histone
D. Anti-ribonucleoprotein

https://openevidence.com/ask/735b79f1-a91f-4c59-b192-f8f4e0585f41

The answer is **A. Anti-cardiolipin**.

This presentation is classic for **antiphospholipid syndrome (APS)**. The key features pointing to this diagnosis include:

- **Recurrent superficial thrombophlebitis** — the cord-like, tender, hardened lesion on the calf represents a thrombosed superficial vein, a venous thrombotic manifestation of APS.
- **Recurrent early pregnancy loss** — three spontaneous abortions at <10 weeks meets the obstetric classification criterion of ≥3 unexplained consecutive spontaneous abortions before 10 weeks of gestation.[1][2]
- **Livedo reticularis** — the lacy, mottled, violaceous rash on multiple extremities is a well-recognized extra-criteria manifestation of APS, present in approximately 25% of patients and serving as a marker for increased arterial thrombotic risk.[3][4]

Per the revised Sapporo classification criteria, APS requires at least one clinical criterion (vascular thrombosis or pregnancy morbidity) and one laboratory criterion: **lupus anticoagulant, anticardiolipin antibodies (IgG/IgM), or anti-β2 glycoprotein I antibodies (IgG/IgM)**,

confirmed on two occasions at least 12 weeks apart.[1][5] Among the answer choices, **anti-cardiolipin** is one of the three criteria antibodies for APS.

Why the other options are incorrect:

- **B. Anti-centromere** — associated with **limited cutaneous systemic sclerosis** (CREST syndrome), which presents with calcinosis, Raynaud phenomenon, esophageal dysmotility, sclerodactyly, and telangiectasias — none of which are present here.
- **C. Anti-histone** — associated with **drug-induced lupus**, which requires a causative drug exposure (e.g., hydralazine, procainamide). This patient takes only OTC analgesics.
- **D. Anti-ribonucleoprotein** — associated with **mixed connective tissue disease**, characterized by features of SLE, scleroderma, and polymyositis, which do not fit this presentation.

Would you like to explore the treatment approach for APS-related recurrent pregnancy loss in women planning future pregnancies?

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Question 149

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:

A. Abrupt hypotension
B. Sudden cardiac death
C. Acute arterial occlusion
D. Septic embolism

https://openevidence.com/ask/d057dd3a-815b-4c14-bd88-749e1c7c1125

The answer is **C. Acute arterial occlusion**.[1][2][3]

The clinical presentation — a young female with a **diastolic murmur** and a **large, pedunculated left atrial mass** on echocardiography — is classic for a **cardiac myxoma**, the most common primary cardiac tumor. The diastolic murmur corresponds to the "tumor plop," a low-frequency sound caused by the pedunculated mass prolapsing through the mitral valve during diastole.[4]

Systemic embolization is the greatest risk for patients with left atrial myxoma. Embolism occurs in **30–50% of patients**, with tumor fragments, thrombi, or surface vegetations detaching and occluding downstream arteries.[1][2][3] The cerebral arteries are affected in over 50% of embolic events, while peripheral arterial occlusion of the extremities, visceral, renal, and coronary arteries also occurs.[2][5] Embolic stroke is often the first presenting symptom, particularly in young adults.[3]

Why the other options are less appropriate:

- **A. Abrupt hypotension** — Large myxomas can obstruct the mitral valve orifice and cause hemodynamic symptoms (dyspnea, syncope), but this patient is asymptomatic, and obstruction-related hemodynamic collapse is far less common than embolization as the primary risk.
- **B. Sudden cardiac death** — While reported in rare cases, this is not the most common or characteristic complication of left atrial myxoma.

- **D. Septic embolism** — Myxomas are benign neoplasms, not infectious. Although constitutional symptoms (fever, elevated ESR) can occur due to IL-6 overproduction, the emboli are composed of tumor or thrombus, not infected material.[4]

Surgical excision is indicated upon diagnosis to prevent embolization, regardless of whether an embolic event has already occurred.[6]

Would you like to explore the surgical approach and perioperative management for cardiac myxoma excision?

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Question 150

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?

A. Endometrial carcinoma
B. Addison disease
C. Wegener granulomatosus
D. Eclampsia

https://openevidence.com/ask/9c9e1e4f-0759-451f-8e19-5a992f09c538

The answer is **A. Endometrial carcinoma**.

This patient presents with a classic picture of **polycystic ovary syndrome (PCOS)**: irregular menses, severe acne, hirsutism, and bilateral enlarged polycystic ovaries on ultrasound — fulfilling the Rotterdam criteria. PCOS is strongly associated with an **increased risk of endometrial carcinoma**, with meta-analyses estimating a **~3- to 5-fold increased risk** compared to women without PCOS, particularly in premenopausal women.[1][2][3]

The mechanism is **chronic anovulation** leading to prolonged exposure of the endometrium to **unopposed estrogen** without the cyclical progesterone-mediated differentiation and shedding that normally occurs with ovulatory cycles.[4][5] This promotes endometrial hyperplasia and, over time, increases the risk of malignant transformation. Additional contributing factors include hyperandrogenism, insulin resistance, and obesity — all common in PCOS.[6]

> "The risk of endometrial cancer is estimated to be 2.7 times as high among women with the polycystic ovary syndrome as among women without the syndrome, and the lifetime risk of endometrial cancer among women with the syndrome has been estimated to be as high as 9%."
>
> —Christopher R. McCartney, M.D. et al., University of Virginia School of Medicine. Polycystic Ovary Syndrome. N Engl J Med. July 07, 2016.

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The other answer choices are not associated with PCOS: **Addison disease** is primary adrenal insufficiency (autoimmune or infectious), **Wegener granulomatosis** (granulomatosis with polyangiitis) is an ANCA-associated vasculitis, and while PCOS does increase risk of pregnancy complications including preeclampsia, **eclampsia** (choice D) is not the best answer given the well-established and much stronger association with endometrial carcinoma.[4]

Would you like to explore screening and prevention strategies for endometrial cancer in PCOS?

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Question 151

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?

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

https://openevidence.com/ask/a3c6a6d7-d133-4c06-9051-59b41162ca4b

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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**.

This lesion — a growing, pigmented neoplasm of melanocytic origin on the sun-exposed neck of a fisherman — is a **melanoma**. The clinical hallmarks of melanoma are captured by the **ABCDE mnemonic**: **Asymmetry, Border irregularity, Color variegation, Diameter >6 mm, and Evolving appearance**.[1][2][3] Color variegation — with different shades of tan, brown, black, and sometimes red, white, or blue within the same lesion — is one of the most characteristic findings.[2][4]

Why the other options are incorrect:

- **B (5 mm macule):** The "D" criterion specifies a diameter **greater than 6 mm**; a 5 mm flat macule would fall below this threshold and is more suggestive of a benign nevus.[3][5]
- **C (Well-circumscribed, smooth borders):** This describes a **benign nevus**, not melanoma. Melanomas characteristically exhibit **irregular, ragged, or notched borders** ("B" criterion). Benign nevi, by contrast, tend to be symmetric with well-defined borders and even-color distribution.[3]
- **D (Itching and pain):** While itching is a minor criterion on the Glasgow 7-point checklist, it is an uncommon presenting symptom. As noted in a landmark NEJM review, **"most patients with melanoma have no skin discomfort whatsoever"**. Pruritus was reported by only 3% of

patients in one prospective cohort. Pain to palpation is not a recognized hallmark feature. [1][2][4][6]

Would you like to explore the recommended biopsy techniques and surgical margins for suspected melanoma?

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Question 152

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?

A. Bitemporal hemianopsia
B. Hypertension
C. Pheochromocytoma
D. Polyostotic fibrous dysplasia

https://openevidence.com/ask/0c67bc1e-cd84-47a0-8559-84a9cf1ad140

The answer is **D. Polyostotic fibrous dysplasia**.

This presentation — **vaginal bleeding and breast development in an 18-month-old girl**, **café-au-lait skin macules**, and **lytic/sclerotic bone lesions in the femur** — is the classic triad of **McCune-Albright syndrome (MAS)**: peripheral (gonadotropin-independent) precocious puberty, café-au-lait hyperpigmented macules, and polyostotic fibrous dysplasia.[1][2][3]

MAS results from postzygotic somatic activating mutations in the **GNAS gene**, which encodes the Gsα subunit, leading to constitutive activation of adenylate cyclase and elevated cAMP in a mosaic distribution of affected tissues.[4][5] The phenotype depends on which tissues harbor the mutation.

Why the other choices are incorrect:

- **A. Bitemporal hemianopsia** — This would suggest a pituitary macroadenoma causing central precocious puberty. The precocious puberty in MAS is **peripheral** (gonadotropin-independent), driven by autonomous ovarian cyst estrogen production, not by a pituitary lesion.[3][5]

- **B. Hypertension** — Not a recognized feature of MAS. This is more associated with conditions such as congenital adrenal hyperplasia or pheochromocytoma.
- **C. Pheochromocytoma** — Associated with MEN 2, neurofibromatosis type 1, and von Hippel-Lindau disease, but not with MAS. While MAS can include neonatal Cushing syndrome from adrenal hyperplasia, pheochromocytoma is not part of the spectrum.[2][3]

The **radiographic findings** described — patchy lytic bone and sclerosis in the femoral metaphysis — are characteristic of fibrous dysplasia, which in MAS is typically **polyostotic** and often involves the femur, with the lower extremities being the most commonly affected site.[6][7]

Would you like to explore the management of precocious puberty and fibrous dysplasia in McCune-Albright syndrome?

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Question 153

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?

A. 64
B. 16
C. 8
D. 4

https://openevidence.com/ask/09403c95-9f31-424e-ac32-ec866d4edfd3

The answer is **B. 16**.

According to **Poiseuille's law**, vascular resistance is inversely proportional to the **fourth power of the vessel radius** ($R = 8\eta L/\pi r^4$).[1] A 50% reduction in diameter corresponds to a 50% reduction in radius. When the new radius is r/2:

$$R_{\text{new}} = \frac{8\eta L}{\pi (r/2)^4} = \frac{8\eta L}{\pi \cdot r^4/16} = 16 \times R_{\text{original}}$$

Resistance therefore increases by a **factor of 16**.[2][3] As stated directly in the literature, "flow is reduced 16-fold when the vessel radius is reduced by one-half".[3]

A key nuance to note: this question specifies a reduction in **diameter**, which equates to the same proportional reduction in radius. Had the question stated a 50% reduction in radius with a different reduction in diameter, the calculation would differ. The fourth-power relationship also explains why even modest stenoses can produce large hemodynamic effects — a stenotic lesion generally must reduce the radius by more than 60% to become hemodynamically significant in the coronary circulation due to compensatory parallel flow pathways.[2]

Would you like to explore the hemodynamic significance thresholds for coronary stenoses and the role of fractional flow reserve?

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Question 154

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?

A. Asthma attack
B. Carbon monoxide (CO) poisoning
C. Neuromuscular disease
D. Acute respiratory distress syndrome (ARDS)

https://openevidence.com/ask/8a6fe9cc-f7d4-46a8-b802-c810482bd3ac

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The correct answer 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 care, **bilateral decreased breath sounds** (reflecting severe airflow limitation/air trapping), a **reduced PEFR of 200 L/min**, and **SpO2 of 89%** — all responding to inhaled SABA. Studies confirm that nearly all patients with severe hypoxemia (PaO2 <60 mmHg) during acute asthma have a PEFR below 200 L/min.[1]

ABG pattern — respiratory alkalosis with hypoxemia — is the hallmark of acute asthma. The most common acid-base disturbance in acute asthma is **simple respiratory alkalosis** (~48% of episodes), driven by hyperventilation in response to bronchospasm and hypoxemia.[2] During an exacerbation, **PaCO2 is often below normal (<40 mmHg)**; a normal or rising PaCO2 is actually a danger sign indicating impending respiratory failure.[3][4] The hypoxemia results from **V/Q**

mismatch due to heterogeneous bronchospasm, which characteristically **improves with supplemental oxygen** — as seen here with PaO2 rising from 59 to 75 mmHg.

Why the other options are incorrect:

- **B. CO poisoning:** PaO2 on ABG measures dissolved oxygen and would typically be **normal** in CO poisoning, since CO affects hemoglobin-bound oxygen. Additionally, pulse oximetry falsely reads normal because it cannot distinguish carboxyhemoglobin from oxyhemoglobin — this patient's SpO2 of 89% argues against CO poisoning.
- **C. Neuromuscular disease:** Would cause **hypoventilation with elevated PaCO2** (respiratory acidosis), not the hypocapnia (PaCO2 26 mmHg) seen here.[5]
- **D. ARDS:** Hypoxemia in ARDS is predominantly due to **intrapulmonary shunting**, which is characteristically more refractory to supplemental oxygen. ARDS also does not present with recurrent exercise-triggered episodes and requires an inciting cause (sepsis, trauma, aspiration) not present here.

Would you like to explore the warning signs of impending respiratory failure in acute asthma and indications for intubation?

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Question 155

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?

A. Thiamine
B. Lactulose
C. Naloxone
D. Rifaximin

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The answer is **B. Lactulose**.

The clinical presentation — **scleral icterus** (indicating liver disease) combined with a **flapping tremor (asterixis)** and **altered mental status** — is classic for **hepatic encephalopathy** in the setting of underlying cirrhosis. The overnight complaints of **multiple episodes of diarrhea and near-constant flatulence**, along with the improvement in mental status and resolution of asterixis, point directly to lactulose as the administered medication.

Lactulose is the **first-line treatment** for overt hepatic encephalopathy.[1][2][3] It is a nonabsorbable disaccharide that works by acidifying the colonic lumen (trapping ammonia as non-absorbable ammonium), exerting an osmotic laxative effect to increase fecal ammonia excretion, and modifying gut microbiota to reduce ammonia production.[1][3] Standard dosing for acute hepatic encephalopathy is **10–20 g (15–30 mL) every 2 hours** until bowel movements occur, then titrated to maintain 2–3 soft stools daily.[1][2]

The most common side effects — **diarrhea, flatulence, bloating, and abdominal discomfort** — are inherent to its mechanism of action.[1][4] The 11 episodes of diarrhea described here suggest relative overdosing, which is common during aggressive initial titration. Overuse can lead to dehydration, hypernatremia, and hypokalemia, which themselves can precipitate further encephalopathy.[1]

Why not the other options:

- **A. Thiamine** — Appropriate in a homeless patient at risk for Wernicke encephalopathy, but would not cause diarrhea/flatulence nor explain the asterixis.
- **C. Naloxone** — Used for opioid overdose reversal; does not explain jaundice, asterixis, or GI symptoms.
- **D. Rifaximin** — Used as **secondary prophylaxis** for hepatic encephalopathy recurrence (added to lactulose after the acute episode resolves), not as the primary acute treatment. It also does not characteristically cause profuse diarrhea and flatulence.[2][3]

Would you like to explore the secondary prophylaxis regimen recommended after resolution of an acute hepatic encephalopathy episode?

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Question 156

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?

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

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The correct answer is **C. Increased glomerular filtration rate, restricted aldosterone release, vascular smooth muscle dilation**.

Atrial natriuretic peptide (ANP) exerts three cardinal physiological effects that are each represented in this answer choice:

- **Increased GFR**: ANP causes **afferent arteriolar dilation and efferent arteriolar constriction** in the glomerulus, raising intraglomerular pressure and thereby increasing the glomerular filtration rate. It also relaxes mesangial cells via cGMP, increasing the effective filtration surface area.[1][2]
- **Aldosterone suppression**: ANP **inhibits both the synthesis and release of aldosterone** from the adrenal glomerulosa, and also suppresses renin secretion, broadly counteracting the renin-angiotensin-aldosterone system.[2][3][4]
- **Vasodilation**: ANP activates guanylate cyclase to generate cGMP in vascular smooth muscle, producing **vasodilation** and reducing systemic vascular resistance and blood pressure.[3][4][5]

Why the other options are incorrect:

- **A** — ANP does the opposite: it **inhibits water reabsorption** in the collecting duct by antagonizing vasopressin, promoting free water clearance.[1]
- **B** — This describes the effects of the renin-angiotensin-aldosterone system (angiotensin II), which ANP functionally opposes at multiple points.[4][6]

- **D** — This describes the actions of **parathyroid hormone (PTH)**, which is unrelated to natriuretic peptide signaling.

Would you like to explore natriuretic peptide resistance in advanced heart failure and how sacubitril/valsartan overcomes it?

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Question 157

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?

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

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D. Informed consent is not needed in this case.

This is the emergency exception to informed consent (doctrine of implied/presumed consent). The patient is unconscious (GCS 9), hemodynamically unstable, and has a clinically diagnosed tension pneumothorax — a condition that will cause death within minutes without decompression. Under this doctrine, a physician may perform any procedure immediately required to prevent death or serious disability when the patient cannot consent and no legally authorized representative is immediately available; the rationale is that a reasonable person would consent if able to be asked.[1][2]

Why the other options are wrong

- **A (closest relatives):** A surrogate should be approached only if immediately available. Delaying needle decompression to transport a spouse, child, or parent to the hospital would be fatal. Efforts to reach family should continue in parallel and the surrogate updated as soon as possible, but treatment is not withheld pending their arrival.[1][3]

- **B (accident witness):** A bystander has no legal standing as a surrogate decision-maker under any surrogate hierarchy.
- **C (ethics committee):** Ethics committees address value conflicts and non-urgent disputes; they are not a consent authority and cannot convene on the timescale of a tension pneumothorax.

Documentation requirement

The emergency exception is not a waiver of charting. Document the nature, immediacy, and magnitude of the threat, and the impossibility of obtaining consent under the circumstances, with date and time.[1] Note also that the exception does **not** apply to a conscious adult with capacity who has refused the intervention, nor does it override a valid advance directive specifically declining life-sustaining treatment.[1][3]

Procedural point

Needle decompression at the 2nd intercostal space midclavicular line or 5th ICS anterior/mid-axillary line is a temporizing measure only; the 5th ICS AAL has superior placement accuracy in cadaveric comparison (misplacement 22% vs 82%).[4] Needle decompression fails to fully relieve tension pressure in a substantial fraction of attempts, so definitive tube thoracostomy must follow immediately and the patient reassessed for persistent tension.[5][6]

Would you like to explore when finger thoracostomy is preferred over needle decompression in trauma?

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Question 158

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?

A. Mixed connective tissue disease
B. Polymyositis
C. Systemic sclerosis
D. Rheumatoid arthritis

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The answer is **A. Mixed connective tissue disease (MCTD)**.

This patient's presentation combines three cardinal features of MCTD: **Raynaud's phenomenon** (triphasic color change: white → blue → red, though the question describes white → red → blue), **myositis** (muscle weakness with elevated creatine kinase), and **positive anti-U1 RNP antibodies**, which are a **sine qua non** for the diagnosis of MCTD.[1] Constitutional symptoms such as fatigue and weight loss are also characteristic.[2]

MCTD is defined by **overlapping features of systemic lupus erythematosus, systemic sclerosis, and polymyositis/dermatomyositis** in the presence of high-titer anti-U1 RNP antibodies.[3][4] The most common clinical manifestations include Raynaud's phenomenon, polyarthritis, puffy/swollen hands, esophageal dysmotility, and muscle weakness.[5]

Why the other choices are incorrect:

- **Polymyositis (B):** While elevated CK and muscle weakness are present, polymyositis does not account for Raynaud's phenomenon and is associated with anti-Jo-1 or anti-Mi-2 antibodies, not anti-U1 RNP.
- **Systemic sclerosis (C):** Raynaud's is a prominent feature of SSc, but the hallmark antibodies are anti-Scl-70 (diffuse) or anti-centromere (limited), not anti-U1 RNP. Myositis with elevated CK is also uncommon as a presenting feature.

- **Rheumatoid arthritis (D):** No articular symptoms are described, and RA is associated with anti-CCP and rheumatoid factor, not anti-U1 RNP.

Anti-U1 RNP antibodies are detected in nearly all MCTD patients and represent the most diagnostically useful serologic marker; when present in high titer with overlapping autoimmune features, they strongly predict MCTD.[6][7]

Would you like to discuss the long-term monitoring and management approach for MCTD, particularly screening for pulmonary arterial hypertension and interstitial lung disease?

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Question 159

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?

A. Bipolar II disorder
B. Cyclothymic disorder
C. Persistent depressive disorder
D. Schizoaffective disorder

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The correct answer is **A. Bipolar II disorder**.

This patient meets DSM-5 criteria for **bipolar II disorder**, which requires at least **one hypomanic episode** and at least **one major depressive episode**, with **no history of mania**.[1][2]

Hypomanic episode: The 5-day episode of **minimal sleep, unusual energy, and impulsive spending** ($2,000 without permission) satisfies the ≥4-consecutive-day duration criterion for hypomania.[1][2] A manic episode would require ≥7 days or hospitalization; this episode resolved spontaneously after 5 days.[3]

Major depressive episodes: The recurrent month-long episodes of **sadness, hypersomnia, anhedonia, fatigue, and guilt** fulfill criteria for major depressive episodes (≥2 weeks of ≥5 symptoms including depressed mood or loss of interest).[2][3]

Why not the other options:

- **B. Cyclothymic disorder** — Requires that depressive symptoms **do not** meet full criteria for a major depressive episode. This patient clearly has recurrent major depressive episodes, which **precludes** a cyclothymic diagnosis.[2][4]
- **C. Persistent depressive disorder** — A chronic depressive condition (≥2 years) that does not account for hypomanic episodes. The presence of hypomania points to a bipolar spectrum diagnosis instead.[2]
- **D. Schizoaffective disorder** — Requires **hallucinations or delusions for ≥2 weeks in the absence of a major mood episode**. The only psychotic symptoms in this patient (seeing monkeys) occurred during **severe meningoencephalitis** in the ICU — most consistent with **delirium secondary to acute CNS infection**, not a primary psychotic process. These symptoms resolved with the medical illness and provide no evidence of an independent psychotic disorder.[2]

Would you like to explore first-line pharmacotherapy options for bipolar II disorder?

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Question 160

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?

A. ERCP
B. MRCP
C. Percutaneous transhepatic cholangiogram
D. CT abdomen

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A. ERCP. This is Reynolds pentad — fever, RUQ pain, jaundice, hypotension, and altered mental status — indicating Tokyo Guidelines Grade III (severe) acute cholangitis with cardiovascular and neurologic organ dysfunction, in the setting of a dilated CBD on ultrasound. The obstruction has already been demonstrated well enough to act on, so the next step is **therapeutic biliary decompression, not further diagnostic imaging**. The ASGE suggests ERCP over percutaneous transhepatic biliary drainage and performance within ≤48 hours, and notes that among patients in septic shock who do not respond to fluid resuscitation, delayed ERCP is associated with adverse events and ERCP in <24 hours may be considered.[1]

Timing and technique

- Tokyo Guidelines 2018: for severe acute cholangitis, drainage should be performed **as soon as possible once the patient has been stabilized** with respiratory/circulatory support — as has occurred here with fluids, pressors, and antibiotics.[2]
- Retrospective data support **decompression within 12–24 hours** in Grade III disease, particularly with neurologic or cardiovascular dysfunction (in-hospital mortality 0% vs 17.3% with neurologic dysfunction; 3.9% vs 9.0% for drainage <24 h in Grade III). A propensity-matched study found urgent ERCP ≤24 h reduced in-hospital mortality in moderate-to-severe CBD stone cholangitis (0.5% vs 21%; adjusted OR 0.09).[3][4]
- ASGE suggests **combining drainage with sphincterotomy and stone extraction** rather than stenting alone, but in an unstable or coagulopathic patient it is reasonable to secure decompression with a stent or nasobiliary drain and defer definitive stone clearance.[1]

Why not the others

- **MRCP** — purely diagnostic; adds delay without source control. Its role is in diagnostic uncertainty about choledocholithiasis in a stable patient, not in confirmed severe cholangitis with ductal dilation.[5]
- **Percutaneous transhepatic cholangiogram/drainage** — second-line. Reserved for failed or unavailable ERCP, surgically altered anatomy (e.g., Roux-en-Y), or proximal/hilar obstruction not decompressible endoscopically. PTBD carries higher rates of bleeding, bacteremia, and abscess, with longer length of stay and higher mortality in registry data (3.3% ERCP vs 8.9% PTBD).[1][6]
- **CT abdomen** — cross-sectional imaging is not required for the diagnosis of cholangitis; it is indicated in patients who fail to improve after drainage, to exclude liver abscess or another concurrent source.[6]

Two adjunctive points on the resuscitation described: norepinephrine, not dopamine, is the first-line vasopressor in septic shock; and this patient warrants ICU-level care with assessment for airway protection given the depressed sensorium prior to sedation for ERCP. Cholecystectomy should follow after recovery if gallstones are the etiology.

Would you like to explore the salvage options when ERCP fails to decompress the biliary tree in severe cholangitis?

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Question 161

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?

A. Medullary sponge kidney
B. Autosomal dominant polycystic kidney disease
C. Autosomal recessive polycystic kidney disease
D. Obstructive cystic dysplasia

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The most likely diagnosis is **B. Autosomal dominant polycystic kidney disease (ADPKD)**.

This presentation is classic for ADPKD: a young adult with **bilateral enlarged kidneys containing multiple parenchymal cysts**, **hypertension**, **recurrent UTIs**, **flank pain**, and **mildly impaired renal function** (creatinine 1.4 mg/dL). ADPKD is the most common inherited kidney disorder worldwide, typically diagnosed between ages **27 and 42 years**.[1] Hypertension affects 70–80% of patients, and UTIs and flank pain are frequent complications of progressive cyst development.[1]

Why the other options are incorrect:

- **A. Medullary sponge kidney** — causes cystic dilation of the collecting ducts confined to the renal medulla, not bilateral parenchymal enlargement with large anechoic cysts. It typically presents with nephrolithiasis and nephrocalcinosis, not palpable abdominal masses.
- **C. Autosomal recessive polycystic kidney disease (ARPKD)** — presents in the **perinatal period or early childhood**, with a first-year mortality of 30–40% in severe cases. Surviving to age 31 without prior diagnosis would be exceedingly unusual. ARPKD kidneys also show diffuse, small cystic dilation of collecting ducts rather than discrete large parenchymal cysts.[2]

- **D. Obstructive cystic dysplasia** — results from abnormal renal development due to urinary tract obstruction in utero, is typically **unilateral**, and is detected in infancy or childhood rather than presenting de novo in adulthood.

Would you like to explore screening recommendations for intracranial aneurysms in ADPKD?

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Question 162

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?

A. Sympathetic block
B. Hypovolemia
C. Acute pulmonary hypertension
D. Aortocaval compression

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The answer is **A. Sympathetic block**.

The **temporal relationship** is the key distinguishing feature: hypotension developed **10 minutes after epidural placement**, directly implicating the neuraxial anesthesia as the cause. Epidural anesthesia blocks sympathetic nerve fibers, producing **vasodilation and decreased systemic vascular resistance (SVR)**, which results in hypotension.[1][2] According to ACOG, **approximately 10% of women develop hypotension** with low-dose neuraxial labor analgesia, and maternal hypotension from sympathetic blockade is a well-recognized adverse effect.[1] The ASA identifies **SVR reduction as the primary mechanism** of neuraxial-induced hypotension and recommends vasopressor infusion (phenylephrine or norepinephrine) as first-line prophylaxis.[3]

The **pulse of 68/min** (normal-to-low, without reflex tachycardia) further supports sympathetic blockade, as the block attenuates the sympathetic-mediated compensatory heart rate response.[4]

Why not the other choices:

- **B. Hypovolemia** — No evidence of hemorrhage or volume depletion. Hypovolemia would be expected to cause compensatory tachycardia, not a pulse of 68/min.
- **C. Acute pulmonary hypertension** — No clinical features suggestive of acute right heart failure (no dyspnea, hypoxia, or tachycardia).
- **D. Aortocaval compression** — While the gravid uterus at 40 weeks can compress the IVC and contribute to hypotension, this would be a positional phenomenon present independent of the epidural. Aortocaval compression can be unmasked when sympathetic compensation is lost due to neuraxial blockade, but the **primary underlying cause** remains the sympathetic block itself. Treatment of aortocaval compression involves left uterine displacement, whereas treatment of sympathetic blockade–induced hypotension centers on **vasopressors** and IV fluid resuscitation.[2][3][5]

Would you like to explore current strategies for preventing and managing neuraxial-induced hypotension in obstetric anesthesia?

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Question 163

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?

A. Urinalysis every 6 months
B. Comprehensive foot exam every year
C. Weekly foot inspections by patient or family member
D. Meningococcal vaccine

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The correct answer is **B. Comprehensive foot exam every year**.

The ADA Standards of Care in Diabetes (2026) explicitly recommend performing **a comprehensive foot evaluation at least annually** in all patients with diabetes to identify risk factors for ulcers and amputations.[1] This exam should include skin inspection, assessment for foot deformities, neurological assessment (10-g monofilament or Ipswich touch test plus at least one additional test), and vascular assessment including pedal pulses.[1] Those with evidence of sensory loss or prior ulceration/amputation should have feet inspected at every visit.[1]

The other options are incorrect:

- **A. Urinalysis every 6 months** — Kidney screening in type 2 diabetes involves a **urine albumin-to-creatinine ratio (UACR)** and eGFR **at least annually** (not every 6 months), starting at the time of diagnosis. More frequent monitoring (1–4 times per year) is recommended only once CKD has been established. Additionally, the recommended test is a UACR, not a routine urinalysis.[2][3]
- **C. Weekly foot inspections** — For patients with neuropathy or loss of protective sensation, **daily** self-inspection is advised, not weekly. General foot self-checks are also promoted, but the key distinction is the frequency: daily, not weekly.[3]
- **D. Meningococcal vaccine** — Meningococcal vaccination is not specifically recommended for diabetes. The vaccines recommended for adults with diabetes include **influenza (annually), pneumococcal, hepatitis B, Tdap, and COVID-19**. Meningococcal vaccine is

indicated for specific high-risk conditions (e.g., asplenia, complement deficiency) but diabetes alone is not an indication.[4][5]

Would you like to explore the full schedule of recommended screening intervals for microvascular complications in type 2 diabetes?

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Question 164

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?

A. Hypertrophic cardiomyopathy
B. Aortic stenosis
C. Takotsubo cardiomyopathy
D. Restrictive cardiomyopathy

https://openevidence.com/ask/b16f6317-b188-4fb3-9c40-0cdd2049370c

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The correct answer is **A. Hypertrophic cardiomyopathy (HCM)**.

This presentation is classic for HCM: a **young athlete with sudden cardiac arrest during vigorous exertion**, combined with examination findings reflecting diastolic dysfunction and ventricular hypertrophy. Each physical finding maps directly to HCM pathophysiology:

- **Prominent A wave on JVP**: Caused by **reduced ventricular compliance**, as forceful atrial contraction against a stiff, hypertrophied ventricle transmits backward into the jugular veins.[1][2]
- **Double apical impulse**: Reflects the **palpable atrial beat (presystolic impulse)** followed by the ventricular systolic impulse, a characteristic finding in HCM occurring in ~27% of patients.[1][2]
- **S4 gallop**: Results from atrial contraction against the noncompliant left ventricle, present in up to **71% of HCM patients**.[2]
- **No audible murmur**: Critically, not all HCM patients have left ventricular outflow tract obstruction (LVOTO). Those without dynamic obstruction — the **nonobstructive form** — may have an entirely normal auscultation, making the diagnosis easy to miss on physical exam alone.[1][3]

HCM remains one of the most common identifiable structural causes of **sudden cardiac death in young competitive athletes**, historically accounting for roughly one-third of autopsy-positive cardiovascular deaths in U.S. athlete registries.[4][5]

Why not the other options?

- **Aortic stenosis (B)**: Would produce a **harsh systolic ejection murmur** radiating to the carotids, with a delayed carotid upstroke (pulsus parvus et tardus). Symptomatic severe AS in a previously healthy 23-year-old without a known valve abnormality is exceedingly unlikely.[6]
- **Takotsubo cardiomyopathy (C)**: Predominantly affects **postmenopausal women** after emotional or physical stress and does not produce the chronic physical findings described (double apical impulse, prominent A wave, S4).
- **Restrictive cardiomyopathy (D)**: Although it can cause elevated filling pressures and a prominent A wave, it is rare in young patients and typically presents with progressive **heart failure symptoms** rather than exertional sudden cardiac arrest.

Would you like to explore current risk stratification and ICD indications in hypertrophic cardiomyopathy?

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Question 165

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?

A. Desensitization
B. Metoprolol
C. Alprazolam
D. Psychotherapy

https://openevidence.com/ask/0a6a5c31-31e7-484f-965a-ac13830c1bc5

The answer is **A. Desensitization**.

This patient presents with a classic **specific phobia (arachnophobia)** — characterized by an extreme, irrational fear of spiders with marked avoidance behavior and significant functional impairment (inability to enter her own home for months). **Systematic desensitization**, a form of exposure therapy involving gradual, progressive exposure to the feared stimulus, is the most effective treatment for specific phobias.[1][2]

Why desensitization over the other options:

- **Desensitization (A)** — Exposure-based therapy is the **treatment of choice** for specific phobias, producing large effect sizes relative to no treatment and outperforming both placebo conditions and alternative psychotherapeutic approaches in meta-analysis. Systematic desensitization pairs graduated exposure to the phobic stimulus (e.g., pictures of spiders → toy spiders → real spiders at a distance → proximity) with relaxation techniques to extinguish the conditioned fear response.[2][3][4]

- **Metoprolol (B)** — Beta-blockers may reduce somatic symptoms of anxiety (e.g., tachycardia, tremor) in performance anxiety but do not address the core phobic avoidance or produce lasting extinction of the fear.[5]
- **Alprazolam (C)** — Benzodiazepines can provide short-term anxiolysis but do not treat the underlying phobia, carry dependence risk, and may actually **interfere with fear extinction learning** that is central to successful exposure therapy.
- **Psychotherapy (D)** — As a generic term, "psychotherapy" encompasses many modalities (psychodynamic, interpersonal, acceptance-based), most of which have a weaker evidence base for specific phobias compared to exposure-based approaches. Meta-analytic data specifically show that exposure-based treatments **outperform alternative active psychotherapeutic approaches** for specific phobia.[2][6]

The critical distinction this question tests is that desensitization is a **specific, behaviorally-based technique** with the strongest evidence for phobia treatment, whereas generic psychotherapy lacks comparable efficacy for this condition.

Would you like to explore how virtual reality exposure therapy compares to traditional in vivo exposure for specific phobias?

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Question 166

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?

A. Skin of the lateral thigh
B. External anal sphincter
C. Skin of the mons pubis
D. Detrusor muscle

https://openevidence.com/ask/6bc8d537-bfc2-4579-aadb-dfeac10dfd83

B. External anal sphincter.

The transvaginal technique described — palpating the ischial spines through the posterolateral vaginal sidewall and injecting just medial/posterior to the spine, where the nerve curves around the sacrospinous ligament — identifies a **pudendal nerve block**.[1][2] Loss of pinprick sensation over the posterior vulva after ~3 minutes confirms successful blockade of the perineal branch.[3]

The pudendal nerve (S2–S4) has three terminal branches:[4][5]

- **Inferior rectal (inferior anal) nerve** — motor to the **external anal sphincter**, sensory to the lower anal canal mucosa and perianal skin[5][6]
- **Perineal nerve** — posterior labial skin, lower vagina, and the superficial/deep perineal muscles including the external urethral sphincter[4][7]
- **Dorsal nerve of the clitoris** — clitoral sensation[5]

Why the other options are wrong:

- **Skin of the lateral thigh** — lateral femoral cutaneous nerve (L2–L3), a lumbar plexus branch not affected by this block.

- **Skin of the mons pubis** — ilioinguinal and iliohypogastric nerves (L1); the anterior vulva/mons is therefore **not** covered by a pudendal block, which is why supplemental local infiltration is often needed for an anterior extension or periurethral laceration.
- **Detrusor muscle** — parasympathetic pelvic splanchnic nerves (S2–S4) via the inferior hypogastric plexus; these are visceral efferents that do not travel in the pudendal nerve. The pudendal nerve supplies the external (striated) urethral sphincter, not the detrusor.

Clinically relevant point for this case: because the block anesthetizes the external anal sphincter and perineum, it is well suited to episiotomy and repair of perineal/anal sphincter lacerations, but it provides no relief of uterine contraction pain (T10–L1).[3][8] Also note the block commonly blunts the bearing-down reflex, so it is typically given immediately before expected delivery, and the pudendal vessels lie adjacent to the nerve — aspirate before injecting to avoid intravascular local anesthetic toxicity.[1][2][3]

Would you like to review maximum local anesthetic doses for pudendal block and management of systemic toxicity?

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Question 167

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?

A. Discontinue antibiotics
B. Perform an arterial blood gas
C. Needle thoracostomy
D. Stat chest X-ray

https://openevidence.com/ask/318b6242-a22e-4c9f-943f-e23dd3435178

The answer is **C. Needle thoracostomy**.

This patient has developed a **tension pneumothorax**, a clinical diagnosis requiring **immediate decompression without delay for imaging**. The classic findings are all present: acute hemodynamic collapse (BP 80/50), **tracheal deviation to the left** (away from the affected side), **absent breath sounds on the right**, **jugular venous distension** from impaired venous return, and worsening hypoxia.[1][2] Tension pneumothorax is diagnosed clinically and treated immediately — before obtaining a radiograph — with needle decompression at the second intercostal space (midclavicular line) or fourth/fifth intercostal space (anterior axillary line), followed by tube thoracostomy.[2][3]

Why the other options are incorrect:

- **A (Discontinue antibiotics):** The presentation — unilateral absent breath sounds, tracheal deviation, JVD — is inconsistent with anaphylaxis, which would produce diffuse wheezing, urticaria, and angioedema rather than focal thoracic findings.

- **B (Arterial blood gas):** While an ABG may be useful after stabilization, it provides no immediately actionable information and would delay life-saving decompression.
- **D (Stat chest X-ray):** Tension pneumothorax is a clinical diagnosis. Waiting for radiographic confirmation in a hemodynamically unstable patient risks cardiovascular collapse and cardiac arrest.[2][4][5]

Underlying context: This HIV-positive patient with a CD4 count of 180, noncompliant with prophylaxis, presenting with subacute dyspnea, fever, and dry cough most likely has **Pneumocystis jirovecii pneumonia (PCP)** — a well-established risk factor for spontaneous pneumothorax. PCP causes subpleural necrosis, cyst formation, and bullous changes that predispose to pneumothorax, with an incidence of **2–9%** in PCP patients.[6][7][8][9] Spontaneous pneumothorax in a person with HIV should raise suspicion for PCP.[6]

Would you like to explore the treatment protocol for PCP in HIV, including corticosteroid indications and dosing?

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Question 168

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?

A. Rectouterine pouch
B. Hepatorenal space
C. Splenorenal angle
D. Rectovesical pouch

https://openevidence.com/ask/400abd18-56d7-42d4-9b42-e3cd05607737

The answer is **A. Rectouterine pouch** (Pouch of Douglas).

In females, the **rectouterine pouch (cul-de-sac of Douglas)** is the **most dependent portion of the peritoneal cavity** in the supine or upright position. When an ovarian cyst ruptures, the leaked fluid (serous or hemorrhagic) gravitates to this space first. On pelvic ultrasound — particularly transvaginal — free fluid in the cul-de-sac is the hallmark finding supporting the diagnosis.[1][2]

Why the other options are incorrect:

- **B. Hepatorenal space (Morrison's pouch)** — This is the most dependent space of the *upper abdomen* in a supine patient. While large-volume hemoperitoneum can track here, a small amount of pelvic free fluid from a ruptured cyst would not preferentially collect in this location.[3]
- **C. Splenorenal angle** — Another upper abdominal space assessed during FAST exams; not the first site of fluid accumulation from a pelvic source.[3]
- **D. Rectovesical pouch** — This is the most dependent peritoneal space in **males** (between the bladder and rectum). In females, the uterus divides this space into the vesicouterine recess anteriorly and the rectouterine pouch posteriorly, making the rectouterine pouch the relevant dependent space.[1][4]

The EFAST protocol explicitly notes this sex-based anatomical distinction: in male patients, free fluid collects behind the bladder in the rectovesical pouch, whereas in female patients, free fluid is found posterior to the uterus and anterior to the rectum in the rectouterine pouch.[1]

Would you like to explore how to differentiate hemorrhagic ovarian cysts from ovarian torsion on ultrasound?

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Question 169

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?

A. Primary hyperparathyroidism
B. Pseudopseudohypoparathyroidism
C. Secondary hyperparathyroidism
D. Tertiary hyperparathyroidism

https://openevidence.com/ask/4a2c1341-060a-47f5-9305-34ca0873fea4

The answer is **A. Primary hyperparathyroidism**.

This patient presents with the classic constellation of **elevated PTH and hypercalcemia** in a previously healthy postmenopausal woman — the hallmark biochemical profile of **primary hyperparathyroidism (PHPT)**. PHPT is the most common cause of hypercalcemia in the outpatient setting, with the highest prevalence (~2%) in postmenopausal women, and is most often caused by a solitary parathyroid adenoma (~80% of cases).[1][2][3]

The clinical picture fits the classic mnemonic of **"bones, stones, abdominal groans, and psychic moans"**: calcium oxalate **nephrolithiasis** with hypercalciuria, **constipation** (abdominal groans), **fatigue** (psychic moans), and **hypertension** — all well-described features of PHPT.[1][4][5]

> "Primary hyperparathyroidism should be distinguished from other causes of elevated levels of intact PTH. Secondary hyperparathyroidism, a physiologic response to hypocalcemia, is seen in association with severe vitamin D deficiency, intestinal calcium malabsorption, and chronic kidney disease. Tertiary hyperparathyroidism occurs in some patients with end-stage renal disease when chronic hypocalcemia, hyperphosphatemia, and impaired synthesis of 1,25-dihydroxyvitamin D lead to parathyroid hyperplasia and eventually to hypercalcemia."

—Karl L. Insogna, M.D., Yale School of Medicine. Primary Hyperparathyroidism. N Engl J Med. September 13, 2018.

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Why the other choices are incorrect:

- **B. Pseudopseudohypoparathyroidism** — This is Albright hereditary osteodystrophy phenotype (short stature, brachydactyly, round facies) **without** PTH resistance; calcium and PTH levels are normal. It does not cause hypercalcemia or nephrolithiasis.
- **C. Secondary hyperparathyroidism** — Characterized by **elevated PTH but low or low-normal calcium**, as the PTH elevation is a physiologic compensatory response to hypocalcemia (e.g., CKD, vitamin D deficiency). This patient has **hypercalcemia**, ruling out secondary disease.[5][6]
- **D. Tertiary hyperparathyroidism** — Also features elevated PTH with hypercalcemia, but arises only after **longstanding secondary hyperparathyroidism**, typically in end-stage renal disease or post-renal transplant. This patient has no history of CKD or chronic hypocalcemic states.[5][6][7]

Would you like to explore the current guidelines for surgical indications in primary hyperparathyroidism?

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Question 170

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?

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

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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)** — secondary amenorrhea in the setting of intentional caloric restriction, excessive exercise, significant weight loss, and decreased bone mineral density. Her vital signs (bradycardia at 55 bpm, hypothermia at 35.9°C, low-normal blood pressure) reflect a hypometabolic adaptation to chronic energy deficit. [1][2]

The mechanism linking **decreased adiposity to hypoestrogenemia** centers on **leptin signaling**. Adipocytes produce leptin in proportion to fat mass; reduced body fat leads to low leptin levels, which suppress hypothalamic **GnRH pulsatility** via kisspeptin neurons in the arcuate nucleus.[3][4] This results in decreased LH and FSH secretion and, consequently, **insufficient ovarian estradiol production** — producing the hypogonadotropic hypogonadism that characterizes FHA. [1][4] Leptin replacement in women with hypothalamic amenorrhea has been shown to restore LH pulsatility, increase estradiol levels, and restore menstrual cycles, confirming the causal role of this pathway.[5][6]

Why the other options are incorrect:

- **A (Insulin resistance):** Insulin resistance is associated with states of excess adiposity such as PCOS. This patient's caloric restriction, low body fat, and intensive exercise produce **increased insulin sensitivity**, not resistance.[7]
- **C (Increased liver metabolism of estrogen):** There is no physiologic basis for increased hepatic estrogen clearance in this condition. The low estrogen results from **suppression of the HPO axis**, not from enhanced hepatic metabolism.[1][4]
- **D (Hyperthyroidism):** The bradycardia, hypothermia, and low blood pressure are signs of a **hypometabolic state**, the opposite of thyroid hyperfunction. Patients with FHA typically develop **low T3 syndrome** as an adaptive energy-conservation response. The weight loss is fully explained by intentional restriction and exercise.[2][8]

Would you like to explore bone health management in adolescents with functional hypothalamic amenorrhea?

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Question 171

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?

A. Factitious disorder
B. Somatic symptom disorder
C. Conversion disorder
D. Acute small bowel hemorrhage

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The most likely diagnosis is **A. Factitious disorder** (imposed on self).

This presentation is classic for **factitious disorder in a healthcare worker who is inducing anemia through self-phlebotomy**. The critical clue is the **numerous crusts along the course of the left arm veins**, which indicate repeated venipuncture — a procedure a nurse would have the skill and access to perform on herself.[1][2] The DSM-5 defines factitious disorder as the

falsification or induction of physical signs or symptoms, associated with identified deception, in the absence of obvious external rewards.[3]

Several features are characteristic of factitious disorder:[1]

- **Healthcare profession**: Up to half of patients with factitious disorder work in health-related occupations. A series of hematologic Munchausen syndrome specifically described young female nurses with self-inflicted phlebotomy.[1][2]
- **Eagerness for invasive procedures**: Requesting diagnostic laparoscopy and insisting "I know I have cancer" despite a negative workup is a hallmark behavioral feature.[1]
- **Laboratory findings inconsistent with reported symptoms**: The **normocytic anemia (Hgb 7.5, MCV 89) with elevated reticulocyte count (13.3%)** indicates blood loss with appropriate marrow compensation, yet the **stool occult blood is negative** and **abdominal ultrasonography is normal** — there is no identifiable organic source of hemorrhage.
- **Hemodynamic compromise** (tachycardia, hypotension) and the **systolic flow murmur** are consequences of severe anemia, not independent pathology.

Why the other options are less likely:

- **B. Somatic symptom disorder**: Involves excessive thoughts, feelings, or behaviors related to somatic symptoms but does **not** involve deliberate production or falsification of signs and symptoms. The venipuncture marks and induced anemia point to active self-harm, not disproportionate worry about genuine symptoms.[3]
- **C. Conversion disorder**: Presents with neurological symptoms (e.g., paralysis, blindness, seizures) incompatible with recognized neurological disease. This patient's presentation is hematologic, not neurological.[3]
- **D. Acute small bowel hemorrhage**: While this could cause anemia with reticulocytosis, the **negative fecal occult blood and normal abdominal ultrasound** argue against it — and critically, this diagnosis cannot explain the **crusts along the arm veins**, which are the most specific finding in this case.

Is there interest in discussing the recommended approach to confronting or managing patients with suspected factitious disorder, including strategies to minimize iatrogenic harm while preserving the therapeutic relationship?

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Question 172

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?

A. Serum transferrin level
B. Bone marrow biopsy
C. Peripheral blood smear
D. Serum porphobilinogen level

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The answer is **B. Bone marrow biopsy**.

This presentation — **pancytopenia** (Hgb 8.7 g/dL, WBC 1,100/mm³, platelets 54,000/mm³) with a **very low reticulocyte count (0.1%)**, normocytic anemia (MCV 93), and **no evidence of hemolysis** (normal bilirubin, low LDH) — is classic for **aplastic anemia**. The recent antibiotic course for a UTI is a potential drug-induced trigger for marrow failure.[1][2]

Bone marrow biopsy is the gold standard for confirming aplastic anemia. A 1–2 cm core biopsy is essential to assess overall cellularity, which reveals a **markedly hypocellular marrow with fat**

replacement and near-complete absence of hematopoietic precursors.[1][3] This also serves to exclude important mimics such as hypoplastic myelodysplastic syndrome, acute leukemia, and marrow infiltration.[4][5][6]

> "Aplastic anemia has long been regarded as the result of a profound deficit in hematopoietic stem and progenitor cells. The marrow is devoid of morphologic precursors to erythrocytes, granulocytes, and platelets."
>
> —Neal S. Young, M.D., National Heart, Lung, and Blood Institute. Aplastic Anemia. N Engl J Med. October 25, 2018.
>
> Used under license from The New England Journal of Medicine.

Why the other options are incorrect:

- **A. Serum transferrin level** — Evaluates iron status; iron deficiency causes microcytic anemia, not normocytic pancytopenia with reticulocytopenia.
- **C. Peripheral blood smear** — Part of the initial workup but cannot confirm aplastic anemia; in aplastic anemia, it typically shows pancytopenia without major morphologic abnormalities. The diagnosis requires direct assessment of marrow cellularity.[7]
- **D. Serum porphobilinogen level** — Tests for acute intermittent porphyria, which presents with abdominal pain and neuropsychiatric symptoms, not pancytopenia.

Would you like to explore first-line treatment options for severe aplastic anemia in adults?

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Question 173

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?

A. Gastroesophgeal sphincter dysfunction
B. Nonsteroidal anti-inflammatory drugs
C. Heliobacter pylori infection
D. Excessive gastrin

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C. Helicobacter pylori infection. The urea breath test detects bacterial **urease** activity, an enzyme produced by *H. pylori* but not by human gastric mucosa — ordering it signals that the physician is pursuing active *H. pylori* infection as the cause of PPI-refractory dyspepsia.[1][2] This patient fits the "test-and-treat" population exactly: under 60, no alarm features (no GI bleeding, no weight loss, no vomiting), no NSAID use, and no family history of gastric cancer.[3]

Why the alternatives are less likely

- **A. Gastroesophageal sphincter dysfunction** — GERD typically produces heartburn and regurgitation rather than isolated epigastric discomfort, generally responds to acid suppression, and is not evaluated with a urea breath test. Routine *H. pylori* testing is in fact not recommended for GERD in the US population.[4]
- **B. NSAIDs** — explicitly excluded by the history that he takes no medications. NSAID use would have been a reason for prompt endoscopy rather than noninvasive testing.[3]
- **D. Excessive gastrin** — Zollinger-Ellison syndrome is rare, usually presents with multiple/refractory ulcers, diarrhea, and complications, and is diagnosed by fasting serum gastrin with secretin stimulation, not a breath test.

Practical caveat on the test as ordered

PPIs suppress *H. pylori* and cause false-negative urea breath tests, so the drug must be stopped before testing. Most guidance specifies **discontinuation for at least 2 weeks** (and antibiotics/bismuth for 4 weeks); US recommendations have advised[1][5] **30 days** off PPIs, while the Maastricht V–Florence guidelines specify 2 weeks.[2] An H2 blocker can bridge symptom control during the washout.[2] Since this patient is currently on a PPI, testing immediately would risk a false-negative result.

Worth noting for expectation-setting: eradication in *H. pylori*–positive functional dyspepsia yields only modest symptom benefit (NNT ~9–14 in the ACG meta-analysis), but it durably reduces the long-term risk of peptic ulcer and gastric cancer.[3][4]

Would you like to explore next steps if he remains symptomatic after eradication and PPI therapy?

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Question 174

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?

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

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The correct answer is **A: HIV, syphilis, and hepatitis B**. These three infections carry **USPSTF Grade A recommendations for universal screening** at the first prenatal visit of every pregnancy, regardless of risk factors.[1][2][3]

Why the other options are incorrect:

- **Option B** (HIV, syphilis, gonorrhea) — **Gonorrhea screening is not universal**; the USPSTF recommends it only for sexually active women **≤24 years** or those ≥25 with increased risk (new/multiple partners, partner with concurrent partners or STI). This 32-year-old monogamous patient would not meet criteria.[4]
- **Option C** (HIV, hepatitis B, hepatitis C) — Omits **syphilis**, which has a longstanding USPSTF Grade A universal screening recommendation. While hepatitis C screening is now recommended universally in pregnancy by **ACOG (2023)**, the **CDC (2020)**, and **AASLD-IDSA**, the USPSTF's HCV recommendation covers all adults aged 18–79 rather than being a pregnancy-specific recommendation. Regardless, dropping syphilis makes this option incorrect.[2][3][5][6][7]
- **Option D** (HIV, syphilis, hepatitis B, gonorrhea, chlamydia) — Both **chlamydia and gonorrhea** screening follow the same USPSTF criteria: universal for women ≤24, **risk-based**

for women ≥25. This patient is 32 with no STI risk factors, so neither would be indicated as part of the universal panel.[4][8]

It is worth noting that current guidelines have evolved to include **universal hepatitis C screening** in pregnancy (ACOG, CDC, SMFM, AASLD-IDSA all recommend it).[5][6][9][10] However, among the available answer choices, **option A** best reflects the core universal prenatal infectious disease screening panel.

Would you like to explore the updated hepatitis C screening guidelines in pregnancy?

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Question 175

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?

A. Schizotypal personality disorder
B. Obsessive-compulsive personality disorder
C. Antisocial personality disorder
D. Personality disorder not otherwise specified

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The answer is **A. Schizotypal personality disorder**.

This patient's presentation — pervasive **distrust and suspiciousness**, interpreting others' motives as malevolent (boss "jealous," neighbors "out to get" him), **pathological jealousy** regarding his wife's fidelity, and believing the counselor is biased — is classic for **paranoid personality disorder (PPD)**.[1] The DSM-5 diagnostic criteria for PPD require four or more features including unjustified suspicions of exploitation/harm, doubts about loyalty, reluctance to confide, reading threatening meanings into benign events, bearing grudges, perceiving attacks on character, and recurrent suspicions of spousal infidelity.[1] This patient meets multiple criteria.

Paranoid personality disorder belongs to Cluster A, along with **schizoid** and **schizotypal** personality disorders.[1][2] Cluster A disorders are unified by their "odd or eccentric" qualities and social aversion.[1][3]

The other answer choices fall into different clusters:

- **Antisocial personality disorder → Cluster B** (dramatic, emotional, erratic)[1]
- **Obsessive-compulsive personality disorder → Cluster C** (anxious, fearful)[1]
- **Personality disorder NOS** → not assigned to any cluster[1]

Schizotypal personality disorder is the only listed option that shares **Cluster A** membership with paranoid personality disorder, making it the correct answer.[1][2]

Would you like to explore treatment approaches for paranoid personality disorder?

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Question 176

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?

A. Amitriptyline
B. Cocaine
C. Ethylene glycol
D. Heroin

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D. Heroin.

The blood gas shows **severe hypercapnic (type 2) respiratory failure** — a markedly elevated $PaCO_2$ with acidemia and a bicarbonate that has not risen enough to indicate any chronic renal compensation. Among the listed agents, only an opioid produces pure hypoventilation of this magnitude in a comatose patient. Mu-opioid agonism in the brainstem respiratory centers (pre-Bötzinger and parabrachial/Kölliker-Fuse complexes) blunts both hypercapnic and hypoxic ventilatory drive, producing decreased respiratory rate and tidal volume with resultant hypoxemia and CO_2 retention.[1][2] Morphine (heroin's active metabolite) is documented to cause both hypoxemia and hypercapnia experimentally.[3] The unremarkable head CT excludes the main structural mimic of coma with hypoventilation in a patient found down.

Why the alternatives don't fit

- **Amitriptyline** — plausible given neuropathic pain, depression, and suicide attempts, but TCA overdose is characterized by sinus tachycardia, QRS >100 ms with terminal R in aVR,

prolonged QTc, anticholinergic signs (mydriasis, hyperthermia), hypotension, and seizures. The acid–base picture is typically metabolic acidosis from seizures and hypoperfusion, not isolated hypercapnia. Management would center on sodium bicarbonate boluses.[4][5][6][7]

- **Cocaine** — sympathomimetic toxicity causes agitation, tachycardia, hyperthermia, and seizures with a lactic (anion-gap) metabolic acidosis and hyperventilation, not respiratory depression.

- **Ethylene glycol** — produces a high anion-gap metabolic acidosis with a low bicarbonate and compensatory hyperventilation (low $PaCO_2$). The opposite pattern is present here, though very early presentation can precede acidosis development.

A note on the numbers as given

The three values are internally inconsistent. By Henderson–Hasselbalch, $PaCO_2$ 95 mm Hg with HCO_3^- 24 mEq/L yields a pH near 7.03; a pH of 7.29 at that $PaCO_2$ would require HCO_3^- near 44. Similarly, a PaO_2 of 70 is not achievable on room air at $PaCO_2$ 95 (alveolar $PO_2 \approx 31$ mm Hg by the alveolar gas equation), implying supplemental oxygen. Additionally, even acute respiratory acidosis raises HCO_3^- roughly 1 mEq/L per 10 mm Hg rise in $PaCO_2$, so a truly normal bicarbonate at this $PaCO_2$ would suggest a concurrent metabolic acidosis. None of this changes the intended answer — the dominant, unambiguous derangement is hypoventilatory hypercapnia.

Clinical management implications

- **Airway and ventilation first** — bag-mask ventilation to restore a rate >10/min is the highest priority, since opioid deaths proceed through loss of airway patency and apnea to hypoxemic cardiac arrest.[6][8]

- **Naloxone** — 0.2–2 mg IV/IM (or 2–4 mg intranasal), repeated every 3 minutes as needed for RR <10/min or hypoxia; titrate to adequate respiration rather than full arousal to limit precipitated withdrawal. Anticipate **resedation**, as heroin's duration exceeds naloxone's, and note that co-ingested sedatives (benzodiazepines, alcohol, gabapentinoids) potentiate respiratory depression and are not reversed.[2][8][9]

- **Watch for naloxone-associated pulmonary edema**, which responds to positive pressure ventilation.[6]

- Given the bruising and prolonged down time, screen for **rhabdomyolysis, compartment syndrome, and occult traumatic injury** despite the normal head CT, and obtain an ECG to exclude a coexisting sodium-channel-blocking co-ingestant.

Would you like to explore observation periods and safe-discharge criteria after naloxone reversal?

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Question 177

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?

A. Systemic lupus erythematosus
B. Polymyalgia rheumatica
C. Polymyositis
D. Dermatomyositis

https://openevidence.com/ask/071ce4ef-0e75-405b-a889-06e7e6a31025

The answer is **C. Polymyositis**.

The combination of **proximal muscle weakness** (difficulty climbing stairs and brushing hair reflecting hip- and shoulder-girdle involvement) with **CD8+ T-cell infiltration in the endomysium** on muscle biopsy is the defining histopathological signature of polymyositis.[1][2]

Why each other option is incorrect:

- **A. Systemic lupus erythematosus** — SLE can cause myalgias but does not produce the characteristic endomysial CD8+ T-cell infiltrate seen here.
- **B. Polymyalgia rheumatica** — Causes proximal pain and stiffness (not true weakness), predominantly affects patients >50 years, and is not associated with endomysial inflammatory infiltrates on muscle biopsy.
- **D. Dermatomyositis** — The key differentiator is the **location and composition** of the inflammatory infiltrate. In dermatomyositis, infiltrates are **perivascular and perimysial** (not endomysial) and consist predominantly of **CD4+ T cells, B cells, macrophages, and plasmacytoid dendritic cells**, with characteristic **perifascicular atrophy** and complement (membrane attack complex) deposition on capillaries. In contrast, polymyositis features **endomysial CD8+ cytotoxic T cells** invading non-necrotic muscle fibers expressing MHC class I antigen — the "**MHC–CD8 complex**".[1][2][3]

  "In polymyositis and inclusion-body myositis, the inflammation is perivascular and is most typically concentrated in multiple foci within the endomysium; it consists

predominantly of CD8+ T cells invading healthy-appearing, nonnecrotic muscle fibers expressing major histocompatibility complex (MHC) class I antigen."

—Marinos C. Dalakas, M.D., Thomas Jefferson University and other institutions. Inflammatory Muscle Diseases. N Engl J Med. April 30, 2015.

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This CD8-mediated, endomysial, cell-mediated cytotoxicity pathway is distinct from the humoral/complement-mediated microangiopathy that drives dermatomyositis.[1][2]

Would you like to explore the current treatment approach and monitoring for polymyositis?

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Question 178

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?

A. Anterior horn cell degeneration
B. Axonal demyelination
C. Decreased acetylcholine receptor density
D. Myonecrosis

https://openevidence.com/ask/1046fcb8-c83e-4b71-b1dc-197224f41588

The answer is **A. Anterior horn cell degeneration**.

This presentation is classic for **Spinal Muscular Atrophy (SMA) Type 1 (Werdnig-Hoffmann disease)**, which results from **degeneration of anterior horn cells** (alpha motor neurons) in the spinal cord. SMA is caused by homozygous deletion or mutation of the *SMN1* gene, leading to deficiency of the survival motor neuron (SMN) protein and progressive motor neuron loss.[1][2][3]

Key clinical features supporting this diagnosis:

- **Symmetric flaccid proximal weakness** with diminished deep tendon reflexes — hallmarks of lower motor neuron disease[4][5]
- **Bell-shaped chest** — caused by intercostal muscle weakness with relative diaphragmatic sparing, a characteristic finding in SMA Type 1[5][6]
- **Weak cry and suck** with preserved facial expression and intact extraocular movements — SMA preferentially affects spinal motor neurons while sparing cranially innervated muscles (face, extraocular muscles), and cognitive function is normal[6]

- **Symptom onset before 6 months** with previously normal appearance — consistent with SMA Type 1 natural history[4][7]

Why the other options are incorrect:

- **B. Axonal demyelination** — Would suggest a peripheral neuropathy (e.g., Guillain-Barré syndrome), which typically presents with ascending weakness and areflexia but not a bell-shaped chest or this pattern of cranial nerve sparing.
- **C. Decreased acetylcholine receptor density** — Describes myasthenia gravis, which features fatigable weakness, ptosis, and ophthalmoplegia — findings absent here. Extraocular movements are intact and weakness is not fatigable.
- **D. Myonecrosis** — Would suggest a primary myopathy (e.g., muscular dystrophy), which typically presents with elevated CK and does not produce the pattern of intercostal weakness with diaphragmatic sparing seen here.

Would you like to explore the current disease-modifying therapies available for SMA Type 1?

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Question 179

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?

A. Methimazole and propranolol therapy
B. Potassium iodide therapy
C. Naloxone therapy
D. Calcium gluconate therapy

https://openevidence.com/ask/e9d1cd94-8e1d-4eeb-92ab-eafe7974f98f

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The answer is **A. Methimazole and propranolol therapy**.

This neonate presents with **neonatal Graves' disease (neonatal hyperthyroidism)** caused by transplacental passage of maternal thyroid-stimulating hormone receptor antibodies (TRAb). The presentation at **day 6 of life** is classic — maternal propylthiouracil (PTU) clears from the neonatal circulation faster than TRAb, unmasking hyperthyroidism toward the end of the first week.[1] The constellation of **tachycardia (180/min), irritability, diarrhea, diaphoresis, weight loss, and a midline neck swelling (goiter)** is characteristic of neonatal thyrotoxicosis.[2]

Why methimazole and propranolol:

- **Methimazole (MMI)** is the antithyroid drug of choice for neonatal hyperthyroidism. PTU is avoided in pediatric patients due to the risk of severe hepatotoxicity. The ATA recommends MMI with propranolol added for **sympathetic hyperactivity** (tachycardia, irritability) in severe cases. Treatment duration is typically **1–3 months** as maternal TRAb levels decline.[1][3][4][5]

Why not the other options:

- **B (Potassium iodide):** Reserved as adjunctive therapy in **refractory cases** that do not respond to methimazole alone — not first-line.[2][3]
- **C (Naloxone):** Although the maternal heroin history raises concern for neonatal abstinence syndrome (NAS), which can share features like irritability and diarrhea, the **goiter** and full thyrotoxic symptom complex point definitively to neonatal Graves' disease. Naloxone is also not standard treatment for NAS; it can precipitate acute withdrawal with seizures in opioid-dependent neonates.
- **D (Calcium gluconate):** Used for **neonatal hypocalcemia**, which presents with jitteriness and tetany — inconsistent with this clinical picture.

Would you like to explore the monitoring strategy and dose titration for methimazole in neonatal Graves' disease?

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Question 180

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?

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

https://openevidence.com/ask/cc351244-8cd5-4317-b2ee-7b1f7a5a7d6b

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The answer is **D. Tenderness at the insertion of the Achilles tendon**.

This presentation is classic for **reactive arthritis** (formerly Reiter syndrome): a young man with the triad of **arthritis** (asymmetric lower-extremity oligoarthritis), **urethritis** (dysuria), and **conjunctivitis** (bilateral conjunctival injection), occurring **1–3 weeks after a dysenteric illness**.[1][2] Common enteric triggers include Salmonella, Shigella, Campylobacter, and Yersinia.[3]

Enthesitis — inflammation at tendon insertion sites — is considered a hallmark of reactive arthritis and all spondyloarthropathies.[1][4][5] The **Achilles tendon insertion** and plantar fascia are among the most frequently affected entheseal sites; heel pain and Achilles tendon tenderness are classic findings.[3][6] A population-based study of post-enteric reactive arthritis found that **enthesitis was the most frequent clinical finding**, even more common than overt arthritis.[7]

Why the other options are incorrect:

- **A. Circular erythematous rash with central clearing** — This describes erythema migrans of Lyme disease, not reactive arthritis. The mucocutaneous findings in reactive arthritis include keratoderma blennorrhagicum and circinate balanitis, neither of which resemble a target lesion.
- **B. Pain on passive extension of the fingers** — This would suggest tenosynovitis (e.g., disseminated gonococcal infection), not the typical pattern of reactive arthritis, which favors lower-extremity large joints and entheses.

- **C. Palpable mass in the right lower quadrant** — This might suggest an appendiceal abscess or Crohn's disease; it is not a feature of reactive arthritis.

Would you like to explore the management of reactive arthritis, including when antibiotics or DMARDs are indicated?

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Question 181

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?

A. Methadone
B. Naloxone
C. Alvimopan
D. Loperamide

https://openevidence.com/ask/25450610-4626-4461-be67-f6b26754d7b5

A. Methadone. The presentation — diarrhea, abdominal cramping, and diffuse myalgias/arthralgias (abdomen, knees, shoulders) during a month-long heroin taper — is spontaneous opioid withdrawal, and a tapering opioid agonist is the only option listed that treats the entire syndrome (GI, musculoskeletal, and autonomic symptoms) with a single agent.[1][2][3] Methadone and buprenorphine tapers are more effective than α2-adrenergic agonists or symptom-targeted adjuncts for reducing withdrawal severity, retaining patients in withdrawal management, and supporting completion.[2][4]

Why the others fail

- **Naloxone** — a μ-opioid antagonist that would displace residual agonist and precipitate severe withdrawal within minutes in a physically dependent patient.[2][5]
- **Alvimopan** — a peripherally acting μ-opioid antagonist indicated for accelerating GI recovery after bowel resection; it is restricted to short-term inpatient use under a REMS because of increased myocardial infarction risk with long-term use. It would aggravate, not relieve, withdrawal-related GI symptoms and does nothing for myalgias.
- **Loperamide** — treats only the diarrhea. It is a reasonable adjunct but should not be used alone unless the patient declines an opioid agonist, and it leaves the pain and other withdrawal symptoms untreated. High-dose loperamide misuse also carries QT prolongation and torsades risk.[6][7]

Practical caveats if methadone is started

- **Dosing/tolerance:** the label supports an initial 20–30 mg with a total day-1 dose not ordinarily exceeding 40 mg, with 5–10 mg supplements if withdrawal persists, but explicitly advises lower initial doses when tolerance is expected to be low — relevant here after a month of tapering — and warns of accumulation and deaths in the first several days of induction.[8][9]
- **Cardiac:** methadone prolongs the QTc; check electrolytes (magnesium, potassium may be depleted by diarrhea) and consider ECG, particularly with concomitant QT-prolonging agents.
- **HIV/HBV:** review the antiretroviral regimen — efavirenz and nevirapine induce methadone metabolism and can precipitate withdrawal at stable doses; ritonavir-containing regimen effects are variable. Significant hepatic impairment from HBV warrants a more cautious induction.
- **Access:** in the US, methadone for opioid use disorder is dispensed through federally certified opioid treatment programs, with limited exceptions for administration/dispensing in acute care and by qualifying clinicians while arranging treatment. Buprenorphine is an equally valid first-line agent and is more accessible in many settings, though it is not among the options.[2][5][6]
- **Do not anchor on withdrawal alone:** in an HIV-positive patient, fever, bloody or persistent diarrhea, or dehydration should prompt evaluation for enteric infection or medication toxicity rather than attribution to withdrawal.[10]

The COWS can be used to grade severity and guide dosing decisions:[5]

Computed value for COWS Score: 5

Mild withdrawal. Patients with a score between 5 and 12 are experiencing mild withdrawal symptoms. Monitoring and supportive care may be sufficient at this stage.[11]

Scores of 5–12 indicate mild, 13–24 moderate, and >24 severe withdrawal.[5] Note also that withdrawal management alone, without transition to ongoing agonist maintenance, carries a high relapse rate and elevated overdose risk after loss of tolerance — the ASAM guidance is to link this patient to continued methadone or buprenorphine treatment rather than complete the taper and stop.[2]

Would you like to explore methadone dose adjustment for antiretroviral drug interactions in HIV-positive patients?

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Question 182

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?

A. Urinary tract infection
B. Bacterial vaginosis
C. Trichomonal vaginitis
D. Chlamydia infection

https://openevidence.com/ask/c8fcdf2f-61c8-4760-8601-b7e1416208f0

The answer is **C. Trichomonal vaginitis**.

This presentation is classic for **Trichomonas vaginalis** infection, with several features pointing specifically to this diagnosis:

- **Greenish-yellow, purulent, malodorous discharge** is the hallmark of trichomoniasis. A JAMA study found that purulent vaginal discharge (OR 8.0), yellow discharge (OR 2.4), and vaginal erythema (OR 4.3) were all significantly and independently associated with *T. vaginalis* infection.[1]
- **Vaginal pH of 5.5** is characteristic; trichomoniasis typically produces a pH **>5**, whereas bacterial vaginosis is >4.5 and candidiasis maintains a normal pH of 3.5–4.5.[2]
- **Inflammatory vaginitis with erythema** distinguishes trichomoniasis from BV. Trichomoniasis is the most common cause of **inflammatory** vaginitis (abundant WBCs, purulent discharge, erythema), while BV is a **noninflammatory** condition with thin, gray, homogeneous discharge and rare WBCs on wet mount.[2][3]
- **Risk factors** — multiple sexual partners and inconsistent barrier use — align with this STI, which is the most common nonviral sexually transmitted infection.[4]

Why the other options are less likely:

- **A. UTI** — While dysuria is present, the dominant findings are vaginal (profuse discharge, vaginal erythema), and there is no fever, flank pain, or urinary frequency/urgency to suggest a primary UTI. Dysuria in trichomoniasis results from urethral involvement by the parasite.[5]
- **B. Bacterial vaginosis** — BV produces a **thin, homogeneous, grayish-white** discharge with a fishy (amine) odor, not a purulent greenish-yellow one. Critically, BV is noninflammatory — vaginal erythema and purulent discharge argue strongly against it.[2][6]
- **D. Chlamydia infection** — Chlamydia primarily causes **cervicitis**, not vaginitis. It is most often asymptomatic and, when symptomatic, produces mucopurulent cervical (not vaginal) discharge without the prominent vaginal erythema and profuse purulent discharge seen here.[7]

Would you like to explore the recommended treatment regimen for trichomoniasis and partner management?

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Question 183

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?

A. 1st pharyngeal arch
B. 2nd pharyngeal arch
C. 3rd pharyngeal arch
D. 6th pharyngeal arch

https://openevidence.com/ask/81cc327f-c089-4bf6-8344-0f485f9fcf20

The correct answer is **D. 6th pharyngeal arch**.

Post-thyroidectomy hoarseness is most commonly caused by injury to the **recurrent laryngeal nerve (RLN)**, a branch of the vagus nerve that innervates all intrinsic laryngeal muscles except the cricothyroid. The RLN is **derived from the 6th pharyngeal (branchial) arch**.[1][2] During embryologic development, as the heart descends and the neck elongates, the RLN is dragged caudally by the 6th aortic arch derivatives — the left RLN loops around the ligamentum arteriosum (6th arch), while the right RLN loops around the right subclavian artery (4th arch).[1][3]

RLN injury is one of the most feared complications of thyroid surgery, with transient vocal fold paralysis occurring in **5–11%** of thyroidectomies.[4] Graves' disease is a recognized risk factor for RLN injury.[1] Unilateral RLN injury typically presents with **hoarseness, breathy voice, and vocal fatigue**, whereas bilateral injury can cause stridor and airway compromise.[1][5]

The other pharyngeal arches are associated with different cranial nerves:

- **1st arch** — trigeminal nerve (V3), innervates muscles of mastication
- **2nd arch** — facial nerve (VII), innervates muscles of facial expression
- **3rd arch** — glossopharyngeal nerve (IX), innervates stylopharyngeus

The **superior laryngeal nerve (SLN)**, which innervates the cricothyroid muscle, is associated with the **4th pharyngeal arch** and can also be injured during thyroidectomy, but its injury typically causes changes in vocal pitch and range rather than frank hoarseness.[1]

Would you like to explore the evidence on intraoperative neuromonitoring for RLN preservation during thyroidectomy?

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Question 184

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?

A. Alteplase
B. Exchange transfusion
C. Heparin
D. Warfarin

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B. Exchange transfusion. In a patient with sickle cell disease presenting with an acute focal neurologic deficit and no hemorrhage on head CT, the presumed diagnosis is acute ischemic stroke from sickle vasculopathy, and the definitive acute therapy is **emergent red cell exchange (erythrocytapheresis) to reduce HbS to <30% while raising hemoglobin to ~10 g/dL**.[1][2][3] The 2014 NHLBI expert panel recommends exchange transfusion, in consultation with a sickle cell expert, for any person with SCD and neuroimaging-confirmed acute stroke, and the AHA gives blood exchange to lower HbS a Class I (Level B) recommendation alongside optimal hydration, correction of hypoxemia, and correction of systemic hypotension.[1][3]

Why not the other options

- **A. Alteplase** — not the best answer, but not absolutely excluded. The American Society of Hematology 2020 cerebrovascular guideline suggests shared decision-making for IV tPA in adults ≥18 years within 4.5 hours with no hemorrhage on CT, with the explicit caveats that **tPA must not delay simple or exchange transfusion** and that **management of younger patients without atrial fibrillation, diabetes, hypertension, or hyperlipidemia should emphasize early transfusion**. This 22-year-old has none of those features. The AHA rates IV alteplase in SCD as Class IIb, Level C, though registry data from Get With The Guidelines-Stroke found no excess symptomatic intracranial hemorrhage or worse outcomes in 832 patients with SCD receiving lytics.[3][4][5]

- **C. Heparin** and **D. Warfarin** — anticoagulation is not a treatment for acute ischemic stroke in SCD. It would become relevant only if cerebral sinus venous thrombosis were identified, which is why MRV is considered in this population.[6]

Practical management sequence

1. Activate stroke pathway in parallel: last-known-well, glucose, NIHSS, neurology consult, and vascular imaging for large-vessel occlusion (thrombectomy remains an option if LVO is present).[2]

2. Type and cross, CBC with reticulocyte count, and begin transfusion urgently — do not wait for MRI. If exchange cannot be initiated promptly and hemoglobin is <10 g/dL, give simple transfusion as a bridge, keeping hemoglobin ≤11 g/dL to avoid hyperviscosity, then proceed to exchange targeting HbS ~15–30%.[6]

3. Supportive care: supplemental oxygen for hypoxemia, hydration, avoidance of hypotension, and adequate analgesia for the concurrent vaso-occlusive pain.[3]

4. MRI with DWI plus MRA to characterize infarct and define vasculopathy/moyamoya; MRV if venous thrombosis is suspected.[6][7]

5. Secondary prevention: initiate a **chronic monthly simple or exchange transfusion program** targeting HbS <30%, with iron chelation as needed; hydroxyurea if a transfusion program cannot be implemented.[1][2]

In an adult with SCD and stroke lacking evidence of sickle vasculopathy, pursue alternative etiologies — patent foramen ovale, antiphospholipid syndrome, dissection, cardioembolism.[2]

Would you like to explore the technical targets and complications of automated erythrocytapheresis in acute sickle cell stroke?

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Question 185

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?

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

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The answer is **D. Polymerase chain reaction for viral genes**.

This presentation — **failure to thrive, oral thrush, chronic diarrhea, bilateral pneumonia, and generalized lymphadenopathy** in a 3-month-old born at home without prenatal care — is classic for **vertically transmitted HIV infection**.[1][2][3] The absence of prenatal care means the mother was never screened for HIV and no antiretroviral prophylaxis was administered during pregnancy or postpartum.

Why PCR and not antibody-based testing:

In infants **<18 months of age**, standard HIV antibody and antigen/antibody immunoassays cannot be used for diagnosis because **transplacentally transferred maternal IgG antibodies** may persist, yielding false-positive results.[4][5] HIV nucleic acid tests (NATs) — including **HIV DNA PCR and HIV RNA PCR** — directly detect viral genetic material and are the gold standard for confirming HIV in this age group.[4][5]

Why not the other choices:

- **A (Karyotyping):** Would evaluate for chromosomal abnormalities (e.g., DiGeorge syndrome/22q11 deletion), but the constellation of oral candidiasis, lymphadenopathy, diarrhea, and pneumonia with no prenatal care points to an acquired rather than congenital immunodeficiency.
- **B (CFTR mutation testing):** Cystic fibrosis can cause failure to thrive and recurrent pulmonary infections, but would not explain oral thrush or lymphadenopathy.
- **C (FTA-ABS):** Congenital syphilis can present with multisystem disease, but the prominent oral thrush and lymphadenopathy pattern is more consistent with HIV-related immunosuppression.

Would you like to explore the recommended initial antiretroviral therapy and PCP prophylaxis for infants with perinatal HIV?

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Question 186

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?

A. HBsAg
B. Anti-HAV IgG
C. Anti-HCV IgG
D. Anti-HEV IgM

https://openevidence.com/ask/4bd9e0bb-c2fd-4ef6-9673-5f0653f4eda5

The answer is **D. Anti-HEV IgM**.

This presentation is classic for **acute Hepatitis E virus (HEV) infection** in a pregnant woman. Several features converge on this diagnosis:

- **Travel to Sudan** — HEV is endemic in Africa, with fecal-oral (waterborne) transmission in regions with inadequate sanitation.[1]
- **Incubation period** — The mean incubation period for HEV is **3–8 weeks (mean ~40 days)**, consistent with symptom onset 3 weeks after returning from travel.[1]
- **Fulminant hepatitis in pregnancy** — HEV uniquely causes severe disease in pregnant women, particularly in the **second and third trimesters**, with maternal mortality as high as **20–30%** and an incidence of acute liver failure of approximately 70% in developing countries. The markedly elevated transaminases (AST >4,000, ALT >3,500), coagulopathy (INR 2.0), jaundice, and **asterixis** (indicating hepatic encephalopathy) all point to fulminant hepatic failure.[1][2][3]
- **Negative workup for other causes** — Autoimmune hepatitis (ANA, anti-smooth muscle antibody negative), CMV, EBV, and HIV have been excluded. Immunizations are up-to-date (likely vaccinated against hepatitis A and B), and she denies blood product exposure (reducing hepatitis B/C risk).

Why not the other choices?

- **A. HBsAg** — Hepatitis B rarely causes acute liver failure in pregnancy and is transmitted via blood/body fluids, not travel-associated waterborne exposure. Up-to-date immunizations would include HBV vaccination.[2]
- **B. Anti-HAV IgG** — IgG indicates **past infection or immunity**, not acute infection; anti-HAV IgM would be needed for acute HAV. Furthermore, HAV follows a similar course in pregnant and non-pregnant individuals and rarely causes acute liver failure.[2]
- **C. Anti-HCV IgG** — HCV rarely presents as acute fulminant hepatitis and has a much longer incubation period. IgG also does not distinguish acute from chronic infection.

Anti-HEV IgM is the appropriate confirmatory test, as IgM antibodies appear at the onset of clinical symptoms during acute infection and remain detectable for approximately 3–12 months.[4][5][6] The IDSA recommends diagnosing acute HEV by the presence of **HEV IgM antibody** (appearing 4–6 weeks post-exposure) combined with the absence of HAV IgM.[7]

Would you like to explore the management of fulminant hepatitis E in pregnancy?

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Question 187

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?

A. Deficiency of vitamin K-dependent clotting factors
B. Phagocytosis of autoantibody-opsonized platelets
C. Excess circulating thrombin
D. Autoantibody-mediated platelet activation

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D. Autoantibody-mediated platelet activation — heparin-induced thrombocytopenia (type II). Six days of prophylactic unfractionated heparin after cardiopulmonary bypass, a platelet count of 48,000/mm^3, and a new proximal venous thrombosis (tender, swollen, erythematous calf)

constitute the classic HIT triad, with essentially normal PT/aPTT arguing against a consumptive or factor-deficiency coagulopathy.

Mechanism

- Heparin binds platelet factor 4 (PF4), inducing conformational neoepitopes; **IgG anti-PF4/heparin antibodies form ~5 days after exposure** and the resulting immune complexes **cross-link platelet FcγRIIa receptors**, causing platelet activation and release of procoagulant microparticles.[1][2][3]
- Parallel activation of monocytes (tissue factor) and endothelium produces **marked thrombin generation**, so HIT is a consumptive thrombocytopenia with a paradoxical prothrombotic state.[2][4]
- Cardiac surgery with UFH carries a HIT incidence of **0.5%–3%**, onset on **POD 5–10 in ~75%**, and thrombosis in **30%–60%** of cases. The hematomas at IV sites reflect thrombocytopenic bleeding, not the antibody target.[5]

Why the other options are wrong

- **A. Vitamin K–dependent factor deficiency** — plausible given daily alcohol use, but would prolong the PT out of proportion (PT is 15 s) and does not cause thrombocytopenia or DVT.
- **B. Phagocytosis of autoantibody-opsonized platelets** — the mechanism of ITP (and most drug-induced immune thrombocytopenias), which produces bleeding without thrombosis.[6]
- **C. Excess circulating thrombin** — describes DIC. Thrombin generation is the downstream consequence in HIT, not the initiating mechanism; overt DIC would typically show prolonged PT/aPTT, hypofibrinogenemia, and high D-dimer, though HIT can be complicated by DIC and near-normal coagulation times do not fully exclude it.[1][7]

Clinical caveats

- Interpret the platelet fall against the **highest postoperative platelet count**, not the preoperative value; a biphasic pattern or a new ≥30% decline beginning on/after POD 5 is what should trigger 4Ts scoring. Formal 4Ts calculation requires the postoperative platelet trend, which is not given here.[5]
- **22%–52% of cardiac surgery patients develop non-pathogenic anti-PF4/heparin antibodies**, so a positive immunoassay alone is not diagnostic — confirm with a functional assay (e.g., serotonin release) while treating empirically if pretest probability is intermediate/high.[5]

- Management: stop all heparin (including flushes and heparin-bonded catheters), start a **therapeutic-dose non-heparin anticoagulant** (argatroban or bivalirudin are preferred over fondaparinux early after sternotomy given short half-life and possible need for procedures), image the leg, avoid routine platelet transfusion, and **defer warfarin until platelet recovery (>150,000/mm³)** because of venous limb gangrene risk.[1][8]

Would you like to explore argatroban versus bivalirudin dosing and monitoring in post-cardiac-surgery HIT?

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Question 188

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?

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

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D. Integration of foreign DNA into host genome.

This patient has hepatocellular carcinoma (chronic HBV, constitutional symptoms, hepatomegaly, AFP 380 ng/mL, and a solitary arterially enhancing liver mass). In HBV-related HCC, the defining direct oncogenic mechanism is integration of HBV DNA into the hepatocyte genome, which causes insertional mutagenesis of cancer-related genes and chromosomal instability.[1][2][3]

Why integration is the mechanism

- During HBV replication, mispriming generates double-stranded linear DNA that integrates at sites of host double-strand breaks via non-homologous end joining; integrants are found in roughly 80% of HBV-related HCC tumors and occur within days of infection.[4]
- Integration drives oncogenesis in two ways: **insertion of the viral enhancer/promoter adjacent to cancer-driver genes** (recurrently *TERT*, *CCNE1*, *MLL4*/*KMT2B*, *FN1*), and **structural rearrangements** producing distant driver alterations such as 8q/*MYC* gains, focal 5p/*TERT* amplification, and 17p/*TP53* deletions.[4][5][6][7]
- Integrated DNA also serves as a persistent transcriptional template for HBx and truncated preS2/S proteins, which transactivate proliferation pathways and impair DNA repair — but these follow from the integration event itself.[2][4]

- Integration explains why HBV-related HCC can arise **in a non-cirrhotic liver**, unlike most other etiologies.[1][7][8]

Why the other options are wrong

- **A. Overexpression of secretory hepatitis antigen** — HBeAg is a marker of high replication and correlates with HCC risk, but the secreted antigen itself is not the transforming event; viral load and integration burden are.[9]
- **B. Intracellular accumulation of misfolded protein** — this describes α1-antitrypsin deficiency (PAS-positive, diastase-resistant globules), which also predisposes to HCC. Retention of mutant preS/S envelope protein can activate the unfolded protein response in HBV, but it is a secondary contributor, not the principal mechanism.[1]
- **C. Gain-of-function mutation of a proto-oncogene** — HCC is not typically driven by classic activating proto-oncogene point mutations; HBV-related tumors show a high rate of chromosomal alterations and TP53 inactivation with a notably **low** frequency of activating β-catenin mutations.[1][10]

Would you like to explore the diagnostic and staging workup for this arterially enhancing liver lesion?

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Question 189

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?

A. Initiate proton pump inhibitor
B. Obtain abdominal ultrasound
C. Reassurance and counseling on positioning
D. Recommend modification of mother's diet

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C. Reassurance and counseling on positioning. This is uncomplicated physiologic gastroesophageal reflux ("happy spitter") in a thriving 8-week-old — effortless, nonbilious, nonprojectile regurgitation that began at ~6 weeks, transient mild fussiness with prompt settling and return of appetite, normal growth (weight 34th → 36th percentile, length tracking), age-appropriate development, and a benign abdomen. GER occurs daily in roughly 40% of infants, typically begins before 8 weeks, peaks around 4 months, and resolves by 12 months; it is self-limited, not pathologic, and does not warrant routine testing or pharmacologic treatment.[1][2] Symptom improvement with smaller-volume feeds already confirms the diagnosis and the appropriate management pathway.

What "positioning" should mean here

- **Upright holding for 20–30 minutes after feeds**, small frequent feeds, avoiding overfeeding, and burping — about 80% of infants with uncomplicated GER improve with these measures alone. NASPGHAN/ESPGHAN also supports modifying feeding volume and frequency to avoid overfeeding.[3][4]
- **Do not elevate the head of the crib or use lateral/prone sleep positioning.** NASPGHAN/ESPGHAN recommends against positional therapy in sleeping infants, and this conflicts with safe-sleep guidance — sleep remains supine on a flat, firm, separate surface.[1][4][5]
- **Anticipatory guidance** that symptoms peak ~4 months and resolve by ~12 months, reinforced by the sibling's identical self-limited course. Parental education and support is itself a formal recommendation.[4]
- Since supply is the mother's stated concern, a **breastfeeding/lactation assessment** is reasonable — NASPGHAN and NICE recommend breastfeeding assessment as the initial step in breastfed infants with reflux. Percentile tracking is reassuring but is best paired with interval weight gain, urine/stool output, and latch/milk-transfer assessment.[6]

Why the other options are wrong

- **A. PPI** — NASPGHAN/ESPGHAN explicitly recommends against H2RAs or PPIs for visible regurgitation or for crying/distress in otherwise healthy infants. Three well-designed placebo-controlled trials (lansoprazole, pantoprazole, omeprazole) in infants failed to show benefit for regurgitation, crying, arching, or feeding refusal. Risks include lower respiratory tract and GI infections, and associations with allergy, NEC in preterm infants, and fracture.[1][4][7][8]
- **B. Abdominal ultrasound** — imaging targets pyloric stenosis, which presents with progressively projectile nonbilious emesis in a 3- to 6-week-old with weight loss, dehydration, and hypochloremic metabolic alkalosis. Here vomiting is nonprojectile, improving with smaller feeds, and weight gain is preserved, so ultrasound is low-yield. That said, escalating force or frequency, a palpable olive, dehydration, or faltering growth should prompt reassessment and imaging.[1]
- **D. Maternal dairy elimination** — a reasonable second-line step for suspected cow's milk protein allergy or for reflux refractory to optimal nonpharmacologic measures, but this infant has no eczema, diarrhea, hematochezia, poor growth, or family history of atopy, and conservative measures have not yet been optimized.[1][6]

Alarm features that would change management: bilious or forceful projectile vomiting, hematemesis or hematochezia, onset of vomiting after 6 months or persistence beyond 12–18 months, poor weight gain or downward percentile crossing, fever, lethargy, bulging fontanelle, dysphagia or feeding refusal, or apnea.[1]

Would you like to explore whether thickened feeds have any role in exclusively breastfed infants with reflux?

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Question 190

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?

A. Anterior cord lesion
B. Posterior cord lesion
C. Right cord hemisection
D. Left cord hemisection

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The correct answer is **D. Left cord hemisection** — this presentation is classic **Brown-Séquard syndrome**, historically described in the setting of penetrating spinal cord trauma such as a stab wound.[1][2]

Localizing the deficits to the left hemicord:

- **Ipsilateral (left) motor weakness** — The corticospinal tracts decussate at the cervicomedullary junction, so a left hemisection disrupts the already-crossed left corticospinal tract, producing left-sided weakness (2/5 strength).[3]
- **Ipsilateral (left) loss of vibration and light touch** — The dorsal columns (fasciculus gracilis/cuneatus) ascend ipsilaterally and do not decussate until the medulla, so a left-sided lesion impairs dorsal column function on the left.[1][4]
- **Contralateral (right) loss of pain and temperature** — The spinothalamic tracts cross within 1–2 levels of their entry into the cord, then ascend contralaterally. A left hemisection therefore disrupts the already-crossed fibers carrying pain and temperature from the right side.[4][5]

Why the other options are incorrect:

- **A. Anterior cord syndrome** — Would produce **bilateral** motor loss and bilateral loss of pain/temperature with **preserved** dorsal column function (proprioception, vibration), which does not match this unilateral pattern.[1]
- **B. Posterior cord syndrome** — Would produce isolated **bilateral proprioceptive loss** with preserved motor and spinothalamic function.[4]
- **C. Right cord hemisection** — Would produce motor weakness and dorsal column deficits on the **right** with pain/temperature loss on the **left** — the mirror image of what is described here.[2]

Would you like to explore the prognosis and management approach for Brown-Séquard syndrome from penetrating trauma?

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Question 191

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?

A. PSA
B. Digital rectal exam
C. Abdominal ultrasound
D. Flexible sigmoidoscopy

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A. PSA — after shared decision-making, PSA is the appropriate screening test for this 58-year-old Black man with a first-degree relative with prostate cancer. He falls squarely within the age window (55–69 years for USPSTF, 40–75 for NCCN high-risk) where PSA screening is recommended or offered, and the other three options are either not indicated or not yet due.[1][2]

Why PSA

- The American Urological Association guideline gives a strong recommendation to offer PSA screening beginning at age 40–45 in men at increased risk, including Black men; increased-risk patients may also warrant shorter re-screening intervals (e.g., annually).[3]
- The National Comprehensive Cancer Network algorithm places Black/African American individuals and those with concerning family history in the age 40–75 risk-assessment group, with **baseline PSA** as the test and DRE only as an optional adjunct.[2]

- The American Cancer Society recommends the informed-decision discussion begin at age 45 for Black men or those with a father/brother diagnosed before age 65.[4]
- The USPSTF (2018) recommends shared decision-making for PSA screening in men 55–69 years and notes that modeling suggests African American men may derive greater benefit, though it could not issue a race-specific recommendation. Life expectancy ≥10 years is a prerequisite — met here.[1]

Why not the others

- **B. DRE** — should not be used as a stand-alone screening test. Pooled sensitivity is ~51% and specificity ~59%, and in PROBASE the positive predictive value of a suspicious DRE at age 50 was 0.87%. Its value is in the workup of an elevated PSA, not in screening.[2][3][5]
- **C. Abdominal ultrasound** — AAA screening is a one-time ultrasound in men aged 65–75 who have ever smoked (Grade B); selective screening in never-smokers 65–75 (Grade C). He is 58, a never-smoker, with no family history of AAA, so he meets no criterion.[6][7]
- **D. Flexible sigmoidoscopy** — his high-quality normal colonoscopy 8 years ago buys a 10-year interval; repeat colorectal screening is due in 2 years, and sigmoidoscopy would be a downgrade in modality.[8]

Other items worth addressing at this visit (not among the options): HbA1c or repeat fasting glucose given BMI 30, maternal type 2 diabetes, and OSA; lipid screening and ASCVD risk assessment; intensive behavioral counseling for weight, with consideration of pharmacotherapy given BMI ≥30. Also worth clarifying the age at which his father was diagnosed, since early-onset or lethal/metastatic prostate cancer in a first-degree relative raises the question of germline testing.[2][3]

Would you like to explore how to act on the PSA result — thresholds and re-screening intervals for a high-risk man in this age group?

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Question 192

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?

A. Pericardiocentesis
B. Chest CT scan
C. Pericardial window
D. Insert chest tube

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The answer is **A. Pericardiocentesis**.

This vignette describes **cardiac tamponade** following blunt chest trauma. The triad of findings — **sinus tachycardia** (compensatory for reduced cardiac output), **enlarged cardiac silhouette** on chest radiograph (pericardial effusion), and **pulsus paradoxus** (loss of palpable radial pulse during inspiration) — is classic for hemodynamically significant tamponade.[1][2] Pulsus paradoxus, defined as a >10 mmHg inspiratory decrease in systolic blood pressure, is the **most specific** physical examination finding for cardiac tamponade.[2][3]

Pericardiocentesis is the appropriate emergent intervention. Per the 2025 ACC Expert Consensus Statement, pericardiocentesis is therapeutically performed in cases of **impending or established cardiac tamponade**, especially in urgent or emergency settings, with a **subxiphoid or apical approach** preferred in emergencies.[1] As stated in the NEJM:

Why not the other options:

- **B (Chest CT scan)** — Would inappropriately delay definitive treatment in a patient with hemodynamic compromise from tamponade physiology.
- **C (Pericardial window)** — A surgical option considered for **recurrent large pericardial effusions and/or tamponade despite prior pericardiocentesis**, not the initial emergent intervention. In traumatic hemopericardium, surgical drainage may ultimately be needed if clotted blood prevents adequate needle drainage, but pericardiocentesis remains the initial step.[1][2]

- **D (Chest tube)** — Treats pneumothorax or hemothorax, not pericardial tamponade. The clinical findings here point to pericardial, not pleural, pathology.

Would you like to explore the echocardiographic findings used to confirm cardiac tamponade and the role of bedside FAST in trauma?

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Question 193

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?

A. Interstitial lung disease
B. Hypersensitivity pneumonitis
C. Chronic obstructive pulmonary disease
D. Bronchiectasis

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The answer is **C. Chronic obstructive pulmonary disease (COPD)**.

This presentation is classic for **emphysema-predominant COPD** based on several converging findings:

- **Obstructive spirometry**: FEV1/FVC of 62% (below the 0.70 threshold) with FEV1 of 60% predicted, consistent with **GOLD stage 2 (moderate) COPD**.[1]
- **Hyperinflation**: TLC of 125% predicted reflects **air trapping and loss of elastic recoil**, a hallmark of emphysema. As the 2026 GOLD Report describes, structural changes cause narrowing of the small airways and destruction of lung parenchyma, diminishing the ability of the airways to remain open during expiration, contributing to "gas trapping and lung hyperinflation".[1]
- **Decreased DLCO**: Parenchymal destruction in emphysema reduces the alveolar-capillary surface area for gas exchange, lowering DLCO. A low DLCO in COPD is also a predictor of oxygen desaturation, coexisting pulmonary hypertension, and increased mortality.[1][2]

- **40-pack-year smoking history**, **low BMI** (19.7 — typical of the "pink puffer" phenotype), **prolonged expiratory phase**, and **end-expiratory wheezing** all further support COPD.

Why the other options are incorrect:

- **Interstitial lung disease (A)** and **hypersensitivity pneumonitis (B)** produce a **restrictive** pattern (reduced TLC, preserved or elevated FEV1/FVC ratio). DLCO is reduced in ILD, but the hyperinflation and obstructive physiology here are inconsistent with either diagnosis.
- **Bronchiectasis (D)** can cause obstruction, but typically presents with **chronic productive cough with purulent sputum**, not a dry cough, and DLCO is usually **normal or only mildly reduced** without significant hyperinflation.

Would you like to explore the recommended pharmacotherapy for moderate COPD?

References

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Question 194

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?

A. Maintain current therapy
B. Add fluticasone daily
C. Add salmeterol twice daily
D. Add zileuton twice daily

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The correct answer is **B. Add fluticasone daily**.

This child's symptom profile — **SABA use 4 times per week, 3 nighttime awakenings per month, and activity limitation** — classifies his asthma as **mild persistent** per NAEPP criteria (symptoms >2 days/week, nighttime awakenings >2/month).[1][2] He is currently on Step 1 therapy (SABA alone), which is insufficient for this level of impairment.

Both the NHLBI 2020 guidelines and GINA 2026 recommend **daily low-dose inhaled corticosteroid (ICS)** as the preferred Step 2 controller therapy for children aged 5–11 years with mild persistent asthma.[3][4][5] Low-dose ICS reduces the risk of severe exacerbations, improves lung function, and controls symptoms compared with SABA-only treatment.[3][6] Fluticasone is the prototypical low-dose ICS used at this step, continued alongside as-needed albuterol for quick relief.

Why the other options are incorrect:

- **A (Maintain current therapy):** The patient's symptoms clearly exceed the thresholds for intermittent asthma; continuing SABA alone leaves him undertreated. Increasing SABA use is itself a marker of inadequate control and an indication to step up therapy.[4]
- **C (Salmeterol):** A long-acting beta-agonist (LABA) should **never be used as monotherapy** without an ICS, due to increased risk of serious asthma-related events. LABAs are reserved as add-on therapy at Step 3 or higher, always combined with an ICS.[4][5]
- **D (Zileuton):** Zileuton (a 5-lipoxygenase inhibitor) is **not approved for children under 12 years**, requires serial hepatic function monitoring, and is not a guideline-preferred option at any pediatric step.[4]

Would you like to explore specific ICS dosing recommendations for this age group?

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Question 195

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?

A. Panic attack
B. Mechanical ventilation
C. Pulmonary embolus
D. Chronic obstructive bronchitis

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The answer is **D. Chronic obstructive bronchitis**.

ABG Interpretation

This ABG shows a **primary respiratory acidosis** (pH 7.33, pCO2 70 mmHg) **with significant metabolic compensation** (HCO3 33 mEq/L). The degree of HCO3 elevation is the critical clue for distinguishing acute from chronic respiratory acidosis:

- **Acute respiratory acidosis**: HCO3 rises ~1 mEq/L per 10 mmHg increase in pCO2 → expected HCO3 ≈ 27 mEq/L[1]
- **Chronic respiratory acidosis**: HCO3 rises ~4–5 mEq/L per 10 mmHg increase in pCO2 → expected HCO3 ≈ 36–39 mEq/L[1]

The observed HCO3 of 33 far exceeds the acute prediction, indicating substantial **renal compensation that develops over days to weeks** as the kidneys increase ammonium chloride excretion, raising plasma bicarbonate.[2] This degree of compensation points to a chronic hypercapnic process.

Chronic obstructive bronchitis is the classic cause of chronic CO2 retention from V/Q mismatch and alveolar hypoventilation.[3][4] In stable COPD patients with chronic hypercapnia, pCO2 values range from 45–77 mmHg with near-normal pH maintained by elevated bicarbonate.[5] A 65-year-old presenting from home with dyspnea and this compensated ABG pattern is the hallmark presentation.

Why the other choices are incorrect:

- **A. Panic attack** — causes hyperventilation and **respiratory alkalosis** (low pCO2, elevated pH), the opposite pattern.
- **B. Mechanical ventilation** — implausible because the patient is presenting from home with no indication of ventilatory support.
- **C. Pulmonary embolus** — typically provokes tachypnea and **respiratory alkalosis**, not chronic hypercapnic respiratory acidosis with renal compensation.[6]

Would you like to explore the management of COPD exacerbation with hypercapnic respiratory failure, including indications for noninvasive ventilation?

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Question 196

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?

A. Hypertrophic pyloric stenosis
B. Biliary cyst
C. Intestinal malrotation
D. Pancreas divisum

https://openevidence.com/ask/19dc5f88-1fcf-4162-8aec-779bf4db8a77

The answer is **D. Pancreas divisum**.

Recurrent episodic epigastric pain radiating to the back with nausea in a child is the hallmark presentation of **recurrent pancreatitis**, and among the listed congenital conditions, pancreas divisum best explains this pattern.[1][2] Pancreas divisum — the **most common congenital anomaly of pancreatic development** (present in ~7% of the general population) — results from failure of the dorsal and ventral pancreatic ducts to fuse during embryogenesis, causing the majority of exocrine secretions to drain through the smaller minor papilla.[3][4] In a subset of affected individuals, this arrangement leads to functional outflow obstruction and recurrent pancreatitis.[1][3]

Notably, pancreas divisum is found in approximately **14–19% of children with recurrent or chronic pancreatitis**, significantly higher than the general population prevalence.[2][5] In one pediatric surgical series, the **mean age of symptom onset was 6 years**, with patients presenting with recurrent episodic epigastric pain and vomiting — closely matching this case.[2]

Why the other options are less likely:

- **A. Hypertrophic pyloric stenosis** — Presents in **neonates (2–8 weeks)** with projectile non-bilious vomiting and a palpable "olive" mass; it would not manifest as episodic epigastric pain in a 6-year-old.
- **B. Biliary cyst (choledochal cyst)** — While choledochal cysts can cause abdominal pain and even secondary pancreatitis, the classic presentation includes **jaundice and/or a right upper quadrant mass**. The isolated pattern of epigastric pain radiating to the back without jaundice or a palpable mass is more consistent with primary pancreatic pathology.[1]
- **C. Intestinal malrotation** — Typically presents in neonates with **bilious vomiting** due to midgut volvulus. Late presentations can occur but usually involve obstructive symptoms rather than episodic pancreatic-type pain.

The mention of the sister's congenital heart disease serves to prime consideration of congenital anomalies as the underlying etiology, though no specific syndromic link between pancreas divisum and congenital heart disease is established.

Would you like to explore the diagnostic workup for suspected pancreas divisum in children?

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Question 197

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?

A. Seizures due to hypocalcemia
B. Catlike cry
C. Hyperthyroidism from transplacental antibodies
D. Increased phenylalanine in the blood

https://openevidence.com/ask/9159c3b6-a1a2-4046-b5de-237e39f3fb13

The answer is **A. Seizures due to hypocalcemia**.

This presentation is classic for **22q11.2 deletion syndrome** **(DiGeorge syndrome)**, remembered by the mnemonic **CATCH-22**: **C**ardiac defects, **A**bnormal facies, **T**hymic aplasia, **C**left palate, **H**ypocalcemia, chromosome **22**q11.2 deletion.

The echocardiographic and radiographic findings describe **Tetralogy of Fallot** (pulmonary stenosis, VSD, overriding aorta, right ventricular hypertrophy producing the "boot-shaped" heart), which is the most common conotruncal cardiac defect in this syndrome, occurring in 17–22% of affected patients.[1] Absent thymus on chest radiograph and cleft palate further confirm the diagnosis.

Hypocalcemia due to hypoparathyroidism is a cardinal feature, present in 17–60% of patients, most typically manifesting in the neonatal period.[2] It results from aplasia or hypoplasia of the parathyroid glands and can present as **neonatal seizures**, jitteriness, tetany, or prolonged QT interval.[2][3] Hypocalcemic seizures are the most common seizure type in neonates with this syndrome and respond to electrolyte correction.[2] Notably, the frequency of hypocalcemia is higher in patients who also have congenital heart disease (~62% vs. ~41% without).[4]

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** — describes neonatal Graves disease; while autoimmune thyroid disease can occur in 22q11.2 deletion syndrome, it is uncommon and not caused by transplacental antibodies in this context.
- **D. Increased phenylalanine** — characteristic of phenylketonuria (PAH deficiency), unrelated to this syndrome.

Would you like to explore the immunologic evaluation and management approach for neonates with DiGeorge syndrome?

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Question 198

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?

A. Bile deposition in the dermis
B. Release of prostaglandins
C. Mast cell degranulation
D. T cell activation

https://openevidence.com/ask/4743ebf2-21fb-41d8-b8ba-74f5846efdcb

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The correct answer is **B. Release of prostaglandins**.

The side effect in question is **niacin-induced cutaneous flushing**, characterized by warmth, redness, and tingling of the face and upper body. This is a **prostaglandin-mediated phenomenon**: niacin activates the G protein-coupled receptor **GPR109A** on dermal Langerhans cells and keratinocytes, triggering the release of **prostaglandin D2 (PGD2)** and **prostaglandin E2 (PGE2)** via cyclooxygenase-1 (COX-1) and COX-2, respectively.[1][2][3] These prostaglandins act on vascular DP1, EP2, and EP4 receptors to cause cutaneous vasodilation.[1][4]

Aspirin (325 mg taken 30 minutes before niacin) reduces flushing by **inhibiting cyclooxygenase and thereby blocking prostaglandin synthesis**.[5][6][7] Clinical studies show this decreases moderate-to-severe flushing events by approximately 30–50%.[8]

Why the other options are incorrect:

- **A. Bile deposition in the dermis** — This describes the mechanism of pruritus in cholestatic liver disease, not niacin flushing.
- **C. Mast cell degranulation** — While one study showed PGD2 release from mast cells in vitro, the primary accepted mechanism involves prostaglandin production by Langerhans cells and keratinocytes, and the reason aspirin works is its inhibition of prostaglandin synthesis, not prevention of mast cell degranulation per se.[9]
- **D. T cell activation** — Not implicated in niacin-induced flushing.

Would you like to explore the current evidence on cardiovascular outcomes with niacin and whether it still has a role in dyslipidemia management?

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Question 199

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?

A. Sofosbuvir and ledipasvir therapy
B. Tenofovir and velpatasvir therapy
C. Interferon and ribavirin therapy
D. Tenofovir and entecavir therapy

https://openevidence.com/ask/15bcc803-cbb0-4dd4-af2e-b6ac1710bc30

The correct answer is **A. Sofosbuvir and ledipasvir therapy**.

This patient has **chronic hepatitis C virus (HCV) genotype 1 infection**, confirmed by positive HCV antibody, detectable HCV RNA, and genotyping. The liver biopsy showing **mononuclear portal infiltrates and periportal hepatocyte necrosis (interface hepatitis)** is characteristic of chronic viral hepatitis. The severe car accident 30 years ago raises the possibility of a blood transfusion prior to universal HCV screening (implemented in 1992).

Ledipasvir/sofosbuvir (Harvoni) is an oral, fixed-dose direct-acting antiviral (DAA) combination — an **NS5A inhibitor (ledipasvir)** plus an **NS5B polymerase inhibitor (sofosbuvir)** — FDA-approved for HCV genotype 1.[1][2] In the ION-1 registration trial, SVR12 rates were **97–99%** in treatment-naive genotype 1 patients, including those with cirrhosis.[3][4] Standard treatment duration is **12 weeks** for treatment-naive patients without cirrhosis or with compensated cirrhosis.[2]

Why the other options are incorrect:

- **B. Tenofovir and velpatasvir** — Tenofovir is a **hepatitis B** antiviral, not an HCV drug. Velpatasvir is a valid HCV NS5A inhibitor, but it is combined with **sofosbuvir** (not tenofovir) in the pangenotypic regimen Epclusa. This is not a recognized combination.[5]
- **C. Interferon and ribavirin** — This was the prior standard of care but has been **supplanted by DAA regimens**, which achieve SVR rates exceeding 95% (vs. ~50% with interferon/ribavirin) with far fewer adverse effects and shorter treatment duration.[5][6]
- **D. Tenofovir and entecavir** — Both are **hepatitis B antivirals** (a nucleotide and nucleoside analog, respectively) with no activity against HCV. Additionally, combining two HBV agents from the same therapeutic class would be unusual even in HBV management.

Would you like to explore the recommended pre-treatment workup before initiating DAA therapy, including fibrosis staging and HBV screening?

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Question 200

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?

A. Islet cell cytoplasm
B. Deamidated gliadin peptide
C. Parietal cells
D. Smooth muscle

https://openevidence.com/ask/669aef00-ccb8-454d-a110-651d82eaf2e2

C. Parietal cells.

This is autoimmune (type A) gastritis with pernicious anemia. The defining lesion is antibody- and T cell–mediated destruction of gastric parietal cells, with the H^+ /K^+ -ATPase (gastric proton pump) as the major autoantigen; parietal cell antibodies are the serologic hallmark.[1][2] Loss of parietal cells eliminates intrinsic factor and acid, causing cobalamin malabsorption.[2]

Why the findings fit

- **Histology:** Corpus/fundus-predominant atrophy with antral sparing is the pattern that distinguishes autoimmune gastritis from H. pylori–associated atrophic gastritis, which begins at the incisura/antrum. Oxyntic (acid-secreting) glands containing parietal cells are confined to body and fundus.[3][4]
- **Neurologic exam:** Decreased proprioception and vibration with ataxic gait is subacute combined degeneration — demyelination of posterior and lateral columns from B12 deficiency.[5][6]
- **Macrocytic anemia + pallor:** Megaloblastic anemia from cobalamin deficiency.[7]

- **Hypothyroidism:** The thyrogastric association is well established; up to one-third of patients with autoimmune thyroid disease have autoimmune gastritis, and the AGA recommends bidirectional screening.[3][8]

Why the others are wrong

- **A. Islet cell cytoplasm** — type 1 diabetes; shares the polyglandular autoimmune background but does not cause gastric corpus atrophy or B12 deficiency.[1]
- **B. Deamidated gliadin peptide** — celiac disease. Can cause malabsorption and neuropathy, but the histologic lesion is duodenal villous atrophy with crypt hyperplasia, not corpus-restricted gastric atrophy.[8]
- **D. Smooth muscle** — anti–smooth muscle antibodies characterize type 1 autoimmune hepatitis; no gastric or hematologic correlate here.

Confirmatory testing: Anti–parietal cell antibody is the most sensitive serologic marker but is less specific (false positives with H. pylori and other autoimmune disease); anti–intrinsic factor antibody has low sensitivity (<30%) but high specificity.[3][7] Elevated serum gastrin with low pepsinogen I supports achlorhydria from oxyntic atrophy.[1][9] Treat with parenteral B12 (1 mg IM weekly for ~1 month, then monthly; high-dose oral 1–2 mg daily is comparably effective) — neurologic deficits may not fully reverse if longstanding.[6][10] These patients also need endoscopic surveillance given elevated risk of gastric adenocarcinoma and type 1 neuroendocrine tumors.[2][4]

Would you like to explore the recommended endoscopic surveillance intervals in autoimmune gastritis?

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Question 201

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?

A. Inpatient treatment with intravenous ciprofloxacin
B. Outpatient treatment with oral levofloxacin
C. Outpatient treatment with trimethoprim-sulfamethoxazole
D. Initiate hemodialysis

https://openevidence.com/ask/c79943c1-b4b4-4aa8-8468-4d15bc0bf509

The correct answer is **A: Inpatient treatment with intravenous ciprofloxacin**.

This patient has **acute pyelonephritis**, supported by fever (39.4°C), left costovertebral angle tenderness, marked pyuria (100 WBC/hpf), positive nitrites, and — critically — **numerous WBC casts**, which indicate intrarenal inflammation and strongly point to renal parenchymal infection in this clinical context.[1]

Inpatient admission with IV antibiotics is warranted here for several reasons:[1]

- **Systemic illness**: High fever, tachycardia (102/min), and leukocytosis (19,000/mm^3) raise concern for sepsis or impending sepsis.
- **Unstable comorbidities**: CKD (creatinine 2.4 mg/dL), poorly controlled diabetes (glucose 240 mg/dL), and an active diabetic foot ulcer all increase the risk of poor outcomes if initial treatment is ineffective.
- Per the NEJM review on acute pyelonephritis in adults, **immediate hospital admission is warranted for patients with severe illness or unstable coexisting medical conditions**. The IDSA 2025 guidelines on complicated UTI recommend fluoroquinolones among first-line empiric options for complicated UTI without sepsis.[1][2]

Why the other options are incorrect:

- **B and C (outpatient treatment)**: Outpatient management is reserved for mildly ill patients with minimal nausea, no vomiting, stable comorbidities, and a reliable psychosocial situation. This patient's systemic toxicity and multiple comorbidities make outpatient therapy inappropriate. Additionally, trimethoprim-sulfamethoxazole should generally not be used empirically for pyelonephritis without known susceptibility and requires a longer treatment course (10–14 days vs. 7 days for fluoroquinolones).[1][3]
- **D (hemodialysis)**: There is no emergent indication for dialysis. Potassium is 5.0 mEq/L (mildly elevated but not dangerous), bicarbonate is 25 mEq/L (normal, no severe acidosis), and there are no signs of uremic encephalopathy, pulmonary edema, or refractory hyperkalemia. The elevated BUN/creatinine likely reflects baseline CKD, possibly with a prerenal component from infection.

Ciprofloxacin dosing should be adjusted for renal impairment, and cross-sectional imaging of the urinary tract should be considered given his diabetes, CKD, and systemic illness to exclude obstruction, abscess, or emphysematous pyelonephritis.[1]

Would you like to explore empiric antibiotic regimens for complicated pyelonephritis in the setting of chronic kidney disease?

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Question 202

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?

A. 0.9% saline IV
B. 5% dextrose IV
C. 5% dextrose IV with 0.45% saline IV
D. Oral free water replacement

https://openevidence.com/ask/0360fdd9-eed1-46de-8b6a-984510804d06

The answer is **A. 0.9% saline IV**.[1]

This patient has **hypovolemic hypernatremia** (Na+ 154 mEq/L) from high-output surgical drain losses following pancreaticoduodenectomy. The critical finding is evidence of **hemodynamic compromise**: tachycardia to 120/min and a markedly **narrowed pulse pressure of 19 mmHg** (107/88), along with dry mucous membranes and altered mental status. These signs indicate significant intravascular volume depletion requiring isotonic resuscitation as the immediate priority.

Why isotonic saline first?

In hypernatremia with concurrent hypovolemia, the management approach is determined by hemodynamic status. As described in the NEJM review on hypernatremia, isotonic saline is generally unsuitable for correcting hypernatremia (1 L of 0.9% NS would lower serum sodium by only ~0.2 mEq/L in this patient).[1] However, the same review specifies that isotonic saline is indicated when there is **"depletion of extracellular-fluid volume sufficient to cause substantial hemodynamic compromise"** — after which a **prompt transition to hypotonic fluids** (0.45% NaCl or D5W) should follow to actually correct the hypernatremia.[1]

> "The sole indication for administering isotonic saline to a patient with hypernatremia is a depletion of extracellular-fluid volume that is sufficient to cause substantial hemodynamic compromise. Even in this case, after a limited amount of isotonic saline has been administered to stabilize the patient's circulatory status, a hypotonic fluid should be substituted."
>
> —Horacio J. Adrogué, M.D. et al., Baylor College of Medicine and other institutions. Hypernatremia. N Engl J Med. May 18, 2000.
>
> Used under license from The New England Journal of Medicine.

Why not the other options?

- **B (D5W):** Distributes as free water after glucose metabolism, providing negligible intravascular volume expansion — inadequate for initial resuscitation in a hemodynamically compromised patient.[1]
- **C (D5 0.45% NS):** A reasonable choice after initial stabilization, but provides less efficient volume resuscitation than NS when the immediate concern is restoring perfusion.[1]
- **D (Oral free water):** The patient is **difficult to arouse**, creating a significant aspiration risk. While oral or enteral free water is the preferred route in alert patients, it is not feasible here.[1][2]

Once hemodynamic stability is achieved with a limited volume of NS, the fluid should be switched to a hypotonic solution to correct the free water deficit, targeting sodium correction of **no more than 10–12 mEq/L per 24 hours** with sodium rechecked every 2–4 hours initially.[1][3]

Would you like to explore the free water deficit calculation and optimal sodium correction strategy for this patient?

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Question 203

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?

A. Giardia intestinalis
B. Shigella species
C. Staphylococcus aureus
D. Enterotoxigenic Escherichia coli

https://openevidence.com/ask/33945a2f-6a0d-4b5c-b3f1-2f6a01a2af8b

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The answer is **D. Enterotoxigenic Escherichia coli (ETEC)**.

ETEC is the most common cause of traveler's diarrhea in visitors to South Asia, including India, accounting for more than half of bacterial cases in this region.[1][2] The clinical presentation here — **watery, non-bloody diarrhea** with abdominal cramps, malaise, and **no fever** — is classic for ETEC, which produces heat-labile and heat-stable enterotoxins that induce secretory diarrhea without mucosal invasion.[3][4] The **1–3 day incubation period** fits the timeline (symptoms began during the return flight from a 2-week stay).[5]

An additional predisposing factor is her use of **ranitidine**, an H2 receptor antagonist. Gastric acid serves as a first-line defense against ingested enteropathogens; acid suppression increases susceptibility to enteric infection.[6][7] While the risk association is stronger with PPIs than H2RAs, the concept of reduced gastric acid barrier remains clinically relevant.[8]

Why not the other options:

- **Giardia intestinalis** — Causes more **chronic, intermittent** diarrhea with prominent bloating and flatulence, and has a longer incubation period (typically 1–2 weeks). Protozoal pathogens account for <5% of traveler's diarrhea.[7]
- **Shigella species** — Causes **inflammatory/dysenteric diarrhea** with bloody stools, fever, and tenesmus. The afebrile, watery presentation here is inconsistent.
- **Staphylococcus aureus** — Causes **rapid-onset** food poisoning (1–6 hours) via preformed toxin, predominantly vomiting, that typically **resolves within 24 hours**. A 3-day course of ongoing watery diarrhea does not fit.

Would you like to explore the recommended empiric treatment for traveler's diarrhea acquired in South Asia?

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Question 204

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?

A. Inadvertent surgical removal of parathyroid glands
B. DiGeorge syndrome
C. Chronic hypomagnesemia
D. Hungry bone syndrome

https://openevidence.com/ask/69bea2b1-2c78-420c-9cc6-a5c62f438121

The correct answer is **A. Inadvertent surgical removal of parathyroid glands**.

This is a classic presentation of **post-thyroidectomy hypoparathyroidism**. The clinical picture — symptomatic hypocalcemia (serum calcium **6.7 mg/dL**) developing on postoperative day 1, with **perioral numbness, hand and foot paresthesias, confusion, and a positive Trousseau sign** — is the hallmark of parathyroid insufficiency following total thyroidectomy.[1][2]
Hypoparathyroidism is the most common complication of bilateral thyroid surgery, with transient rates of 19–38% and permanent rates of 0–3%.[1] The mechanism may involve inadvertent excision, devascularization, or direct injury to the parathyroid glands.[2]

The positive **Trousseau sign** — carpal spasm elicited by inflating a blood pressure cuff above systolic pressure for 3 minutes — is a specific bedside sign of hypocalcemia-induced neuromuscular excitability.[2][3]

Why not the other options:

- **B. DiGeorge syndrome** — A congenital disorder (22q11.2 deletion) causing parathyroid aplasia/hypoplasia that presents in infancy or childhood. It would not first manifest as acute hypocalcemia in a 55-year-old with no prior history.
- **C. Chronic hypomagnesemia** — While the serum magnesium is low (1.1 mEq/L), the acute onset of symptoms immediately following thyroidectomy points to a surgical etiology rather than a chronic condition. Hypomagnesemia can impair PTH secretion and cause PTH resistance, worsening hypocalcemia, but it would not explain the temporal relationship to surgery.[4]
- **D. Hungry bone syndrome** — This occurs in states of preoperative **high bone turnover** (thyrotoxicosis, severe hyperparathyroidism), where postoperative mineral deposition into demineralized bone causes hypocalcemia with simultaneous drops in calcium, magnesium, and phosphorus. This patient had **papillary thyroid carcinoma** with no indication of thyrotoxicosis or a high bone turnover state. In euthyroid patients undergoing thyroidectomy for benign nodules or cancer, hungry bone syndrome is not observed.[5]

Would you like to explore the acute management of symptomatic post-thyroidectomy hypocalcemia?

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Question 205

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?

A. Regular blood transfusions
B. Methylphenidate
C. Iron supplementation
D. Allogenic stem cell transplantation

https://openevidence.com/ask/43874d31-b8af-485d-aa01-e032ab90b29a

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The answer is **C. Iron supplementation**.

This patient presents with a classic constellation of **iron deficiency anemia (IDA)**. The key findings include:

- **Microcytic anemia** (hemoglobin 11.5 g/dL, MCV 76 fL) with **elevated RDW (18%)**, reflecting anisocytosis characteristic of IDA[1]
- **Conjunctival pallor**, **angular cheilitis** (cheilosis), and **koilonychia** (spoon-shaped nails) — all well-recognized physical signs of iron deficiency[2][3]
- **Dietary risk factor**: subsisting primarily on cereal, which is low in bioavailable heme iron[4]

The AAP's 2026 clinical report recommends that for adolescents with IDA, initial therapy should consist of **ferrous sulfate, 65 mg elemental iron, administered once daily**, along with dietary counseling and identification of the underlying etiology.[4] Oral iron is first-line in this setting given mild-to-moderate anemia in a clinically stable patient.[5]

Why the other options are incorrect:

- **A. Regular blood transfusions** — Reserved for severe, hemodynamically unstable anemia (generally Hb <7 g/dL); this patient has mild anemia with stable vital signs.[4]
- **B. Methylphenidate** — Though his declining academic performance and inattention could superficially suggest ADHD, these symptoms are explained by iron deficiency and anemia, which cause fatigue, poor concentration, and decreased activity.[3][4]
- **D. Allogeneic stem cell transplantation** — Indicated for conditions such as severe aplastic anemia or hemoglobinopathies, not nutritional IDA.

Would you like to explore the expected timeline and follow-up monitoring after starting oral iron in adolescents?

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Question 206

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?

A. Hyperbaric oxygen
B. Protein C concentrate
C. Argatroban
D. Tranexamic acid

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The answer is **B. Protein C concentrate**.

This presentation is classic **warfarin-induced skin necrosis (WISN)** — onset **3 to 5 days after warfarin initiation**, with painful purpura, hemorrhagic bullae, and necrosis over adipose-rich areas (thighs, buttocks, genitalia).[1][2] The underlying mechanism is a **transient hypercoagulable state** caused by the rapid decline of protein C (half-life ~8 hours) before adequate reduction of procoagulant factors II, IX, and X, leading to microvascular thrombosis in the skin and subcutaneous tissue.[2][3]

> "People with hereditary deficiency of protein C, a natural anticoagulant protein, are at highest risk, even if they are heterozygotes and thus have no history of recurrent thrombosis. In these persons, warfarin greatly depresses protein C levels before decreasing other vitamin K-dependent coagulation factors, inducing a transient hypercoagulable state and thrombus formation."
>
> —Jean Claude Roujeau et al., Henri Mondor Hospital and other institutions. Severe Adverse Cutaneous Reactions to Drugs. N Engl J Med. November 10, 1994.
>
> Used under license from The New England Journal of Medicine.

Treatment of WISN includes **discontinuing warfarin**, administering **vitamin K**, providing **heparin** anticoagulation, and giving **protein C concentrate** to directly replete the depleted

protein C and halt the thrombotic process.[1][4] Case reports and clinical studies demonstrate that protein C concentrate halts necrosis progression, often within 24 hours of administration.[4][5]

Why not the other options:

- **A. Hyperbaric oxygen** — Used for certain wound-healing indications (e.g., chronic non-healing wounds, gas gangrene) but does not address the underlying prothrombotic mechanism.
- **C. Argatroban** — A direct thrombin inhibitor used in heparin-induced thrombocytopenia (HIT). While anticoagulation is part of WISN management, heparin (not argatroban) is the standard choice, and argatroban does not correct the protein C deficiency driving the pathology.
- **D. Tranexamic acid** — An antifibrinolytic agent that would be contraindicated in this prothrombotic state, as it could worsen microvascular thrombosis.

Would you like to explore how to safely reinitiate anticoagulation in patients with a history of warfarin-induced skin necrosis?

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Question 207

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?

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

https://openevidence.com/ask/4c0fc4fe-5d9a-4941-b1bf-1f5513b43728

The answer is **B. Long face and large everted ears**.

The clinical presentation — a 15-year-old male with **learning disability, hyperactivity, social interaction difficulties**, and **CGG trinucleotide repeat expansion** — is diagnostic of **Fragile X syndrome (FXS)**, the most common inherited cause of intellectual disability and the most common single-gene cause of autism.[1][2]

FXS results from expansion of CGG repeats (>200 repeats = full mutation) in the 5' UTR of the *FMR1* gene on the X chromosome, leading to gene silencing and loss of FMRP production.[2][3] The characteristic physical features of FXS include a **long, narrow face**, **large prominent ears**, **prominent jaw and forehead**, joint hyperlaxity, flat feet, and **macroorchidism** after puberty.[1][4][5] These craniofacial features become more obvious with age and may be subtle in younger children.[5][6]

Why the other options are incorrect:

- **A. Frontal balding and cataracts** — characteristic of **myotonic dystrophy type 1**, caused by a CTG trinucleotide repeat expansion (not CGG).
- **C. Almond-shaped eyes and downturned mouth** — features of **Prader-Willi syndrome**, caused by loss of paternally expressed genes on chromosome 15q11-13.
- **D. Thin upper lip and receding chin** — suggestive of **fetal alcohol spectrum disorder**, not a trinucleotide repeat disorder.

Would you like to explore the current treatment options for Fragile X syndrome?

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Question 208

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?

A. Cleave immunoglobulin
B. Inhibit phagocytosis
C. Inhibit ribosomal function
D. Trigger widespread inflammation

https://openevidence.com/ask/cad030ac-d54b-4c21-8852-324b67ae3086

The correct answer is **B. Inhibit phagocytosis**.

This presentation — **fever, painful lymphadenopathy (buboes), and acral ischemic necrosis** (black hemorrhagic eschars on fingertips) in a traveler returning from **rural Madagascar** with animal exposure — is classic for **plague caused by *Yersinia pestis***, with features of both bubonic and septicemic plague.[1][2][3] Madagascar is one of the world's most active plague-endemic regions, and this patient's occupation as a zoologist studying lemurs placed him at high risk for flea bites from infected rodents.[2]

The hallmark virulence factors of *Y. pestis* function primarily to **inhibit phagocytosis**:[1][3]

- **F1 capsular antigen** (encoded by *caf1* on the pFra plasmid): forms a polypeptide capsule at 37°C that **inhibits macrophage phagocytosis**.[3]
- **Yersinia outer proteins (Yops)**: effector proteins delivered into host immune cells via a **Type III secretion system** that disrupt actin cytoskeleton signaling, **prevent phagocytosis**, and induce apoptosis in macrophages, dendritic cells, and neutrophils.[3][4]

The black fingertip eschars represent **acral ischemic necrosis** from disseminated intravascular coagulation (DIC) in septicemic plague — the historical origin of the term "Black Death."

Why the other options are incorrect:

- **A. Cleave immunoglobulin** — characteristic of IgA protease–producing organisms (e.g., *Neisseria*, *Haemophilus influenzae*).
- **C. Inhibit ribosomal function** — describes exotoxin mechanisms such as Shiga toxin or diphtheria toxin.
- **D. Trigger widespread inflammation** — while septicemic plague involves endotoxin-mediated shock, the specific virulence factors of *Y. pestis* are designed to **suppress and evade** immune responses, not to trigger inflammation as their primary function.[3][5]

Would you like to explore the recommended antimicrobial treatment regimens for plague?

References

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Question 209

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?

A. Phosphodiester bonds
B. Glycosidic bonds
C. Cystine bonds
D. Hydrogen bonds

https://openevidence.com/ask/0d5b800f-5773-4a56-8879-1f0408e220c1

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 α-1,4-glycosidic bonds** in oligosaccharides and disaccharides, cleaving them into glucose and other absorbable monosaccharides.[2] By inhibiting this enzymatic activity, miglitol prevents the cleavage of glycosidic bonds, delaying carbohydrate digestion and glucose absorption, thereby reducing postprandial hyperglycemia.[1][3]

The other answer choices are not relevant to this mechanism:

- **Phosphodiester bonds** link nucleotides in DNA and RNA — unrelated to carbohydrate digestion.
- **Cystine (disulfide) bonds** are covalent linkages between cysteine residues in proteins — unrelated to carbohydrate digestion.
- **Hydrogen bonds** are ubiquitous non-covalent interactions; alpha-glucosidase does not act on hydrogen bonds.

The instruction to take miglitol **with the first bite of the meal** reflects the need for the drug to be present in the intestinal lumen at the same time as dietary carbohydrates, so it can competitively inhibit alpha-glucosidase before glycosidic bonds are cleaved.[1][4]

Would you like to explore how miglitol compares to acarbose in efficacy and tolerability?

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Question 210

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?

A. Oral acyclovir
B. Oral cephalexin
C. Smoking cessation
D. Washing thoroughly

https://openevidence.com/ask/f3121838-4c0a-46bf-ad7d-57d7b839a83e

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A. Oral acyclovir. This is herpetic whitlow — a primary HSV inoculation infection of the fingertip, classically an occupational hazard for dental personnel exposed to oral secretions.[1][2] The presentation is diagnostic: burning/tingling prodrome followed by abrupt swelling, erythema, and clustered small vesicles on the distal pulp, often with mild leukocytosis and reactive lymphangitis or epitrochlear/axillary adenopathy.[3][4] Acyclovir is the treatment of choice for HSV, and antiviral therapy started early in a primary episode speeds healing and reduces pain.[3][5] Typical regimen: acyclovir 400 mg PO TID (or 200 mg five times daily) for 7–10 days; valacyclovir or famciclovir are equally acceptable.[5][6]

Critical management point: do not incise and drain. Herpetic whitlow is self-limited (2–4 weeks) and surgical drainage prolongs morbidity and risks bacterial superinfection or systemic spread; the IDSA states surgery should be avoided in HSV infections unless a documented bacterial or fungal abscess is present.[2][5][7] Misdiagnosis as a bacterial felon is common — 65% of pediatric cases in one review.[7]

Occupational counseling matters here: lesions shed virus, so he should cover the digit with an occlusive dressing and avoid direct patient contact until lesions have crusted/re-epithelialized. Universal glove use is what prevents this in dental practice.

Why the other options are wrong:

- **Oral cephalexin (B):** grouped 3-mm vesicles on the pulp with a burning prodrome are viral, not staphylococcal. A felon is a tense, exquisitely tender pulp abscess without vesicles, and paronychia involves the nail fold. Antibiotics are unnecessary absent documented secondary bacterial infection.[4][8][9]
- **Smoking cessation (C):** the family history of thromboangiitis obliterans is a distractor. Buerger disease causes ischemic digital pain, claudication, and ulceration in a smoker — not acute vesicles over 24 hours.
- **Washing thoroughly (D):** poison oak (Toxicodendron) dermatitis is intensely pruritic, linear/streaky, and typically appears 1–3 days after exposure; this exposure was a week ago, the lesions are painful rather than itchy, and they are confined to one digital pulp. Decontamination is also futile more than a few hours after contact.

Diagnosis is clinical; if uncertain, unroof a vesicle for HSV PCR (highest yield) — it does not change initial management.[4] Counsel that recurrences occur in roughly a quarter of cases, usually milder, and suppressive therapy can be considered for frequent recurrences.[7]

Would you like to explore suppressive antiviral regimens for recurrent herpetic whitlow?

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Question 211

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?

A. Lifestyle modification
B. Combined antacid therapy
C. Continue on Omeprazole
D. Surgical gastropexy

https://openevidence.com/ask/41c7ab6a-d551-4eb5-9d16-6e0837151ed2

The answer is **D. Surgical gastropexy**.

The barium swallow findings — a **subdiaphragmatic gastroesophageal junction (GEJ) with herniation of the gastric fundus into the left hemithorax** — are characteristic of a **Type II (paraesophageal) hiatal hernia**. In this hernia type, the GEJ remains in its normal position below the diaphragm, but the gastric fundus herniates through the esophageal hiatus alongside the esophagus.[1]

Why surgical repair is indicated here:

- **Surgical repair is recommended for symptomatic type II and III paraesophageal hernias**, particularly those unresponsive to medical therapy. This patient has progressive dysphagia and heartburn refractory to multiple GERD therapies, making continued conservative management inappropriate.[1]
- Paraesophageal hernias carry risk for serious complications including **volvulus, obstruction, and strangulation**, reinforcing the need for definitive repair in symptomatic patients.[1][2]

- Elective repair is associated with significantly better outcomes (88% textbook outcomes) compared with urgent (58%) or emergent (47%) repair, supporting proactive surgical intervention rather than watchful waiting in a symptomatic patient.[3]

Why the other options are incorrect:

- **A (Lifestyle modification), B (Combined antacid therapy), C (Continue omeprazole):** The patient has already failed multiple medical therapies. These approaches address acid-related symptoms but do not correct the underlying **structural defect** — the herniation of the gastric fundus. When symptoms do not respond to medical therapy, especially with dysphagia as the predominant presentation, surgical repair should be pursued.[1]

In practice, paraesophageal hernia repair typically involves reduction of the hernia, crural closure, and often an anti-reflux procedure (fundoplication) in addition to gastropexy to anchor the stomach in its intra-abdominal position.[2][4][5]

Would you like to explore the classification and management differences between the four types of hiatal hernias?

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Question 212

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?

A. Distributive shock with warm skin
B. Hypovolemic shock with warm skin
C. Neurogenic shock with cold skin
D. Obstructive shock with cold skin

https://openevidence.com/ask/8a190434-67ea-46da-8c65-5a6c4d486deb

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The correct answer is **A. Distributive shock with warm skin**.

This patient has **septic shock from a gram-negative wound infection** acquired in the Gulf of Mexico, most consistent with **Vibrio vulnificus**. Septic shock is the prototypical form of **distributive shock**, characterized by systemic vasodilation with decreased systemic vascular resistance (SVR) and typically preserved or increased cardiac output in a hyperdynamic state.[1] [2] This peripheral vasodilation produces the characteristic finding of **warm, flushed skin**.

As described in a classic NEJM review of septic shock pathogenesis:

> "If this hypovolemia is corrected by aggressive intravenous administration of fluids, it will lead to low systemic vascular resistance, normal or increased cardiac output, tachycardia, and elevated oxygen concentrations in pulmonary-artery blood -- a hyperdynamic shock syndrome -- in more than 90 percent of patients. This constellation of hemodynamic abnormalities has been categorized as distributive shock."

None

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Why the other options are incorrect:

- **B (Hypovolemic shock with warm skin):** Hypovolemic shock produces **cold, clammy skin** due to compensatory sympathetic vasoconstriction and elevated SVR. The clinical picture here — fever, spreading cellulitis, gram-negative bacteremia — points to a septic, not hypovolemic, etiology.[2]
- **C (Neurogenic shock with cold skin):** Neurogenic shock results from loss of sympathetic tone (e.g., spinal cord injury), which can cause warm skin — but the mechanism is entirely different, and this clinical scenario has no neurological insult. Additionally, cold skin would be atypical for neurogenic shock.
- **D (Obstructive shock with cold skin):** Obstructive shock (e.g., cardiac tamponade, tension pneumothorax, massive PE) features impaired cardiac output with elevated SVR and cold extremities. There is no evidence of an obstructive process here.[2]

Early septic shock produces **warm** peripheries due to vasodilation, whereas **hypovolemic, cardiogenic, and obstructive** shock all produce **cold** peripheries from compensatory vasoconstriction.[3] In late or decompensated sepsis, cold extremities can develop as cardiac output falls, but the classic and tested presentation of septic/distributive shock emphasizes warm skin.[3]

Would you like to explore the management of Vibrio vulnificus infections, including antibiotic selection and the role of surgical intervention?

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Question 213

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?

A. Intravenous thiamine
B. Oral naltrexone
C. Intravenous vitamin B12
D. Intravenous glucose

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The answer is **A. Intravenous thiamine**.

This patient presents with the **classic triad of Wernicke encephalopathy (WE)**: **confusion/ altered mental status**, **oculomotor dysfunction** (horizontal nystagmus on lateral gaze), and **gait ataxia** (difficulty walking without assistance), in the setting of chronic alcohol use disorder.[1][2] The **macrocytic anemia** (MCV 110 µm³) further supports chronic alcohol misuse and nutritional deficiency.

Intravenous thiamine is the cornerstone of WE treatment and must be initiated immediately, as WE is a medical emergency — untreated, it carries approximately **20% mortality** and progresses to **irreversible Korsakoff syndrome in ~85% of survivors**.[3][4] Acute thiamine replacement is typically given at **100–500 mg IV three times daily for 2–3 days**, followed by oral maintenance.[3][5] The IV route is essential because oral absorption is unreliable in malnourished, alcohol-dependent patients.[6]

Why not the other options:

- **D (IV glucose)** — Glucose administration in a thiamine-depleted patient can **precipitate or worsen** Wernicke encephalopathy, as carbohydrate metabolism consumes thiamine as a cofactor. Thiamine must be given **before or concurrently with** glucose, never glucose alone first.[3][5]
- **B (Oral naltrexone)** — Used for long-term treatment of alcohol use disorder to reduce cravings, not for acute neurological emergencies.
- **C (IV vitamin B12)** — While B12 deficiency can cause macrocytic anemia and neurologic findings, the classic WE triad with alcohol use points to thiamine deficiency. B12 deficiency typically presents with peripheral neuropathy and subacute combined degeneration, not this acute constellation.

Would you like to explore the optimal thiamine dosing regimen and treatment duration for Wernicke encephalopathy?

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Question 214

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?

A. Chlamydia trachomatis
B. Ureaplasma urealyticum
C. Trichomonas vaginalis
D. Enterobius vermicularis

https://openevidence.com/ask/ae07bb80-3834-4a49-a1d2-679e9d307029

The answer is **C. Trichomonas vaginalis**.

This vignette presents the classic triad of trichomoniasis: **frothy, malodorous yellow-green discharge**; "**strawberry cervix**" (colpitis macularis — punctate erythematous spots on an inflamed cervix); and **motile trichomonads on saline wet mount**.[1][2][3]

Key distinguishing features pointing to *Trichomonas vaginalis*:

- **Strawberry cervix** is highly specific (approaching 100%) for trichomoniasis, though it is observed in only ~2–5% of cases. The description of "pink and inflamed nulliparous cervix with small red punctate spots" is the classic gross appearance of colpitis macularis.[3][4]
- **Motile organisms on wet mount** in the setting of squamous cells is diagnostic of trichomoniasis. *T. vaginalis* is a flagellated protozoan that displays characteristic tumbling motility on saline microscopy.[3][5]
- The **greenish-yellow frothy discharge** with malodor is the hallmark symptomatic presentation.[6]

Why not the other options:

- **Chlamydia trachomatis** — an obligate intracellular bacterium that cannot be visualized as motile organisms on wet mount; it typically causes mucopurulent cervicitis, not a frothy vaginal discharge with strawberry cervix.
- **Ureaplasma urealyticum** — a mycoplasma that is too small to visualize on light microscopy and does not produce frothy discharge or colpitis macularis.
- **Enterobius vermicularis** (pinworm) — a helminth causing perianal pruritus, not a vaginal STI with this presentation. While vaginal migration can rarely occur, the wet mount would show ova or large worms, not motile organisms of this type.

Would you like to explore the recommended treatment regimen for trichomoniasis, including partner management?

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Question 215

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?

A. γ-aminobutyric acid
B. Acetylcholine
C. Dopamine
D. Glutamate

https://openevidence.com/ask/cc867117-9c71-4951-82bb-e3fd73324261

The answer is **B. Acetylcholine**.

This vignette describes **moderate-to-severe Alzheimer's disease**: progressive cognitive decline over 3 years with impaired IADLs (requires help with cooking/cleaning), getting lost in familiar areas, oriented only to person, both short- and long-term memory deficits, and **anosognosia** (indifference to deficits). The **initial pharmacotherapy** for Alzheimer's disease is an **acetylcholinesterase inhibitor** (donepezil, rivastigmine, or galantamine), which enhances cholinergic neurotransmission by inhibiting the breakdown of **acetylcholine** at synaptic clefts.[1][2][3]

Why not the other options:

- **A. GABA** — No GABA-targeting agents are approved for Alzheimer's disease. Drugs targeting GABA have not shown cognitive benefits in AD.[1]

- **C. Dopamine** — Though dopaminergic deficits exist in AD, dopamine-targeting agents have not demonstrated cognitive benefit.[1]

- **D. Glutamate** — This refers to **memantine**, an NMDA receptor antagonist approved for **moderate-to-severe AD**. However, memantine is not the initial agent; it is typically **added to a cholinesterase inhibitor** once disease progresses to moderate-to-severe stages, or used when cholinesterase inhibitors are insufficient. A JAMA review notes that cholinesterase inhibitors are the first-line therapy, and memantine is approved specifically for moderate-to-severe disease and is most commonly used as adjunctive therapy.[2][3][4][5]

The key distinction is that cholinesterase inhibitors (acting on acetylcholine) represent the **initial** pharmacotherapy across all stages of AD, whereas memantine (glutamate) is reserved as an add-on or alternative for more advanced disease.[3][6]

Would you like to explore the comparative profiles of the three available cholinesterase inhibitors for Alzheimer's disease?

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Question 216

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?

A. Succinylcholine
B. Inhaled ipratropium and oxygen
C. Atropine and pralidoxime
D. Inhaled albuterol and oxygen

https://openevidence.com/ask/dbcdfd63-69a7-473a-bd24-45f2a64fd9a2

The answer is **C. Atropine and pralidoxime**.

This presentation is classic for **organophosphate poisoning**. The key contextual and clinical clues include:

- **Agricultural exposure**: A mechanic working on a plowing tractor — agricultural equipment commonly contaminated with organophosphate pesticides[1][2]
- **Cholinergic toxidrome (muscarinic excess)**: Acute-onset dyspnea with diffuse wheezes (bronchospasm), **miosis** (contracted pupils), **diaphoresis**, and relative **bradycardia** (HR 65) — all hallmarks of acetylcholinesterase inhibition and parasympathetic overstimulation[1][3]

Why the other options are incorrect:

- **A. Succinylcholine** — A depolarizing neuromuscular blocker metabolized by plasma cholinesterase (pseudocholinesterase). In organophosphate poisoning, cholinesterase is already inhibited, so succinylcholine would have a dangerously **prolonged duration of action** and would worsen paralysis. It is contraindicated.
- **B. Inhaled ipratropium and oxygen** — While ipratropium is an anticholinergic, inhaled delivery alone is insufficient to address the systemic cholinergic crisis. Organophosphate

poisoning requires **systemic atropine** to counteract bronchorrhea, bradycardia, and bronchospasm, plus an oxime to reactivate acetylcholinesterase.[1][3]

- **D. Inhaled albuterol and oxygen** — This would treat simple bronchospasm (e.g., asthma) but does not address the underlying cholinergic toxidrome. The miosis and diaphoresis distinguish this from a primary airway disease.

Cornerstones of organophosphate poisoning management per the AHA (2023/2025) include:[1][4]

- **Atropine** — Blocks muscarinic effects (bronchospasm, bronchorrhea, bradycardia); initial dose 1–3 mg IV, doubled every 5 minutes until atropinization (clear lungs, HR >80, SBP >80)
- **Pralidoxime** — Reactivates acetylcholinesterase before irreversible "aging" occurs, reversing nicotinic effects (fasciculations, weakness, paralysis); 1–2 g IV over 30 minutes, followed by infusion[2][3]
- **Decontamination** — Removal of clothing and soap/water irrigation to prevent ongoing absorption
- **Benzodiazepines** — For seizure prophylaxis in severe cases

Would you like to explore the intermediate syndrome that can complicate organophosphate poisoning days after initial treatment?

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Question 217

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?

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

https://openevidence.com/ask/20387e85-c7d5-439b-a0a5-c5572b85703d

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The answer is **C. Na+/Cl- cotransporter in the membranes of epithelial cells in the distal convoluted tubule**.

This patient's constellation of **constipation, fatigue, and decreased motivation** developing after initiation of a new antihypertensive medication points to **thiazide diuretic–induced hypercalcemia**. Thiazide diuretics (e.g., hydrochlorothiazide, chlorthalidone) are first-line agents for hypertension, and their cellular target is the **Na+/Cl- cotransporter (NCC)** in the distal convoluted tubule.[1]

Mechanism linking thiazides to these symptoms:

- By inhibiting the NCC, thiazides reduce intracellular sodium in distal tubular epithelial cells, which enhances basolateral Na+/Ca2+ exchange and increases calcium reabsorption. This leads to **decreased urinary calcium excretion and elevated serum calcium**.[1][2]
- Hypercalcemia, even when mild, classically presents with **fatigue and constipation** — the two cardinal nonspecific symptoms. As a JAMA review notes, "mild hypercalcemia is typically asymptomatic or characterized by nonspecific constitutional symptoms, such as

fatigue and constipation". Elevated ionized calcium causes hyperpolarization of neuromuscular membranes, resulting in slowed gastrointestinal peristalsis (constipation) and neuropsychiatric symptoms (fatigue, lethargy).[3]

Why not the other options:

- **A (ARBs)** and **B (ACE inhibitors)** — Neither class is typically associated with constipation or hypercalcemia.
- **D (Loop diuretics)** — Loop diuretics inhibit Na+/K+/2Cl- transporters in the ascending loop of Henle and cause **hypercalciuria** (the opposite effect on calcium), leading to hypocalcemia rather than hypercalcemia.

The hydrochlorothiazide FDA label explicitly lists **constipation** and **weakness** among reported adverse reactions and warns that thiazides may cause **elevation of serum calcium**.[2][4]

Would you like to explore the evaluation and management of thiazide-induced hypercalcemia, including when to suspect underlying hyperparathyroidism?

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Question 218

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:

A. Iodine deficiency
B. Thryoglossal duct cyst
C. Infection
D. Chronic renal disease

https://openevidence.com/ask/2a005cd0-d3df-4bfa-a421-c981dc95d7ea

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The answer is **C. Infection**.

The clinical and histopathological findings are classic for **subacute granulomatous thyroiditis (de Quervain thyroiditis)**, which is characteristically preceded by a **viral upper respiratory tract infection**. Viruses commonly implicated include coxsackievirus, adenovirus, Epstein-Barr virus, mumps, measles, influenza, and SARS-CoV-2.[1][2][3]

Why this presentation fits de Quervain thyroiditis:

- **Tender neck and jaw pain** — anterior neck pain radiating to the jaw or ear is the hallmark presentation, occurring most commonly in middle-aged women.[3][4]
- **Hypothyroid symptoms** (fatigue, constipation, decreased appetite, bradycardia at 60 bpm) — this patient is in the **hypothyroid phase** of the typical triphasic course (thyrotoxicosis → hypothyroidism → euthyroidism).[5][6]
- **Biopsy with granulomatous inflammation, multinucleate giant cells, and fragmented colloid** — these are the defining histopathological features. The multinucleate giant cells (often foreign-body type) surrounding and phagocytosing fragmented colloid are characteristic of this condition.[1][2][7]

Why the other choices are incorrect:

- **A. Iodine deficiency** — causes endemic goiter and hypothyroidism but does not produce granulomatous inflammation or a tender thyroid.

- **B. Thyroglossal duct cyst** — a developmental anomaly presenting as a midline neck mass that moves with swallowing/tongue protrusion; unrelated to granulomatous thyroiditis.
- **D. Chronic renal disease** — can cause secondary hypothyroidism through altered thyroid hormone metabolism but does not cause granulomatous inflammation of the thyroid.

Would you like to explore the management of subacute granulomatous thyroiditis across its triphasic course?

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Question 219

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?

A. Denial
B. Displacement
C. Projection
D. Regression

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The answer is **C. Projection**.

Projection is the defense mechanism in which an individual **attributes their own unacceptable thoughts, feelings, or behaviors to another person**, thereby avoiding the shame or guilt associated with acknowledging those qualities in themselves.[1][2] In this vignette, the patient has a well-documented alcohol use disorder that has led to job loss, yet rather than acknowledging his own substance abuse problem, he accuses his ex-boss of being a cocaine addict. He is attributing his own unacceptable quality (addiction) to someone else.

Projection is classified alongside denial and rationalization as a **disavowal defense**, in which the individual refuses to acknowledge their role in a problem and misattributes it to another source.[3]

The other options differ in key ways:

- **Denial** would involve the patient refusing to acknowledge his alcohol problem altogether (e.g., "I don't have a drinking problem"). While denial may also be at play here, the specific behavior of accusing his boss of addiction is projection.[1]

- **Displacement** involves redirecting an emotion (e.g., anger) from its true target to a safer or less threatening one. If the patient were angry at his boss but instead yelled at a nurse, that would be displacement.[4]
- **Regression** involves reverting to behaviors characteristic of an earlier developmental stage (e.g., an adult throwing a tantrum or becoming clingy like a child). Although the patient is agitated, his behavior is specifically accusatory toward his boss rather than a reversion to childlike behavior.[4][5]

Would you like to explore how projection differs from projective identification?

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Question 220

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?

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.

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The correct answer is **C. Accept the patient's wishes and ensure he receives appropriate care.**

This patient — an incarcerated individual presenting with **acute variceal hemorrhage** in the setting of known cirrhosis — is hemodynamically unstable and clearly, coherently expressing his desire for full resuscitative efforts. **Incarcerated patients retain full decision-making autonomy** when they have capacity, and are entitled to the **same standard of care as non-incarcerated patients**.[1][2]

Several key principles support this:

- **Eighth Amendment protections** guarantee incarcerated individuals' right to healthcare. The landmark case *Estelle v. Gamble* (1976) established that "deliberate indifference to serious medical needs of prisoners" constitutes cruel and unusual punishment.[1]
- Per ACEP best practice guidelines, **patients in custody make their own medical decisions** if they have decision-making capacity. This patient is alert, communicating coherently, and expressing a clear preference for treatment.[2]
- Incarcerated persons have a **legally protected right to consent to or refuse treatment**, including life-sustaining interventions.[3][4]

Why the other options are incorrect:

- **A (Ethics committee consultation):** There is no ethical dilemma. The patient has capacity and is requesting standard-of-care treatment. Ethics committees are appropriate for disputes or uncertainty about goals of care — neither exists here.
- **B (Psychiatric evaluation):** A psych evaluation would be relevant if there were concerns about capacity or if the patient were refusing treatment in a way that raised questions about competence. This patient is expressing a rational, coherent desire to live — no psychiatric evaluation is warranted as a prerequisite to treatment.
- **D (Emergency court order):** Court orders may be relevant when the state seeks to override a patient's treatment refusal. Here, the patient is *requesting* treatment, so judicial intervention is unnecessary and would only delay life-saving care.

The abnormal labs (elevated beta-hydroxybutyrate, ammonia, lactate) reflect his decompensated liver disease and hemodynamic shock but do not alter the ethical framework: the patient is expressing coherent wishes and should receive aggressive resuscitation without delay.

Would you like to explore the acute management of variceal hemorrhage in this clinical scenario?

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Question 221

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?

A. CT pulmonary angiography
B. Compression ultrasonography
C. D-dimer level
D. 2 sets of blood cultures

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The answer is **B. Compression ultrasonography**.

This patient has a **high pretest probability for deep vein thrombosis (DVT)** based on multiple major risk factors: **active pancreatic cancer**, **recent major abdominal surgery** (Whipple procedure 3 days prior), and **postoperative immobilization**. Unilateral leg swelling from thigh to ankle is a classic presentation of acute DVT. Note that a negative Homans sign does not reliably exclude DVT.

Why compression ultrasonography is preferred here

In patients with high clinical suspicion for DVT — particularly those with active cancer — guidelines recommend **proceeding directly to compression ultrasonography** rather than using D-dimer as a triage step.[1][2][3] An individual participant data meta-analysis demonstrated that the prevalence of DVT in cancer patients with suspected symptoms is approximately **37.5%**, compared to 15% in patients without cancer, and concluded that **direct referral for compression ultrasonography is the preferred diagnostic approach** in this population.[2] The NCCN

guidelines for cancer-associated VTE similarly list **venous ultrasound as the primary imaging modality** in the workup of suspected acute DVT.[1]

Why not the other options

- **A. CT pulmonary angiography** — There are no cardiopulmonary symptoms (dyspnea, chest pain, tachypnea) or hemodynamic instability to suggest pulmonary embolism. Lungs are clear on auscultation. CTPA is not indicated without clinical suspicion for PE.[1]
- **C. D-dimer level** — D-dimer has **limited utility in cancer patients** because specificity is markedly reduced by malignancy, recent surgery, and the associated hypercoagulable state. In cancer patients, the combination of a low pretest probability and negative D-dimer occurred in only 9% of patients and still carried a 2.2% probability of DVT. With this patient's high pretest probability, D-dimer testing would not meaningfully change management regardless of the result.[3][4]
- **D. Blood cultures** — While there is a low-grade fever (38°C/100.4°F), this is common in the early postoperative period. The clinical picture — **unilateral leg swelling without signs of wound infection, peritonitis, or sepsis** — points much more strongly to DVT. Blood cultures would not address the primary concern.

Would you like to explore the recommended anticoagulation regimens for cancer-associated DVT in this patient?

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Question 222

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?

A. Internal laryngeal nerve injury
B. Recurrent laryngeal nerve injury
C. External laryngeal nerve injury
D. Laryngeal edema

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The answer is **B. Recurrent laryngeal nerve injury**.

The **recurrent laryngeal nerve (RLN) has an intimate and highly variable anatomical relationship with the inferior thyroid artery (ITA)**, making it vulnerable during ITA ligation. A meta-analysis found the RLN courses posterior to the ITA in approximately 52% of cases, anterior in ~30%, and between the arterial branches in ~18%.[1] This variability is why the ITA serves as a key intraoperative landmark for identifying the RLN.[2][3]

Why ligation "close to the poles" matters: The American Head and Neck Society consensus statement emphasizes that the ITA should not be ligated as it approaches the gland; ligatures should be placed distally on the trunk or preferably on the terminal branches just before entry to the gland to mitigate RLN injury risk.[3] By ligating close to the poles, the young surgeon likely placed the ligature at or near the point where the RLN crosses the ITA branches, entrapping or injuring the nerve. When the nerve courses between the ITA branches (the "interposed" pattern), it is most susceptible to injury from careless ligation.[3] The anterior crossing pattern increases vocal cord paralysis risk by approximately 2.8-fold.[4]

RLN injury causes **vocal fold immobility and lateral displacement**, producing a breathy voice, vocal fatigue, and hoarseness — exactly as described in this patient.[5] RLN paralysis occurs in approximately 5–11% of thyroidectomies transiently and is a well-recognized complication at 2 weeks postoperatively.[6]

Why not the other options:

- **A. Internal laryngeal nerve injury** — The internal branch of the superior laryngeal nerve provides sensory innervation above the vocal folds. Injury causes loss of supraglottic sensation (increasing aspiration risk), not hoarseness.
- **C. External laryngeal nerve (EBSLN) injury** — The EBSLN is at risk during ligation of the **superior** thyroid artery, not the inferior. It innervates the cricothyroid muscle and causes subtle changes in pitch range and vocal projection rather than frank hoarseness.[5]
- **D. Laryngeal edema** — Intubation-related edema typically resolves within the first few days and would not persist at 2 weeks postoperatively.

Would you like to explore techniques for intraoperative RLN identification and preservation during thyroidectomy?

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Question 223

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?

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

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B. Isolated gonadotropin-releasing hormone (GnRH) deficiency.

The combination of absent puberty at 17 (Tanner stage 1, micropenis) with impaired olfaction is Kallmann syndrome — congenital hypogonadotropic hypogonadism from **isolated GnRH deficiency**, with anosmia.[1][2] GnRH neurons and olfactory neurons both originate in the olfactory placode and co-migrate to the forebrain along olfactory axons; failure of this migration leaves GnRH neurons stranded in the frontonasal region and the olfactory bulbs hypoplastic, producing simultaneous anosmia and absent gonadotropin secretion.[3][4][5] The pituitary and gonads are intrinsically normal, so the biochemical signature is low testosterone with low or inappropriately normal LH/FSH.[6][7] Mutations in more than 20–30 genes (ANOS1/KAL1, FGFR1, FGF8, PROK2, PROKR2, CHD7, SEMA3A) account for roughly 30–40% of cases, with X-linked, autosomal dominant, autosomal recessive, and oligogenic inheritance.[3][4][8] Normal height and normal cardiopulmonary exam fit; eunuchoidal proportions and delayed bone age would be expected.

Why the other options are wrong

- **A. CTG trinucleotide repeat expansion** — myotonic dystrophy type 1. Causes testicular atrophy and primary (hypergonadotropic) hypogonadism in adults, alongside myotonia, cataracts, frontal balding, and cardiac conduction disease. No anosmia, and puberty is not absent.

- **C. Sex-specific epigenetic imprinting** — Prader-Willi syndrome (paternal 15q11-q13 loss). Also causes hypogonadotropic hypogonadism with micropenis and cryptorchidism, but with hyperphagia, obesity, short stature, hypotonia, and intellectual disability. This patient's normal height/weight (BMI ~19.6) and isolated anosmia do not fit; anosmia is the discriminating finding.
- **D. Non-disjunction of sex chromosomes** — Klinefelter syndrome (47,XXY). Produces hypergonadotropic hypogonadism with elevated LH/FSH, small firm testes, gynecomastia, and tall stature, but puberty typically initiates and progresses partially rather than being absent, and olfaction is normal.[9][10]

Practical next steps in such a patient

- Morning total testosterone with LH and FSH; inhibin B; formal olfactory testing (e.g., UPSIT) since patients often under-report hyposmia.[7]
- Rule out other causes of central hypogonadism before labeling it isolated: full anterior pituitary panel (prolactin, TSH/free T4, IGF-1, cortisol) and sellar MRI to exclude tumor or infiltration; screen for chronic systemic illness or malnutrition.[7][11]
- Look for associated Kallmann features: renal ultrasound (unilateral renal agenesis), bimanual synkinesia, cleft lip/palate, hearing loss, cryptorchidism.[6][12]
- Bone age and DXA; genetic testing for counseling.[8]

The main diagnostic caveat at 17 is that **constitutional delay of growth and puberty cannot be reliably distinguished from congenital hypogonadotropic hypogonadism on basal gonadotropins or GnRH stimulation alone**.[11] Anosmia here strongly favors Kallmann syndrome, but formal diagnosis of CHH conventionally requires absent puberty by age 18.[2] Note also that 10–15% of CHH cases undergo reversal after treatment, warranting periodic reassessment off therapy.[1]

Would you like to explore the hormonal regimens used to induce puberty and later fertility in adolescents with congenital hypogonadotropic hypogonadism?

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Question 224

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?

A. Irreversible cyclooxygenase inhibitor
B. Thromboxane synthase inhibitor
C. Adenosine diphosphate receptor inhibitor
D. Phosphodiesterase inhibitor

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The correct answer is **D. Phosphodiesterase inhibitor**.

Cilostazol is a **phosphodiesterase type III (PDE III) inhibitor** indicated for the reduction of symptoms of intermittent claudication in peripheral artery disease (PAD).[1] By inhibiting PDE III, cilostazol increases intracellular **cyclic AMP (cAMP)** concentrations, which mediates its vasodilatory, antiplatelet, and antithrombotic effects.[2][3] It promotes vasodilation (particularly in femoral arteries), inhibits platelet aggregation, and inhibits vascular smooth muscle cell proliferation.[4][5]

The other answer choices correspond to different drug classes:

- **A. Irreversible cyclooxygenase inhibitor** — aspirin
- **B. Thromboxane synthase inhibitor** — ozagrel
- **C. Adenosine diphosphate (ADP) receptor inhibitor** — clopidogrel, prasugrel, ticagrelor

An important clinical consideration: because another PDE III inhibitor (milrinone) was associated with increased mortality in heart failure patients, cilostazol carries a **black box warning** contraindicating its use in patients with heart failure of any severity.[5][6]

Would you like to explore the role of supervised exercise therapy in managing intermittent claudication?

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Question 225

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?

A. Streptococci viridans
B. Staphylococcus aureus
C. Aspergillus fumigatus
D. Staphylococcus epidermidis

https://openevidence.com/ask/0af50fbb-56ae-4753-b73b-76be6514de72

The answer is **B. Staphylococcus aureus**.

This presentation is classic for **acute infective endocarditis (IE) in a person who injects drugs (PWID)**. The key clinical clues include:

- **Track marks** ("small scars in the antecubital region of both arms") indicating IV drug use
- **Acute high fever** (40°C), new **systolic murmur radiating to the left axilla** (mitral regurgitation), and **petechiae** on the hard palate and palms — all hallmarks of IE[1][2][3]
- **Respiratory symptoms with bilateral crackles**, suggesting **septic pulmonary emboli**, a frequent complication of IE in PWID[4]
- Young, poorly kept male with signs of substance use

Why Staphylococcus aureus?

S. aureus is the predominant pathogen in drug use–associated IE (DUA-IE), responsible for **43–69% of cases**, compared with only 5–10% for viridans group streptococci.[4] A prospective

international cohort study confirmed that S. aureus caused **more than two-thirds** of IE cases among PWID.[5] S. aureus also classically produces the **acute, aggressive presentation** seen here — high fever, rapid progression, and embolic complications — in contrast to the more indolent course typical of viridans streptococci.[6]

Why not the other options?

- **A. Streptococcus viridans** — the leading cause of **subacute** native-valve IE in non-IVDU patients, but accounts for only 5–10% of DUA-IE[4]
- **C. Aspergillus fumigatus** — fungal endocarditis is rare even in PWID (<1–5.7%) and typically occurs in severely immunocompromised hosts[4]
- **D. Staphylococcus epidermidis** — the predominant organism in **early prosthetic valve** endocarditis (within 2 months of surgery), not native-valve IE in IVDU[7]

Would you like to explore the recommended empiric antibiotic regimen for suspected IE in IV drug users?

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Question 226

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?

A. Breast milk jaundice
B. Breastfeeding jaundice
C. Sepsis
D. Physiologic hyperbilirubinemia

https://openevidence.com/ask/3da9ed5c-eafa-402b-92ae-2fe0d1db98c7

The answer is **B. Breastfeeding jaundice**.

This infant's presentation — jaundice at **day 3 of life** with a **poor latch**, **inadequate milk intake**, **prolonged uninterrupted sleep** (7–8 hours, suggesting low caloric drive to wake), and **decreased stool frequency** — is classic for **breastfeeding jaundice** (also termed "suboptimal intake hyperbilirubinemia").[1][2]

Why breastfeeding jaundice and not the other options:

- **Breast milk jaundice (A):** This is a distinct entity that occurs **later** (typically after day 5–7, peaking around 2 weeks) in an otherwise well-thriving infant with **adequate intake and weight gain**. It results from substances in breast milk (e.g., β-glucuronidase) that increase enterohepatic circulation of bilirubin. This infant is clearly not feeding well, making breast milk jaundice the wrong diagnosis.[1][3]
- **Physiologic hyperbilirubinemia (D):** While physiologic jaundice does peak around days 2–5, the clinical scenario specifically highlights **inadequate feeding** as the driving problem — poor latch despite lactation consultation, maternal concern about insufficient intake, and only 2 stools per day. When there is a clear pathologic contributor (suboptimal intake), the jaundice should not be attributed to physiology alone.[1][2]

- **Sepsis (C):** There are no signs of infection — the infant was born full-term by uncomplicated vaginal delivery, is crying appropriately, and has no fever, lethargy, or other systemic signs suggesting sepsis.

Mechanism: Low caloric intake leads to **decreased stool frequency** and **increased enterohepatic circulation of bilirubin**, as intestinal clearance of bilirubin depends on adequate stooling.[1][4] The AAP notes that breastfeeding fewer than 8 times per day is associated with higher TSB concentrations, and this infant's prolonged nighttime sleep further reduces feeding frequency.[1][3]

Would you like to explore the AAP phototherapy thresholds and management approach for this infant's hyperbilirubinemia?

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Question 227

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?

A. Baroreceptor reflex
B. Increased activation of the vagal nuclei
C. Sympathetic nervous system activation
D. Vasopressin release from the pituitary

https://openevidence.com/ask/8741bf6f-9ee7-4fb9-aae8-ca6b4bf50db7

The answer is **C. Sympathetic nervous system activation**.

During dynamic exercise, the **sympathetic nervous system is the primary driver** of both the increase in heart rate and systolic blood pressure observed in this scenario.[1][2] Central command (feedforward from motor cortex) and the exercise pressor reflex (feedback from skeletal muscle mechano- and metaboreceptors) converge to **increase sympathetic outflow and withdraw parasympathetic tone**, resulting in increased heart rate, myocardial contractility, and cardiac output.[1][3][4]

The hemodynamic pattern here — **elevated systolic BP with a preserved diastolic BP** — is classic for dynamic exercise: sympathetically mediated increases in cardiac output raise systolic pressure, while vasodilation in active skeletal muscle keeps diastolic pressure relatively stable.[5]

Why the other choices are incorrect:

- **A. Baroreceptor reflex** — During exercise, the baroreflex is **reset to operate around higher pressures** rather than driving the cardiovascular response. Its role is modulatory (preventing excessive BP swings), not the primary mechanism raising HR and BP.[1][6][7]
- **B. Increased activation of the vagal nuclei** — The opposite occurs: parasympathetic (vagal) activity to the heart **decreases** during exercise, contributing to the rise in heart rate.[8][9]

- **D. Vasopressin release from the pituitary** — While vasopressin may be released during prolonged or intense exercise, it plays a **minor role** compared to sympathetic activation in mediating the acute cardiovascular response shown here.

Would you like to explore how autonomic mechanisms drive heart rate recovery after exercise cessation?

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Question 228

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?

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

https://openevidence.com/ask/9b396d25-8547-4c71-96a7-c102de081204

D. Surgical pinning of the right hip.

This is a slipped capital femoral epiphysis (SCFE) — the classic presentation of an obese adolescent male with weeks of limp and poorly localized hip/knee pain, an externally rotated leg, restricted hip motion (particularly internal rotation), afebrile with normal labs, and radiographic posterior-inferior displacement of the epiphysis relative to the femoral neck.[1][2] Referred knee pain is the presenting complaint in roughly 23% of cases, which is why SCFE is one of the most commonly missed pediatric diagnoses.[2][3]

Definitive management is urgent orthopedic surgical stabilization, since SCFE will not resolve spontaneously and continued weight bearing risks further slippage:

- **In situ fixation with a single cannulated screw** is the standard treatment for stable SCFE, favored over multiple pins, epiphysiodesis, osteotomy, or spica casting because of fewer long-term complications.[2][4]
- **Immediate non–weight-bearing status** (crutches or wheelchair) and urgent referral pending surgery; acute worsening after three weeks of symptoms suggests an acute-on-chronic slip that may have become unstable.[2]
- **Avoid forceful reduction** — closed manipulation risks disrupting the femoral head blood supply and precipitating avascular necrosis.[2][5]
- If the slip is **unstable** (unable to bear weight even with crutches), osteonecrosis rates reach 50%; surgery is generally recommended within 24 hours, with reduction/decompression or a modified Dunn procedure as options depending on surgeon preference.[2][4]

Why the other options are wrong

- **Reassess in 3 months** — delay allows progression of the slip and markedly increases the risk of avascular necrosis, chondrolysis, and femoroacetabular impingement.[1][3]
- **Intra-articular corticosteroid injection** — SCFE is a mechanical physeal failure, not an inflammatory arthropathy; the absence of fever, effusion, and abnormal inflammatory markers argues against septic arthritis or juvenile idiopathic arthritis.
- **Pavlik harness** — used for developmental dysplasia of the hip in infants (typically <6 months), not for an adolescent physeal slip.

Additional points: obtain **bilateral hip radiographs** (AP pelvis plus frog-leg lateral for stable slips; cross-table lateral if unstable), since SCFE is bilateral in a substantial proportion of patients and the contralateral hip should be assessed for a slip or considered for prophylactic fixation.[1][3] Endocrine workup (thyroid, parathyroid, metabolic panel, vitamin D, growth hormone) is recommended for patients under 10 or over 16 years, or those below the 10th percentile for height or weight — this 14-year-old with obesity as the sole risk factor does not routinely require it.[2]

Would you like to explore when prophylactic fixation of the contralateral hip is indicated in SCFE?

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Question 229

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?

A. Leydig cell tumor
B. Obesity
C. Klinefelter syndrome
D. Trauma to testis

https://openevidence.com/ask/2d28d10c-30bd-498e-adb3-255b13d0fade

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The answer is **A. Leydig cell tumor**.

The unifying diagnosis here is a **Leydig cell tumor**, which explains both the **progressive gynecomastia** (18 months) and the **solid testicular mass** (1.5 cm, transillumination-negative). Leydig cell tumors are the most common sex cord-stromal tumors of the testis, and they are frequently hormonally active — they can **directly secrete estradiol**, producing an elevated estrogen-to-testosterone ratio that drives breast tissue proliferation.[1][2] Approximately **15–30% of Leydig cell tumors in adults present with gynecomastia**, which may appear well before the testicular mass becomes clinically apparent.[2][3]

Why the other options are less likely:

- **B. Obesity** — While obesity increases peripheral aromatization of androgens to estrogens and can contribute to gynecomastia, this patient's weight gain occurred only **3 months ago**, whereas gynecomastia has been progressive for **18 months**. Obesity also does not explain the solid testicular mass.[1]

- **C. Klinefelter syndrome** — This can cause gynecomastia due to primary hypogonadism, but patients typically have **small, firm testes** and are often **tall** with eunuchoid body habitus. A discrete solid testicular mass is not a feature of Klinefelter syndrome.[4]

- **D. Trauma to testis** — The testicular injury occurred only **3 months ago**, well after the onset of gynecomastia at 18 months. Trauma could cause a hydrocele or hematocele, but these would **transilluminate**; the negative transillumination test here indicates a **solid mass**, pointing toward neoplasm rather than a traumatic fluid collection.[5]

The **negative transillumination** is a key distinguishing finding — it confirms the mass is solid rather than fluid-filled, raising concern for a testicular neoplasm. The classic presentation of a hormonally active Leydig cell tumor is gynecomastia with a testicular mass and elevated estradiol, sometimes with suppressed testosterone.[6][7] Endocrine manifestations in adults often **precede** detection of the testicular mass by months or even years.[3]

Would you like to explore the recommended workup and management of a suspected Leydig cell tumor in this patient?

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Question 230

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?

A. Amoxicillin
B. Amoxicillin-clavulanic acid
C. Clindamycin
D. Levofloxacin

https://openevidence.com/ask/9f32e07f-0452-4211-b37e-4f1db0fdd007

The answer is **B. Amoxicillin-clavulanate**, the recommended first-line empirical antibiotic for **acute bacterial sinusitis (ABS)** in children.[1][2][3]

This child meets clinical criteria for ABS: **persistent symptoms ≥10 days** without improvement (cough, rhinorrhea, headache), **purulent nasal discharge**, **maxillary sinus tenderness**, and **fever**. [1][4] These findings distinguish bacterial from viral sinusitis and warrant antibiotic therapy.

Why amoxicillin-clavulanate over amoxicillin alone

The three predominant pathogens in ABS are *S. pneumoniae*, nontypeable *H. influenzae*, and *M. catarrhalis*.[5][6] In the post-pneumococcal conjugate vaccine era, **H. influenzae has become the most common cause** (~30–40% of cases), and nearly all *M. catarrhalis* and ~50% of *H. influenzae* isolates produce β-lactamases that confer amoxicillin resistance.[1][6] Clavulanate inhibits these β-lactamases, providing more comprehensive coverage.

The **IDSA recommends amoxicillin-clavulanate as first-line** therapy, while the[1][3] **AAP allows amoxicillin with or without clavulanate**.[3] While recent data show similar treatment failure

rates between the two agents in outpatient settings, amoxicillin-clavulanate remains the preferred answer in the guideline-based and exam context given its broader microbiologic coverage.[5]

Recommended dosing for this child is **amoxicillin-clavulanate at 45 mg/kg/day** of the amoxicillin component in 2 divided doses for 10–14 days; **high-dose therapy (90 mg/kg/day)** is reserved for children at higher risk for resistant organisms (age <2, daycare attendance, recent antibiotic use, or high local resistance rates).[1][3]

Why the other options are incorrect

- **A. Amoxicillin** — Lacks β-lactamase inhibitor coverage, making it less effective against the increasingly prevalent β-lactamase-producing *H. influenzae* and *M. catarrhalis*. While clinically similar outcomes have been observed, amoxicillin-clavulanate is the guideline-preferred first-line agent.[1][5][6]
- **C. Clindamycin** — Does not reliably cover *H. influenzae* or *M. catarrhalis*; its role in ABS is limited to combination therapy (e.g., with cefixime) for treatment failure or in patients with non–type I penicillin allergy.[1][4]
- **D. Levofloxacin** — Reserved for children with **type I hypersensitivity** to penicillin. Fluoroquinolones carry risks of musculoskeletal toxicity in children and are not first-line.[1]

Notably, this child also has **moderate bilateral expiratory wheezing unresponsive to home albuterol**, which warrants concurrent assessment with pulse oximetry, in-office bronchodilator administration, and consideration of systemic corticosteroids for an acute asthma exacerbation — though the question specifically tests antibiotic selection.

Would you like to explore the management of this child's concurrent asthma exacerbation?

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Question 231

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?

A. Antisocial personality disorder
B. Borderline personality disorder
C. Normal grief response
D. Post-traumatic stress disorder

https://openevidence.com/ask/0fd9c5ac-8c27-4cd7-8a4d-e6b4fc24b54a

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

This vignette illustrates several hallmark features of BPD:

- **Splitting (idealization → devaluation)**: The patient initially idealizes the medical team ("extremely grateful," "saving her baby"), then abruptly shifts to devaluation ("incompetent, evil," threatening lawsuits) upon receiving unwelcome news. This alternation between extremes of idealization and devaluation of others is a core diagnostic criterion of BPD.[1] [2]
- **Self-mutilating behavior**: The new wrist lacerations discovered upon re-entering the room represent **recurrent self-injurious behavior**, another cardinal BPD criterion. Self-harming

behaviors are part of the diagnostic criteria for BPD but not for complex PTSD or normal grief.[3][4][5]

- **Inappropriate, intense anger**: The explosive rage and destructive behavior (broken medical equipment) reflect the criterion of **intense anger or difficulty controlling anger**.[3][4]
- **Affective instability**: The rapid, dramatic mood shift from profound gratitude to intense rage exemplifies the **marked reactivity of mood** characteristic of BPD.[1]
- **Impulsivity**: The history of **substance abuse** is consistent with the impulsivity criterion (impulsivity in ≥2 areas that are potentially self-damaging).[3][4]

Why not the other options:

- **Antisocial personality disorder** is characterized by a pattern of disregard for and violation of others' rights, deceitfulness, lack of remorse, and irresponsibility — not the idealization-devaluation pattern or self-harm seen here.
- **Normal grief response** does not typically include splitting, self-laceration, or destruction of property. While anger can be part of grief, the intensity and pattern here are pathological.
- **PTSD** requires re-experiencing a traumatic event (flashbacks, nightmares), avoidance of trauma-related stimuli, and hyperarousal symptoms persisting over time. The acute behavioral pattern here — particularly the splitting and self-harm — is far more consistent with BPD.[1][5]

Would you like to explore the evidence-based treatment approaches for borderline personality disorder?

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Question 232

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:

A. Diffuse cortical necrosis
B. Chronic pyelonephritis
C. Papillary necrosis
D. Acute Nephrolithiasis

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The answer is **C. Papillary necrosis**.

The combination of **high-dose acetaminophen and aspirin** used over several weeks is the classic cause of **analgesic nephropathy**, which is characterized pathologically by **renal papillary necrosis** and chronic interstitial nephritis.[1][2] This patient's presentation — **gross hematuria, colicky flank pain, and proteinuria** — directly matches the clinical syndrome of papillary sloughing, in which necrotic papillary fragments detach and pass into the collecting system, causing ureteric obstruction and renal colic.[3][4]

The pathogenesis involves concentration of acetaminophen in the renal papillae, where it undergoes oxidative metabolism to a reactive quinoneimine. When aspirin is co-ingested, salicylate depletes glutathione in the papillae, leaving the reactive metabolite free to cause lipid peroxidation and tissue protein arylation, ultimately leading to papillary necrosis.[2][4]

Why not the other choices:

- **A. Diffuse cortical necrosis** — occurs in the setting of obstetric catastrophes (e.g., abruptio placentae), septic shock, or DIC, not analgesic overuse. It causes **oliguria/anuria**, not colicky flank pain.
- **B. Chronic pyelonephritis** — associated with recurrent urinary tract infections and vesicoureteral reflux, not analgesic use. Presentation is typically insidious with chronic kidney disease, not acute colic.

- **D. Acute nephrolithiasis** — while the colicky pain overlaps, the history of combined analgesic abuse with proteinuria strongly points to papillary necrosis rather than a primary stone. Sloughed papillary tissue can mimic stone-like ureteral obstruction, but the clinical context makes papillary necrosis the unifying diagnosis.[4][5]

Would you like to explore the diagnostic workup and imaging approach for renal papillary necrosis?

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Question 233

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?

A. Medication side effect
B. Excess weight
C. Infection
D. Occult malignancy

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The answer is **B. Excess weight**.

Obesity (BMI 41) is the single unifying factor responsible for this patient's bilateral knee pain as well as his fatigue, daytime somnolence, and unrefreshing sleep. Specifically:

Knee osteoarthritis — The clinical picture is classic for OA: bilateral knee pain that worsens with activity and at the end of the day, brief morning stiffness (~20 minutes, well under the >30–60 minutes expected in inflammatory arthritis), crepitus on exam, and absence of warmth, erythema, or joint swelling.[1][2][3] Obesity is the most important modifiable risk factor for knee OA; a meta-analysis found a pooled OR of **2.66** (95% CI 2.15–3.28) for knee OA with obesity, and risk rises sharply with BMI — up to an OR of **13.6** at BMI ≥36.[4][5] Mechanisms include mechanical overloading of weight-bearing joints and systemic low-grade inflammation mediated by adipokines.[4][6]

Obstructive sleep apnea — The daytime sleepiness, dozing off at work, and unrefreshing sleep are hallmark symptoms of OSA. Obesity is identified as **the one major modifiable risk factor** for OSA per the AHA Scientific Statement.[7] In morbidly obese populations, OSA prevalence reaches

50–98%.[4] Excess pharyngeal fat deposition narrows the upper airway, and central adiposity further compromises respiratory mechanics during sleep.[8][9]

Type 2 diabetes — The patient's metformin use implies T2DM, for which obesity is likewise the primary modifiable risk factor, completing the triad.

Why the other options are incorrect:

- **A (Medication side effect):** Metformin's main adverse effects are gastrointestinal (nausea, diarrhea). While long-term metformin use can cause vitamin B12 deficiency and contribute to fatigue, it does not cause the mechanical knee pain or crepitus described here.
- **C (Infection):** Septic arthritis presents acutely with joint warmth, erythema, effusion, and often fever — none of which are present.
- **D (Occult malignancy):** There are no red-flag features such as unexplained weight loss, night sweats, or lymphadenopathy, and the pain pattern is entirely consistent with OA.

The **family history of RA** is a distractor; this patient's presentation — end-of-day pain, brief morning stiffness, no synovitis, and crepitus — is incompatible with RA, which typically involves prolonged morning stiffness (>30 minutes), soft tissue swelling, and joint tenderness.[1][2]

Would you like to explore evidence-based weight management strategies for patients with concurrent knee OA and obstructive sleep apnea?

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Question 234

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?

A. CMV
B. HIV
C. HSV-1
D. HSV-2

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The correct answer is **C. HSV-1**.

This presentation is classic for **primary herpetic gingivostomatitis (PHGS)**, caused by **herpes simplex virus type 1 (HSV-1)**. More than **90% of PHGS cases** are attributable to HSV-1.[1] The disease has a peak incidence between **6 months and 5 years of age**, precisely matching this patient's age.[2][3]

The key clinical features that point to this diagnosis include:

- **Vesicular lesions on the tongue, gingiva, and lips** with rupture and ulceration — the hallmark oral manifestation of PHGS[4][5]
- **High fever** (39.1°C) — present in nearly 100% of PHGS cases[6]
- **Cervical and submandibular lymphadenopathy** — a characteristic finding[4][7]
- **Inability to eat or drink** due to pain — a common and clinically important sequela that may lead to dehydration[2][8]
- **Myalgias and irritability** — consistent with the systemic prodrome of primary HSV-1 infection, which includes malaise, fever, and irritability[4][9]

Why not the other options:

- **CMV (A):** Primary CMV in children is typically asymptomatic or causes a mononucleosis-like syndrome; it does not characteristically produce vesicular oral lesions with gingivostomatitis.
- **HIV (B):** HIV does not cause acute vesicular gingivostomatitis. While HIV-associated gingivitis exists, it presents differently (e.g., linear gingival erythema, necrotizing ulcerative gingivitis) and would not explain this acute vesicular presentation.[10]
- **HSV-2 (D):** HSV-2 primarily causes genital herpes and is uncommon as a cause of oral disease in children. PHGS is caused "predominantly by HSV-1" and "only rarely by HSV-2, the latter affecting mostly adults".[3][4]

Would you like to explore the management of primary herpetic gingivostomatitis in children, including antiviral dosing and hospitalization criteria?

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Question 235

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?

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

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The answer is **B. Respect the patient's prior wishes and do not resuscitate**.

A **written advance directive** is the strongest expression of a patient's autonomous wishes, made while the patient had decision-making capacity. The fundamental ethical and legal principle is that **decision-makers must give first priority to known preferences expressed by the patient when capacity was present**, such as in an advance directive.[1][2][3] The wife's request, while understandable, is based on her own emotional needs rather than a representation of the patient's wishes — a form of "projection bias" in which surrogates make decisions based on their own values rather than the patient's.[4]

The 2025 AHA Guidelines for CPR and Emergency Cardiovascular Care state explicitly that when there is disagreement between a patient's advance care plan and a surrogate decision-maker's preferences, **"the patient's wishes, as expressed in person or via ACP, are principal,"** and a surrogate's preference should only be honored when the patient's wishes are uncertain.[5] In this scenario, the patient's wishes are clearly documented and not uncertain.

Why the other options are incorrect:

- **A (Respect the wife's wishes):** A surrogate's role is to represent what the patient would want, not to impose their own preferences. Here, the patient's own wishes are already documented.[4][6]
- **C (Consult a judge):** There is no legal ambiguity requiring judicial intervention when a valid advance directive exists.

- **D (Consult the ethics committee):** Ethics consultation is appropriate when a patient's wishes are unknown and there is intractable conflict. Here, the patient's wishes are clearly stated, so ethics consultation would not override the directive.[5]

Would you like to explore the limitations of advance directives in acute care settings, such as when clinical circumstances may not match the directive's intended scope?

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Question 236

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?

A. Hypersegmented neutrophils
B. Sideroblasts
C. Spherocytes
D. Dacrocytes

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The answer is **C. Spherocytes**.

This vignette describes a classic presentation of **hereditary spherocytosis (HS)**, the most common hereditary hemolytic anemia in populations of European ancestry.[1] The key findings that establish the diagnosis are:

- **Normocytic hemolytic anemia** with reticulocytosis and indirect hyperbilirubinemia — indicating extravascular hemolysis
- **Negative Coombs test** — ruling out autoimmune hemolytic anemia, the other major cause of spherocyte-mediated hemolysis[2]
- **Increased osmotic fragility** in hypotonic solution — the hallmark confirmatory test, reflecting the reduced surface area-to-volume ratio of spherocytes[2]
- **Gallstones in a 14-year-old** — cholelithiasis (pigmented bilirubin stones) is a well-recognized complication of chronic hemolysis in HS, often presenting in the second or third decade of life[3]

The peripheral blood smear in HS characteristically shows **spherocytes** — small, dense, round, hyperchromic red blood cells that lack central pallor.[2] These cells result from defects in

erythrocyte membrane proteins (ankyrin, band 3, spectrin, protein 4.2) that cause progressive membrane loss and the adoption of a spherical morphology.[1][4]

Why the other choices are incorrect:

- **A. Hypersegmented neutrophils** — seen in megaloblastic anemias (B12/folate deficiency), which cause macrocytic, not normocytic, anemia.
- **B. Sideroblasts** — ringed sideroblasts are characteristic of sideroblastic anemias; these would not show increased osmotic fragility.
- **D. Dacrocytes (teardrop cells)** — associated with myelofibrosis and other marrow infiltrative processes, not hemolytic membrane disorders.

Would you like to explore the indications and outcomes of splenectomy in hereditary spherocytosis?

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Question 237

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?

A. Vasculitis
B. Hyperhomocysteinemia
C. Arterial emboli
D. Arterial trauma

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The answer is **C. Arterial emboli**.

This patient presents with classic **acute limb ischemia (ALI)** — sudden onset of severe leg pain, paresthesia, pallor, cool extremity, and diminished popliteal pulse — the hallmarks of the "6 Ps" (pain, pallor, pulselessness, paresthesia, poikilothermia, paralysis).[1] The key clinical clue pointing to the etiology is the **irregular pulse at 100/min**, consistent with **atrial fibrillation**, the most common cardiac source of peripheral arterial emboli.

Arterial embolism is the most common cause of acute (non-traumatic) limb ischemia. Per the American College of Chest Physicians, approximately **80% of peripheral emboli originate in the heart** — most commonly from the left atrial appendage in the setting of atrial fibrillation — with the remainder arising from aortic or peripheral arterial sources.[2] The 2024 ACC/AHA PAD guidelines similarly list **cardiac embolization** (particularly atrial fibrillation) as a leading cause of ALI, with atrial fibrillation identified as the presumed embolic source in approximately 30% of cardioembolic ALI cases.[3]

Why the other options are incorrect:

- **A. Vasculitis** — can cause ALI but is far less common and typically presents with systemic inflammatory features, not an isolated sudden embolic event with an irregular pulse.

- **B. Hyperhomocysteinemia** — a risk factor for arterial and venous thrombosis but not a common acute cause of ALI.
- **D. Arterial trauma** — an important cause of ALI but there is no history of trauma, instrumentation, or vascular access in this patient.

The irregular pulse in an older patient with hypertension strongly implicates **undiagnosed atrial fibrillation** with cardioembolism as the mechanism, making arterial emboli the most common and most likely cause.[2][3]

Would you like to explore the initial management of acute limb ischemia, including anticoagulation and revascularization?

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Question 238

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?

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

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The answer is **A. Increase in false negative test results**.

Raising the diagnostic threshold from **6.5% to 7.0%** makes the criterion more stringent — a higher HbA1c value is required to declare the test "positive." This is a classic sensitivity–specificity tradeoff. As described in a review of diagnostic test performance, "a more stringent requirement to declare a test positive would yield fewer false-positive findings and more false-negative findings".[1]

Applying this principle to HbA1c:

- **False negatives increase (answer A):** Individuals with true diabetes whose HbA1c falls between 6.5% and 7.0% would now be classified as "negative" — these are missed cases (false negatives). This corresponds to **decreased sensitivity**.
- **False positives decrease (not B):** A stricter threshold means fewer non-diabetic individuals are incorrectly labeled as diabetic.
- **True negatives increase (not C):** More non-diabetic individuals are correctly classified as negative, reflecting **increased specificity**.
- **True positives decrease (not D):** Fewer truly diabetic individuals meet the higher threshold, so true positives fall.

The current **HbA1c ≥ 6.5%** threshold was established based on the observation that this level marks a significantly increased risk of diabetic retinopathy, as recommended by the International Expert Committee in 2009 and subsequently adopted by the ADA and WHO.[2][3] Some evidence actually suggests the 6.5% threshold may already be too high, as glucose-based criteria identify

more individuals with diabetes — raising the cutoff further would compound this problem by missing even more cases.[4]

Would you like to explore how the sensitivity and specificity of HbA1c at 6.5% compares with other diagnostic tests for diabetes?

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Question 239

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?

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)

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The correct answer is **B. Increases levels of fetal hemoglobin (HgbF)**.

Hydroxyurea is a **ribonucleotide reductase inhibitor** whose **primary direct effect on hemoglobin physiology in sickle cell disease is the induction of fetal hemoglobin (HbF) production**.[1][2] HbF is normally suppressed after birth, but hydroxyurea reactivates its synthesis through stress erythropoiesis and other metabolic pathways involving guanylyl cyclase and SAR1.[3]

The therapeutic rationale is that **HbF interferes with intracellular HbS polymerization** — the fundamental pathologic event in sickle cell disease.[3][4] Higher HbF concentrations reduce red cell rigidity, hemolysis, and sickling, thereby decreasing vaso-occlusive crises, acute chest syndrome, hospitalizations, and transfusion requirements.[1][2] Randomized controlled trials have demonstrated a statistically significant increase in HbF levels with hydroxyurea compared to placebo (pooled mean difference ~6–10%).[4]

Why the other options are incorrect:

- **A (Decreases oxygen carrying capacity):** Hydroxyurea does not reduce oxygen-carrying capacity; it actually improves anemia and overall hemoglobin levels.
- **C (Decreases levels of HgbS):** While the proportion of HbS relative to total hemoglobin may shift as HbF rises, hydroxyurea does not directly suppress HbS gene expression or production. The benefit comes from HbF induction, not HbS reduction.
- **D (Decreases levels of HbF):** This is the opposite of hydroxyurea's effect; it increases HbF.

Would you like to explore the additional non-HbF-related mechanisms by which hydroxyurea benefits sickle cell disease?

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Question 240

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?

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

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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 **moderate-to-severe croup (laryngotracheobronchitis)**: a 2-year-old with a URI prodrome, **abrupt onset of barky/hacking cough at night**, and **inspiratory stridor** with respiratory distress.[1][2] The absence of small objects in the environment effectively rules out foreign body aspiration (eliminating C), and the viral prodrome without signs of toxicity argues against bacterial tracheitis or epiglottitis (eliminating D).

Why B and not A:

The distinguishing factor between answers A and B is the presence of **stridor at rest and respiratory distress**, indicating **moderate-to-severe croup**. Per AAFP and AAP guidelines, nebulized racemic epinephrine should be added to dexamethasone when stridor is present at rest.[1][3] Humidified oxygen and dexamethasone alone (answer A) would be appropriate for **mild** croup without resting stridor, but is insufficient here.

Observation period:

The clinical effect of racemic epinephrine wears off within approximately 2 hours, and symptoms may recur.[4] Evidence-based guidelines recommend monitoring for **2 to 4 hours** after epinephrine administration before discharge.[1][5] A retrospective study found that patients observed for 3.1–4 hours had significantly lower rates of treatment failure compared to those observed for only 2.1–3 hours (7.1% vs 16.7%).[6] Discharge criteria include resolution of stridor at rest, no signs of increased work of breathing, and adequate oral intake.[5]

Would you like to explore dexamethasone dosing and alternative corticosteroid options for croup?

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Question 241

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?

A. Anti-Sjögren's syndrome type B (SS-B) antibody
B. Anti-centromere antibody
C. Anti-Jo-1 antibody
D. Anti-Scl-70 antibodies

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The answer is **A. Anti-Sjögren's syndrome type B (SS-B) antibody**.

This presentation — **eye dryness with foreign body sensation, oral mucosal ulceration/atrophy, and lymphocytic infiltration of minor salivary glands on lip biopsy** — is classic for **Sjögren's syndrome**. The hallmark autoantibodies are **anti-Ro/SSA and anti-La/SSB**, with anti-SSA/SSB seroprevalence up to **90%** among patients with overt disease.[1] The 2016 ACR/EULAR classification criteria require either anti-SSA antibodies or a positive lip biopsy (focal lymphocytic sialadenitis with focus score ≥1) as a key diagnostic element.[2][3]

Why the other options are incorrect:

- **B. Anti-centromere antibody** — Associated with **limited cutaneous systemic sclerosis** (CREST syndrome), not Sjögren's syndrome.
- **C. Anti-Jo-1 antibody** — A marker of **antisynthetase syndrome**, a subset of inflammatory myopathy associated with interstitial lung disease, mechanic's hands, and arthritis.
- **D. Anti-Scl-70 (anti-topoisomerase I) antibody** — Associated with **diffuse cutaneous systemic sclerosis**, particularly with pulmonary fibrosis risk.

The lip biopsy finding of dense lymphocytic infiltration surrounding salivary ducts and blood vessels (focal lymphocytic sialadenitis) is one of the histopathological hallmarks of Sjögren's syndrome and is included as a major criterion in classification systems.[4][5]

Would you like to explore the extraglandular manifestations and systemic complications of Sjögren's syndrome?

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Question 242

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?

A. Fluticasone
B. Montelukast
C. Tiotropium
D. Cromolyn

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The answer is **C. Tiotropium**.

Vagal (parasympathetic) stimulation causes bronchoconstriction through postganglionic release of acetylcholine, which acts on **muscarinic M3 receptors** on airway smooth muscle to induce contraction and glandular secretion.[1] Tiotropium is a **long-acting muscarinic antagonist (LAMA)** that directly blocks this pathway by binding to M3 receptors with slow dissociation, providing bronchodilation lasting over 24 hours.[2][3][4] This makes it the only listed drug that "directly antagonizes the effects of vagal stimulation on the airways."

The clinical scenario — chronic bronchitis, 20-pack-year smoking history, increased anteroposterior diameter, productive cough, and dyspnea — is classic for **COPD**, for which tiotropium is a first-line maintenance bronchodilator recommended in GOLD groups B through D.[5]

The other options do not act on the vagal-muscarinic pathway:

- **Fluticasone** — an inhaled corticosteroid; reduces airway inflammation but does not antagonize vagal stimulation.
- **Montelukast** — a leukotriene receptor antagonist; blocks cysteinyl leukotrienes, primarily used in asthma.

- **Cromolyn** — a mast cell stabilizer; prevents release of inflammatory mediators but has no direct anticholinergic activity.

Would you like to explore how tiotropium compares with long-acting beta-agonists as initial COPD maintenance therapy?

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Question 243

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?

A. Compression of pituitary stalk
B. Hyperprolactinemia
C. Impaired migration of GnRH neurons
D. Decreased thyroxine production

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C. Impaired migration of GnRH neurons.

This is Kallmann syndrome — congenital hypogonadotropic hypogonadism with anosmia. During embryogenesis, GnRH-secreting neurons originate in the olfactory placode and migrate along olfactory/terminalis nerve axons through the cribriform plate into the hypothalamus.[1][2] When this shared migratory pathway fails, olfactory axons do not reach the olfactory bulb (anosmia/hyposmia) and GnRH neurons never populate the hypothalamus, producing GnRH deficiency with low LH/FSH and low testosterone.[3][4][5]

Why the features fit

- **Anosmia**: inability to detect gas odor and failure to identify common odors reflects olfactory bulb hypoplasia/aplasia.[2]
- **Cryptorchidism**: fetal GnRH deficiency impairs testosterone-driven testicular descent; cryptorchidism and micropenis are the classic neonatal presentation of congenital hypogonadotropic hypogonadism, present in ~70% of boys in a pediatric series.[6]
- **Tanner 1 genitals, sparse sexual hair, falling height percentile at 14**: absent pubertal activation of the HPG axis and absent pubertal growth spurt, so linear growth crosses percentiles downward relative to peers.[3]

Causative variants involve genes governing GnRH/olfactory neuron ontogeny and axon guidance — ANOS1 (KAL1), FGFR1, FGF8, PROK2, PROKR2, CHD7, SEMA3A, FEZF1 — with X-linked, autosomal dominant, and autosomal recessive inheritance; roughly half of cases still lack a molecular diagnosis.[1][3][7]

Why not the others

- **A. Pituitary stalk compression** (e.g., craniopharyngioma) causes hypogonadotropic hypogonadism but with mass effects — headache, visual field loss, multiple pituitary deficits, diabetes insipidus — and does not cause congenital anosmia or infantile cryptorchidism.
- **B. Hyperprolactinemia** suppresses GnRH pulsatility and can delay puberty, but is not associated with anosmia or cryptorchidism dating to infancy.
- **D. Decreased thyroxine production** causes growth failure and delayed puberty, but with characteristic hypothyroid features (bradycardia, delayed relaxation of reflexes, goiter) and normal olfaction.

Confirmatory workup: low/inappropriately normal LH and FSH with low morning testosterone, delayed bone age, formal smell testing, and MRI showing olfactory bulb/sulcus hypoplasia.[3][8] Check for associated anomalies — unilateral renal agenesis, bimanual synkinesis, cleft lip/palate, hearing loss, dental agenesis.[3][9] Treatment is testosterone for virilization, with gonadotropin or pulsatile GnRH therapy when fertility is desired; note that 10–20% of patients show spontaneous reversal of hypogonadism.[7]

Would you like to explore pubertal induction regimens and fertility management in adolescent Kallmann syndrome?

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Question 244

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?

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.

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The correct answer is **A. Inform the patient that romantic relationships with current patients are unethical.**

Romantic or sexual relationships between a physician and a current patient are always unethical, regardless of the complexity of the case, who initiates the interaction, or whether the patient consents.[1][2][3] The AMA Council on Ethical and Judicial Affairs has concluded that "sexual contact or a romantic relationship concurrent with the physician-patient relationship is unethical".[3] The ACOG Committee on Ethics similarly states that such interactions constitute misconduct "regardless of whether a patient appears to initiate or consent to such behavior".[2]

Why the other options are incorrect:

- **B** is wrong because the complexity of the case is irrelevant — the ethical prohibition on romantic relationships with current patients is absolute and does not depend on the nature or difficulty of the clinical decision-making involved.[1][2]

- **C** is wrong because it is overly restrictive. The AMA position is that romantic relationships with **former** patients *may* be unethical under certain circumstances — specifically when the physician "uses or exploits trust, knowledge, emotions, or influence derived from the previous professional relationship". A relationship is not permanently prohibited in all cases after the physician-patient relationship ends (except in psychiatry and cases involving vulnerable patients).[1][3][4]
- **D** is wrong because transferring care does not retroactively make it appropriate to accept the invitation while the physician-patient relationship is still active. The patient is currently mid-treatment (rabies post-exposure prophylaxis series), and the physician-patient relationship has not been formally terminated.[1]

The physician should decline the invitation, citing the ethical obligation to maintain professional boundaries with current patients, while recognizing that a future relationship after appropriate termination of the professional relationship and passage of sufficient time may not be categorically prohibited.[1][3]

Would you like to explore the ethical guidelines for pursuing a relationship with a former patient after the physician-patient relationship has ended?

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Question 245

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?

A. Monochorionic-diamniotic monozygotic
B. Dichorionic-diamniotic dizygotic
C. Monochorionic-monoamniotic monozygotic
D. Conjoined twins

https://openevidence.com/ask/c42ebcf9-e7d7-42bd-bf0f-74ed8bcd9d41

The answer is **A. Monochorionic-diamniotic monozygotic**.

This vignette describes **twin-to-twin transfusion syndrome (TTTS)**, which by definition occurs in **monochorionic-diamniotic (MCDA)** pregnancies.[1][2][3] The key findings pointing to this diagnosis:

- **Hematocrit discordance**: The larger twin (recipient) has a markedly elevated hematocrit of 71% (polycythemia from volume overload), while the smaller twin (donor) has a hematocrit of 42% (relative anemia from chronic volume depletion).
- **Growth discordance**: The donor twin (2050 g) is significantly smaller than the recipient (2850 g), consistent with chronic hypovolemia and growth restriction.
- **Deformation sequence in the donor**: The flattened nose and clubfoot in the smaller twin are compressive deformities resulting from **oligohydramnios** — the donor twin becomes oliguric, leading to severely decreased amniotic fluid and physical compression ("stuck twin" phenomenon).[1]

Why diamniotic and not monoamniotic (ruling out C)?

TTTS is diagnosed by the **oligohydramnios-polyhydramnios sequence** between two separate amniotic sacs.[3] In monochorionic-monoamniotic twins, both fetuses share a single amniotic cavity, so the characteristic differential fluid accumulation and compressive deformation

sequence of the donor cannot develop. TTTS is a complication essentially unique to MCDA pregnancies, occurring in approximately **10–15%** of them.[2][4]

Why not dichorionic-dizygotic (ruling out B)?

Dichorionic placentas lack the shared vascular anastomoses (arteriovenous connections) required for inter-twin transfusion.[3]

Would you like to explore the management and interventional options for twin-to-twin transfusion syndrome?

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Question 246

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?

A. Increased water intake
B. Increased adrenocorticotropin hormone secretion
C. Decreased antidiuretic hormone secretion
D. Decreased adrenocorticotropin hormone secretion

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The answer is **C. Decreased antidiuretic hormone secretion**, consistent with **central diabetes insipidus** from a likely intracranial mass lesion.

Hypernatremia (Na+ 148 mEq/L) with inappropriately dilute urine (240 mOsm/kg) is the hallmark finding. At a plasma sodium above 145 mmol/L, vasopressin should be sufficiently stimulated to produce maximally concentrated urine (~1200 mOsm/kg).[1] A urine osmolality of 240 in this setting implies either **deficient vasopressin (ADH) secretion** (central DI) or renal resistance to vasopressin (nephrogenic DI).[1] The clinical context — **progressive headaches,**

visual impairment, and seizures — points to a hypothalamic-pituitary/suprasellar mass destroying vasopressin-producing neurons, making central DI the diagnosis.[2][3]

> "The presence of a dilute urine when the plasma sodium concentration is above 145 mmol per liter implies either deficient vasopressin secretion (as in neurogenic diabetes insipidus) or failure of the kidneys to respond to vasopressin (as in nephrogenic diabetes insipidus)."
>
> —Richard H. Sterns, M.D., University of Rochester School of Medicine and Dentistry and other institutions. Disorders of Plasma Sodium — Causes, Consequences, and Correction. N Engl J Med. January 01, 2015.
>
> Used under license from The New England Journal of Medicine.

Normally, even complete central DI does not produce hypernatremia because intact thirst drives sufficient water intake to compensate.[1][3] This patient's hypernatremia likely reflects an **inability to adequately replace water losses** due to altered mental status (oriented only to person, confused, lethargic), with dehydration supported by the prolonged capillary refill time.[4] Destruction of hypothalamic osmoreceptors (adipsic DI) is another mechanism that can impair thirst and lead to severe hypernatremia.[3]

Why the other options are incorrect:

- **A. Increased water intake** — would dilute serum sodium and cause hyponatremia, the opposite of what is observed.
- **B. Increased ACTH secretion** — excess cortisol (Cushing's syndrome) does not produce this pattern of dilute urine with hypernatremia.
- **D. Decreased ACTH secretion** — secondary adrenal insufficiency impairs free water excretion and tends to cause **hypo**natremia, not hypernatremia. Notably, in panhypopituitarism, cortisol deficiency can actually mask DI; polyuria may only be unmasked when glucocorticoid replacement is initiated.[5]

Would you like to explore the diagnostic workup and management approach for central diabetes insipidus?

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Question 247

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?

A. Dry eyes
B. High-risk sexual behaviour
C. Oral ulcers
D. Sensory loss

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The correct answer is **D. Sensory loss**.

This presentation is classic for **optic neuritis**: a young woman with acute unilateral painful vision loss (pain with eye movement), a **relative afferent pupillary defect (RAPD)** on swinging flashlight test, optic disc swelling, and decreased color vision.[1][2][3] The pupillary findings described — bilateral constriction when the left eye is illuminated but bilateral dilation when the right eye is illuminated — are the hallmark **Marcus Gunn pupil**, indicating impaired afferent conduction through the right optic nerve.[1][3]

Why sensory loss matters: Optic neuritis is the presenting manifestation of **multiple sclerosis (MS)** in at least 20% of cases, and approximately 50% of patients with isolated optic neuritis go on to develop clinically definite MS.[1][2] Classic MS presentations beyond optic neuritis include **partial myelitis with extremity/torso sensory impairment, limb paresthesias, and focal sensory disturbances**.[4] Eliciting a history of prior sensory symptoms would suggest dissemination in time — a cornerstone of the McDonald diagnostic criteria for MS.[4]

Why the other options are less appropriate:

- **A. Dry eyes** — Sjögren syndrome can rarely cause optic neuropathy, but the classic optic neuritis presentation in a young woman points strongly toward demyelinating disease.
- **B. High-risk sexual behavior** — Syphilitic optic neuritis exists but typically occurs with other features (e.g., uveitis, meningitis) and is not the leading concern here.
- **C. Oral ulcers** — Behçet disease causes ocular involvement, but characteristically as **uveitis** rather than isolated optic neuritis with RAPD.

Would you like to explore the recommended workup and MRI predictors of MS conversion after a first episode of optic neuritis?

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Question 248

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?

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

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The correct answer is **A: pH = 7.5, PCO2 = 50 mm Hg, $HCO3^-$ = 38 mEq/L**.

Metabolic alkalosis with appropriate respiratory compensation is the expected acid-base disturbance in this patient with 3 days of vomiting. Loss of gastric hydrochloric acid raises plasma bicarbonate, producing alkalemia. The body compensates via **hypoventilation** (reflected by the respiratory rate of 9/min), which raises PCO2 to partially restore pH toward normal.[1][2][3]

Verifying with the compensation formula from Berend et al.:[4]

$$\text{Expected } P_{CO_2} = 40 + 0.7 \times ([HCO_3^-] - 24)$$

With $HCO3^-$ of 38, the expected PCO2 is **49.8 mm Hg (±2)**, aligning closely with the 50 mm Hg in option A.[4][5] A nearly identical case is presented in the NEJM by Seifter: a 31-year-old woman vomiting for 2 days had pH 7.54, PaCO2 48 mm Hg, and $HCO3^-$ 40 mEq/L.[1]

Why the other options are incorrect:

- **B (pH 7.2, PCO2 25, $HCO3^-$ 30):** Internally inconsistent — an elevated bicarbonate of 30 with a low PCO2 of 25 should produce alkalemia, not a pH of 7.2.

- **C (pH 7.5, PCO2 34, $HCO3^-$ 38):** The $HCO3^-$ of 38 indicates metabolic alkalosis, but the PCO2 of 34 is inappropriately low (expected ~50), suggesting a concurrent respiratory alkalosis — inconsistent with the low respiratory rate of 9/min seen here.[5]
- **D (pH 7.5, PCO2 30, $HCO3^-$ 24):** This represents a **primary respiratory alkalosis** (low PCO2, normal bicarbonate), not the metabolic alkalosis expected from vomiting.

The volume depletion (sunken eyes, dry tongue, tachycardia, positional dizziness) is critical to **maintenance** of the alkalosis: hypovolemia activates the renin-angiotensin-aldosterone system, driving avid renal bicarbonate reabsorption and paradoxical aciduria, preventing correction of the alkalosis until volume is repleted with normal saline and potassium chloride.[1][5]

Would you like to explore the distinction between chloride-responsive and chloride-resistant metabolic alkalosis?

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Question 249

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?

A. Punch biopsy
B. Surgical excision
C. Thyroxine administration
D. Ultrasound

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The answer is **B. Surgical excision**.

FNA cytology showing **follicular architecture suspicious for malignancy** corresponds to **Bethesda Category IV** (follicular neoplasm/suspicious for follicular neoplasm), which carries a **25–40% risk of malignancy**.[1] The critical principle is that **follicular carcinoma cannot be definitively diagnosed on FNA** — distinguishing follicular adenoma from carcinoma requires histological evaluation for capsular and/or vascular invasion, which can only be assessed on a surgical specimen.[2][3][4] Per the NCCN Thyroid Carcinoma guidelines, the recommended management is **diagnostic lobectomy** (or molecular testing as an alternative to help guide further management).[2] The Bethesda System similarly recommends molecular testing or lobectomy for this category.[1]

Why the other options are incorrect:

- **A. Punch biopsy** — Punch biopsy has no role in thyroid nodule evaluation; FNA has already been performed and provided the maximum diagnostic information obtainable without surgery.
- **C. Thyroxine administration** — TSH suppressive therapy is not indicated as initial management. The patient is euthyroid (normal TSH), and there is no evidence that thyroxine suppression alters outcomes for an undiagnosed suspicious nodule.[5]

- **D. Ultrasound** — While thyroid and neck ultrasound is an important part of preoperative planning if not already done, it does not change the fundamental need for surgical excision after a suspicious FNAB result. The question implies imaging has already been performed (radionuclide scan), and the decisive diagnostic step at this point is surgery, not additional imaging.

Would you like to explore the role of molecular testing in managing indeterminate thyroid nodules?

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Question 250

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?

A. Adenoidectomy
B. Tympanostomy tube insertion
C. Antihistamine therapy
D. Corticosteroid therapy

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The answer is **B. Tympanostomy tube insertion**.

This child has **chronic bilateral otitis media with effusion (OME)** — retracted, immobile tympanic membranes bilaterally, recurrent ear infections since birth, 8 months of speech and hearing difficulties, and **bilateral mild conductive hearing loss** (26–28 dB). Per the **AAO-HNS 2022 Clinical Practice Guideline** on tympanostomy tubes (Key Action Statement 3), clinicians should offer **bilateral tympanostomy tube insertion** to children with bilateral OME for ≥3 months **and** documented hearing difficulties.[1][2] This child meets both criteria: chronic bilateral effusion with mild conductive loss (16–40 dB range) and clear functional impact on speech and language development.[2]

Why not the other options:

- **Adenoidectomy alone (A):** Per the same guideline (KAS 11), adenoidectomy may be performed as an **adjunct** to tympanostomy tubes — for symptoms directly related to the adenoids or in children **≥4 years old** — but it is not a standalone first-line intervention. For children <4 years, tympanostomy tubes are the recommended initial procedure.[3]

- **Antihistamine therapy (C):** Antihistamines and decongestants have demonstrated **no clinical benefit** in OME and are recommended against by both the AAO-HNS and AAFP guidelines.[4]
- **Corticosteroid therapy (D):** Oral and nasal corticosteroids offer only limited short-term benefit and are **not routinely recommended** for OME.[5]

Notably, if speech and language delays persist after tube placement and restoration of hearing, further developmental and speech-language evaluation should be pursued, as the functional deficits described (failure to follow 1-step commands, not responding to name) may have additional contributing factors beyond conductive hearing loss.[2]

Would you like to explore the role of adjunctive adenoidectomy with tympanostomy tubes in pediatric OME?

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Question 251

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?

A. Fumarate
B. Citrate
C. Malate
D. Succinate

https://openevidence.com/ask/2e482a35-b6da-4173-a002-a064d1eb1d32

The answer is **B. Citrate**.

Sodium fluoroacetate undergoes **"lethal synthesis"** in cells: it is converted to fluorocitrate, which acts as a potent **competitive inhibitor of aconitase** (aconitate hydratase), the enzyme that converts citrate to isocitrate in the TCA cycle.[1][2] With aconitase blocked, **citrate accumulates** in the cells. Experimental studies confirm that fluoroacetate poisoning causes a **4.2-fold increase in citrate concentrations** in cardiac tissue, with concurrent ATP depletion.[3] In brain tissue, inhibition of aconitase similarly leads to citrate accumulation, which may contribute to toxicity through chelation of free calcium ions.[4]

The other answer choices — fumarate, malate, and succinate — are TCA cycle intermediates that occur downstream of the aconitase step. Since the block is at aconitase (citrate → isocitrate),

these downstream metabolites would not accumulate; rather, their production would be impaired due to reduced flux through the cycle beyond the block.

Would you like to explore the clinical management and available antidotes for sodium fluoroacetate poisoning?

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Question 252

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?

A. Ceftriaxone and azithromycin
B. Ertapenem
C. Colistin
D. Cefepime and levofloxacin

https://openevidence.com/ask/4b991264-b62e-4cbc-a160-6c999aa83eb1

The correct answer is **D. Cefepime and levofloxacin**, which provides **dual antipseudomonal coverage** appropriate for this patient's severe pneumonia with risk factors for **Pseudomonas aeruginosa**.[1][2]

Why antipseudomonal coverage is needed

This patient has several established risk factors for P. aeruginosa pneumonia:

- **Severe COPD** with frequent exacerbations — COPD patients are at increased risk of gram-negative infections, including Pseudomonas, particularly with advanced disease[2][3][4]
- **Repeated antibiotic exposure** (three courses in the past year) — prior antibiotic use is among the strongest predictors of Pseudomonas and MDR Pseudomonas[5][6]

- **Systemic and inhaled corticosteroid use** (prednisolone for exacerbations, fluticasone inhaler) — systemic steroid therapy is an independent risk factor for Pseudomonas isolation in COPD (pooled aOR 2.67)[5]
- **Immunosuppression** from recent chemotherapy for metastatic colon cancer
- **Gram-negative rods** on endotracheal aspirate, consistent with Pseudomonas (though nonspecific)

The ATS/IDSA community-acquired pneumonia guidelines recommend empiric antipseudomonal coverage when locally validated risk factors for P. aeruginosa are present, using agents such as **cefepime (2 g every 8 hours), piperacillin-tazobactam, meropenem, or imipenem**.[1] For severe cases, guidelines recommend pairing an antipseudomonal β-lactam with an antipseudomonal fluoroquinolone such as **levofloxacin (750 mg/day)** or ciprofloxacin.[1][7]

Why not the other options

- **A. Ceftriaxone and azithromycin** — standard CAP regimen with no antipseudomonal activity, inadequate given this patient's risk profile[1]
- **B. Ertapenem** — a Group 1 carbapenem that **lacks activity against P. aeruginosa**, unlike meropenem or imipenem[6][8][9]
- **C. Colistin** — a last-resort agent reserved for **multidrug-resistant gram-negative infections**; inappropriate as empiric first-line therapy[10][11]

Empiric coverage should be reassessed once blood and respiratory culture results with susceptibilities are available, with de-escalation if Pseudomonas is not isolated.[1]

Would you like to explore empiric antibiotic management of febrile neutropenia in cancer patients?

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Question 253

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?

A. Brief psychotic disorder
B. Schizoaffective disorder
C. Schizophreniform disorder
D. Schizotypal personality disorder

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The answer is **B. Schizoaffective disorder** (bipolar type).

This presentation combines two co-occurring syndromes — **persistent psychotic symptoms** and **recurrent manic episodes** — which is the hallmark of schizoaffective disorder.[1][2]

Why schizoaffective disorder fits:

- **Criterion A for schizophrenia is met**: The patient has auditory hallucinations (command hallucinations about the end of the world) and disorganized speech (jumping from topic to topic) persisting over 7 months.[1][3]
- **Major mood episodes are present**: The 2-week periods of markedly decreased need for sleep, excessive spending, and increased goal-directed activity (redecorating the apartment) meet criteria for **manic episodes**.[1][2]
- **Psychotic symptoms persist outside of mood episodes (Criterion B)**: The auditory hallucinations have been present for 7 months continuously, while manic episodes occur intermittently (~2 weeks every other month). This means hallucinations are present for **at**

least 2 weeks in the absence of a manic episode, which distinguishes schizoaffective disorder from bipolar disorder with psychotic features.[1][4]

Why the other options are incorrect:

- **A. Brief psychotic disorder** requires symptom duration of **1 day to <1 month**. This patient has been symptomatic for 7 months.[1]
- **C. Schizophreniform disorder** requires duration of **1–6 months** and that schizoaffective disorder has been ruled out (i.e., no major mood episodes, or mood episodes present for a minority of illness duration). This patient exceeds 6 months and has prominent manic episodes, eliminating this diagnosis on both criteria.[1]
- **D. Schizotypal personality disorder** involves eccentric behavior, magical thinking, and unusual perceptual experiences — but **not frank psychosis** with overt hallucinations or full manic episodes. This patient's symptoms are far too severe for a personality disorder.[1]

The **bipolar type** subtype is specified because the mood episodes include mania. Typical onset of schizoaffective disorder is in **early adulthood**, consistent with this 21-year-old's presentation.[1]

Would you like to explore first-line treatment strategies for schizoaffective disorder, bipolar type?

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Question 254

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?

A. Alzheimer's disease
B. Lewy body dementia
C. Normal-pressure hydrocephalus
D. Vascular dementia

https://openevidence.com/ask/dbe63efe-ac60-46a2-b65e-59d6ed8738b6

The answer is **D. Vascular dementia**. This patient's presentation is a classic case of **multi-infarct vascular dementia**, supported by several converging features:

- **Documented cerebrovascular disease**: A left basal ganglia hemorrhage (12 years ago) and a right MCA infarction (4 years ago) provide clear temporal association between cerebrovascular events and cognitive decline.[1]
- **Stepwise cognitive decline**: Progressive memory worsening over years with a recent acute exacerbation is the hallmark course of vascular dementia caused by multiple strokes — "an acute stepwise or fluctuating decline in cognition, and intervening periods of stability".[1][2]

- **Transient monocular vision loss**: The episode of right eye vision loss resolving within a day is consistent with **amaurosis fugax** (a TIA), indicating ongoing cerebrovascular disease and likely representing the cause of the recent acute worsening.
- **Focal neurological deficits**: Right-sided weakness (4/5), reduced tone, **exaggerated reflexes**, and **hemiparetic gait** are directly attributable to prior strokes. Per DSM criteria, focal neurologic signs such as "exaggeration of deep tendon reflexes, gait abnormalities, weakness of an extremity" are key diagnostic features of vascular dementia.[3]
- **Vascular risk factors**: Diabetes mellitus type 2 and hypertension are major risk factors for VCID.[2][4]
- **Inconclusive MMSE**: The MMSE was designed to detect Alzheimer's disease and is **less sensitive for vascular dementia**, which preferentially affects attention, processing speed, and executive function rather than episodic memory.[5]

Why not the other options:

- **Alzheimer's disease**: Typically presents with **early episodic memory loss** and **gradual, continuous progression** without focal neurological deficits. The stepwise decline, lateralized motor findings, and strong cerebrovascular history argue against AD as the primary diagnosis.[6]
- **Lewy body dementia**: Characterized by **visual hallucinations**, **fluctuating cognition/alertness**, **parkinsonism** (rigidity, bradykinesia), and **REM sleep behavior disorder** — none of which are present here. The focal lateralized deficits reflect stroke, not LBD.[6]
- **Normal-pressure hydrocephalus**: The classic triad is dementia, **magnetic/apraxic gait**, and **urinary incontinence**. This patient has no incontinence, and the gait abnormality is hemiparetic (from stroke), not the wide-based shuffling gait of NPH.

Would you like to explore evidence-based strategies for secondary prevention and management of vascular dementia?

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Question 255

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?

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.

https://openevidence.com/ask/4f0b7650-0a00-48d8-b834-e402b91e9d6a

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The correct answer is **A: "Let's talk about what makes it difficult for you to take your medications."**

The most appropriate first step when addressing ART nonadherence is to **explore the patient's individual barriers** using an **open-ended, nonjudgmental approach**. The NIH Office of AIDS Research Advisory Council (OARAC) guidelines recommend that clinicians "assist people with HIV in identifying facilitating factors and potential barriers to adherence and develop multidisciplinary plans to attempt to overcome those barriers".[1] Adherence should be assessed "in a constructive and nonjudgmental manner," normalizing less-than-perfect adherence to allow honest disclosure.[1] The HIVMA/IDSA guidelines similarly emphasize that adherence discussions "should use an empathetic lens with the goal of identifying barriers" and should be "provided carefully and thoughtfully so as not to perpetuate (or lead to) a sense of self-guilt or anxiety about missed doses".[2]

Why the other options are inferior:

- **B** ("Are you aware that it is essential...") — This is a closed-ended question that assumes a knowledge deficit and risks being perceived as lecturing. The patient was previously adherent for 3 years, making it unlikely she is unaware of the importance of daily dosing.

- **C** (social worker to subsidize medications) — This presumes the barrier is financial. While cost is a recognized driver of nonadherence, the physician must first identify the actual barrier before offering a targeted solution.[2]
- **D** (reviewing medication instructions) — This assumes the barrier is misunderstanding of how to take the medications. Again, given 3 years of successful prior adherence, this is unlikely and does not explore the root cause.

Motivational interviewing techniques — which emphasize open-ended questions about barriers — have demonstrated efficacy in improving ART adherence and are specifically recommended by guidelines.[1][3]

Would you like to explore evidence-based interventions for improving ART adherence in patients facing socioeconomic barriers?

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Question 256

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?

A. Ultrasonography of the neck
B. Echocardiography
C. Warfarin therapy
D. CT angiography of the head

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The correct answer is **A. Ultrasonography of the neck**.

This patient presents with **transient contralateral hemispheric symptoms** (episodic left hand weakness and numbness) and a **right-sided cervical bruit**, in the setting of extensive atherosclerotic risk factors (PAD, type 2 diabetes, hypertension, hypercholesterolemia, 50-pack-year smoking history). This constellation is highly suggestive of **right internal carotid artery stenosis causing TIAs**.

Duplex ultrasonography is the recommended initial diagnostic test for evaluating carotid stenosis in patients with focal neurological symptoms referable to the carotid territory.[1][2] The AHA/ACC/ASA guidelines give this a **Class I recommendation**, noting that the initial evaluation of patients with transient hemispheric neurological symptoms of possible ischemic origin should include noninvasive imaging, with duplex ultrasonography recommended as the first-line modality.[1][3] It is noninvasive, low-cost, and accurate for estimating stenosis severity.[4][5] CTA

or MRA is indicated when sonography is unavailable, yields equivocal results, or when further anatomical detail is needed to plan revascularization.[1][3]

Why the other options are not the best next step:

- **B. Echocardiography** — Appropriate for evaluating cardioembolic sources, but in a patient with a localizing cervical bruit and contralateral hemispheric symptoms, **vascular imaging of the carotid arteries takes priority**. Guidelines specify that echocardiography should be pursued when extracranial vascular disease is insufficient to explain the symptoms.[1][2]
- **C. Warfarin therapy** — No indication exists here. There is no evidence of atrial fibrillation, venous thromboembolism, or mechanical valve. The patient is already on aspirin, which is appropriate antiplatelet therapy.
- **D. CT angiography of the head** — This evaluates **intracranial** vasculature. While intracranial imaging may be part of a complete TIA workup, it does not directly assess the **cervical carotid bifurcation**, which is the most likely culprit lesion given the right neck bruit.[3][6]

Identifying significant carotid stenosis is also important in the preoperative context — if high-grade stenosis is found, the **elective femoropopliteal bypass may need to be deferred** while urgent carotid evaluation and potential revascularization are pursued, given the elevated perioperative stroke risk and the time-sensitive nature of symptomatic carotid disease.[7]

Would you like to explore the indications and timing for carotid revascularization in symptomatic carotid stenosis?

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Question 257

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?

A. Continue methimazole
B. Discontinue methimazole, start propylthiouracil
C. Add glucocorticoids
D. Refer for radioiodine therapy

https://openevidence.com/ask/07e26796-0257-4153-b005-e374faaabe6f

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The correct answer is **B: Discontinue methimazole, start propylthiouracil**.

This patient is in the **early first trimester** with confirmed pregnancy while on methimazole for hyperthyroidism. **Methimazole is associated with a well-characterized embryopathy** when used in the first trimester, including **aplasia cutis, esophageal atresia, choanal atresia, and abdominal wall defects**.[1][2] Propylthiouracil (PTU) carries a lower teratogenic risk, with milder associated anomalies (facial/neck cysts, urinary tract abnormalities).[1] A meta-analysis of 13 studies confirmed that methimazole-exposed pregnancies had a significantly **higher risk of congenital anomalies** compared to PTU (OR 0.80 favoring PTU; 95% CI 0.69–0.92).[3]

Both the **ATA guidelines** and **ACOG** recommend **PTU over methimazole as the antithyroid drug of choice in the first trimester**.[2][4] The FDA label for methimazole similarly recommends considering an alternative antithyroid medication in early pregnancy during organogenesis.[5] When switching, an approximate **dose ratio of 1:20** (e.g., methimazole 5 mg/day ≈ PTU 50 mg twice daily) can be used.[4][6] PTU should be given at the **lowest effective dose**, targeting maternal free T4 at or just above the upper reference limit, to minimize the risk of fetal hypothyroidism.[1][7]

Why the other options are incorrect:

- **A (Continue methimazole):** First-trimester methimazole exposure carries a significantly higher teratogenic risk than PTU, making continuation inappropriate.[1][2]
- **C (Add glucocorticoids):** Glucocorticoids have no role in routine management of well-controlled hyperthyroidism in pregnancy; they are reserved for thyroid storm or severe Graves ophthalmopathy.
- **D (Radioiodine therapy): Absolutely contraindicated in pregnancy** — radioiodine crosses the placenta and can ablate the fetal thyroid, causing severe hypothyroidism.[1][6]

Notably, the **2026 ATA guidelines** also raise the possibility of **ATD discontinuation altogether** in select patients with well-controlled disease (as suggested by this patient's TSH of 2.0), given that the average time to Graves relapse is approximately 3 months, potentially beyond the critical teratogenic window.[4] However, this approach requires careful patient selection (low-dose ATD, stable thyroid function >6 months, negative TRAb) and close monitoring every 1–2 weeks.[4] Among the answer choices provided, switching to PTU is the best step.

Would you like to explore the monitoring strategy for thyroid function and TRAb throughout pregnancy in Graves' disease?

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Question 258

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?

A. Compression fracture
B. Herniated nucleus pulposus
C. Musculoskeletal strain
D. Spinal stenosis

https://openevidence.com/ask/1a7ca05b-ffcd-409a-8459-6f59aefc63e3

The answer is **D. Spinal stenosis**. This presentation is classic for **lumbar spinal stenosis with neurogenic claudication**.

Several features are diagnostic:

- **"Shopping cart sign"**: Symptom relief with activities that flex the lumbar spine — riding a bike and pushing a grocery cart — is a hallmark of lumbar spinal stenosis. Lumbar flexion increases the cross-sectional area of the spinal canal and neural foramina, relieving nerve root compression.[1][2]
- **Neurogenic claudication**: Numbness and weakness in the legs with walking, gradually worsening over time, is the most common symptom of lumbar spinal stenosis.[1][3]
- **Non-tender spine with normal mobility**: Physical examination in spinal stenosis characteristically shows a **non-tender spine**, unlike compression fractures (midline tenderness) or musculoskeletal strain (paraspinal tenderness, reduced range of motion).[1][4][5]

- **Age and risk factors**: After age 60, spinal stenosis surpasses herniated disc as the leading cause of radicular leg symptoms.[6]

Why the other options are less likely:

- **A. Compression fracture** — Would be expected to cause **midline tenderness** on exam, particularly given his osteoporosis risk. The positional relief pattern (improvement with flexion) does not fit compression fracture.
- **B. Herniated nucleus pulposus** — Typically presents more acutely with a **positive straight leg raise**, dermatomal pain distribution, and peaks in the 30–50 age range. Trunk flexion is often more impaired in disc herniation, which is the opposite of what is seen here.[4][6]
- **C. Musculoskeletal strain** — Would present with **paraspinal muscle tenderness, spasm, and reduced range of motion** without neurological symptoms such as bilateral leg numbness and weakness.[5]

> "Some patients with spinal stenosis report that walking is more comfortable when leaning on a shopping cart, when the spine is flexed. Worsening of spinal stenosis symptoms when the back is extended and improvement of symptoms when the lower back is flexed occurs because spinal extension reduces the cross-sectional area of the central spinal canal and neural foramina."
>
> —Jeffrey N. Katz, MD, MSc et al., Orthopedic and Arthritis Center for Outcomes Research, Brigham and Women's Hospital, Boston, Massachusetts and other institutions. Diagnosis and Management of Lumbar Spinal Stenosis. JAMA. May 03, 2022.
>
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Would you like to discuss the workup and management approach for lumbar spinal stenosis, including indications for advanced imaging or surgical referral?

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Question 259

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?

A. Change lisinopril to propanolol
B. Change lisinopril to amlodipine
C. Change atorvastatin to to lovastatin
D. Change lisinopril to losartan

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The answer is **D. Change lisinopril to losartan**.

Dry cough is a well-known adverse effect of ACE inhibitors such as lisinopril, occurring in **5–35% of patients**.[1] The mechanism involves accumulation of bradykinin and substance P due to ACE inhibition, leading to bronchoconstriction and cough.[2][3] The standard management is to **switch to an angiotensin receptor blocker (ARB)**, such as losartan, which does not inhibit kininase and is associated with a significantly lower incidence of cough.[4][5]

Why the other options are incorrect:

- **A (propranolol):** Non-selective beta-blockers are **contraindicated in asthma**, which this patient has. Propranolol can precipitate bronchospasm.
- **B (amlodipine):** While a calcium channel blocker could treat hypertension, an **ARB is preferred** over a CCB in this patient because it preserves renin-angiotensin system blockade, which confers renal protection in a patient with type 2 diabetes and mildly elevated creatinine.[3]
- **C (lovastatin):** Statins are not a recognized cause of dry cough; switching within the statin class would not address the symptom.

The 2022 AHA/ACC/HFSA guidelines explicitly state that **patients intolerant to ACE inhibitors because of cough should be started on an ARB**.[4] A systematic review confirmed that ACE inhibitors carry **3.2 times the risk of cough compared with ARBs**.[3]

Would you like to explore the renal protective benefits of ARBs in this patient's context of diabetes and mildly elevated creatinine?

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Question 260

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?

A. Mu receptor agonist
B. Nicotinic acetylcholine receptor agonist
C. Monoamine reuptake antagonist
D. Thyroperoxidase inhibitor

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The answer is **A. Mu receptor agonist** (i.e., opioid).

This presentation is classic **neonatal opioid withdrawal syndrome (NOWS)**, formerly termed neonatal abstinence syndrome (NAS). Opioids such as heroin, methadone, and oxycodone are mu-opioid receptor agonists. After chronic in utero exposure, abrupt discontinuation of the transplacental opioid supply at birth triggers a withdrawal syndrome.

The AAP identifies the cardinal signs of NOWS as:[1][2]

- **CNS irritability:** high-pitched continuous crying, tremors, hyperreflexia (hyperactive Moro reflex), increased muscle tone, excessive startle response, seizures
- **Gastrointestinal dysfunction:** poor feeding, vomiting, loose stools
- **Autonomic activation:** fever, sweating, sneezing, nasal stuffiness/rhinorrhea, tachypnea

This infant exhibits nearly every hallmark — **high-pitched crying, poor feeding, rhinorrhea, low-grade fever, hyperreflexia, tremors, and excessive startle** — presenting at 24 hours of life, which aligns with the typical onset of heroin withdrawal (within 24 hours).[1] The lack of prenatal care is an additional clue suggesting possible illicit substance use.

Why not the other options?

- **B (Nicotinic acetylcholine receptor agonist — nicotine/tobacco):** Neonatal nicotine withdrawal can cause irritability but does not produce this full constellation of CNS hyperexcitability, GI dysfunction, and autonomic signs.
- **C (Monoamine reuptake antagonist — cocaine):** Cocaine is a stimulant; neonatal cocaine exposure causes irritability and jitteriness but classically does not produce the organized withdrawal syndrome seen here (rhinorrhea, hyperreflexia, GI symptoms).
- **D (Thyroperoxidase inhibitor — e.g., propylthiouracil):** This would cause neonatal hypothyroidism (lethargy, poor feeding, constipation, hypothermia) — the opposite of the hyperexcitable state described.

Would you like to explore the current management approaches for neonatal opioid withdrawal syndrome, including the Eat, Sleep, Console method?

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Question 261

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?

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

https://openevidence.com/ask/3cfcbfdc-8020-4bd7-9eda-3abcbe70aa08

The answer is **B: Muscle relaxation time: increased, cytosolic calcium concentration: increased**.

The ATP2A1 gene encodes the **SERCA1 (sarco/endoplasmic reticulum calcium-ATPase 1)** pump, which is responsible for **transporting calcium ions from the cytosol back into the sarcoplasmic reticulum** to trigger muscle relaxation.[1][2] Loss-of-function mutations in ATP2A1 cause **Brody myopathy (Brody disease)**, a rare autosomal recessive myopathy characterized by exercise-induced impairment of muscle relaxation, stiffness, and cramps.[3][4]

The physiologic consequences of SERCA1 loss of function are:

- **Increased cytosolic calcium concentration** — Without functional SERCA1, calcium ions cannot be efficiently sequestered back into the SR lumen after contraction. SERCA-mediated reuptake is the primary mechanism for clearing myoplasmic calcium in skeletal muscle, maintaining a 10,000-fold calcium gradient across the SR membrane. Loss of this pump leaves calcium accumulated in the cytosol.[5]
- **Increased muscle relaxation time** — Since relaxation depends on removal of calcium from the cytosol (allowing calcium to dissociate from troponin C and permitting actin-myosin cross-bridge detachment), impaired calcium reuptake directly **delays muscle relaxation**. This manifests clinically as the "silent cramps" seen in Brody disease — electrically silent contractures on EMG, distinguishing them from myotonia.[1][6][7]

The other answer choices are incorrect because a loss of SERCA1 function cannot decrease cytosolic calcium or leave it unchanged; the pump's sole role is cytosolic calcium clearance. Similarly, relaxation time cannot decrease or remain unchanged when the primary mechanism driving relaxation is impaired.

Would you like to explore the diagnostic workup and management of Brody myopathy?

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Question 262

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?

A. Chronic inflammatory bowel disease
B. Ibuprofen
C. History of abdominal surgery
D. Alcohol

https://openevidence.com/ask/921fc734-a0ab-47c8-a887-eaf448fd8e48

C. History of abdominal surgery. The presentation is a mechanical small bowel obstruction — crampy abdominal pain, bilious vomiting, obstipation, distension, high-pitched bowel sounds, empty rectum, and ultrasound showing dilated small bowel with nonpropulsive ("to-and-fro") peristalsis — and postoperative adhesions from his prior laparoscopic appendectomy are the single most common cause, accounting for roughly 60–75% of adult SBO.[1][2][3] Prior abdominal surgery, constipation/obstipation, distension, and abnormal bowel sounds are the most reliable clinical predictors of SBO.[4]

Why the surgical history fits

- Adhesions form when fibrin bridges between injured serosal surfaces fail to undergo fibrinolysis and are organized by fibroblasts; they may band, kink, or angulate bowel loops and precipitate obstruction years to decades later.[5]
- Post-appendectomy SBO occurs in about 2.8% of adults over ~4 years of follow-up, with risk persisting long-term; laparoscopic approach lowers but does not eliminate the risk.[6][7]
- The well-healed laparoscopic scars with no hernia, no fever, normal WBC, and normal chemistries argue for simple adhesive obstruction rather than an inflammatory, infectious, or neoplastic cause.

Why the other options are less likely

- **Chronic inflammatory bowel disease (A):** Crohn stricture causes ~5% of SBO, but he has no history of chronic diarrhea, weight loss, perianal disease, anemia, or elevated inflammatory markers.[2]
- **Ibuprofen (B):** Chronic NSAID use can produce diaphragm-like small bowel strictures, but this is rare and would typically present with iron-deficiency anemia and recurrent subacute obstruction; his hematocrit is normal.
- **Alcohol (D):** Two beers daily (mildly elevated GGT alone, normal transaminases and lipase-independent picture) does not cause mechanical SBO. Alcohol-related pancreatitis would give ileus, not the hyperactive high-pitched sounds and nonpropulsive peristalsis of mechanical obstruction.

Next steps: CT abdomen/pelvis with IV contrast to confirm the transition point and screen for closed-loop obstruction, strangulation, or an unsuspected hernia/mass; NPO, IV fluid resuscitation, and nasogastric decompression; surgical consultation.[2][4][8] Most adhesive SBOs resolve nonoperatively, but strangulation, closed-loop obstruction, or failure of nonoperative management within ~48–72 hours mandates operative intervention.[8][9]

Would you like to explore which CT findings predict strangulation or failure of nonoperative management in adhesive SBO?

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Question 263

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?

A. Involvement of terminal ileum
B. Noncaseating granulomas
C. Transmural inflammation
D. Continuous mucosal damage

https://openevidence.com/ask/71b59a9e-ccc4-4d5d-869a-283489ad3065

The answer is **D. Continuous mucosal damage**.

Ulcerative colitis characteristically affects the rectum and extends proximally in a **continuous, circumferential pattern** with inflammation limited to the **mucosa and submucosa**.[1][2] This continuous pattern of mucosal involvement — beginning at the anorectal junction and extending proximally without skip areas until a clear transition zone to normal mucosa — is the hallmark endoscopic and histologic finding that most strongly supports a UC diagnosis.[1][3][4]

The remaining options are features of **Crohn's disease**, not UC:

- **A. Terminal ileum involvement** — The terminal ileum is the most commonly affected site in Crohn's disease. While "backwash ileitis" can occur in UC pancolitis, isolated terminal ileum involvement points toward Crohn's.[3][5]
- **B. Noncaseating granulomas** — These are a distinguishing histopathologic feature of Crohn's disease (detected in ~40–60% of resection specimens), and their presence helps differentiate CD from UC.[5][6]
- **C. Transmural inflammation** — Crohn's disease is characterized by transmural (full-thickness) inflammation, whereas UC inflammation is confined to the mucosal layer.[4][5][7]

Would you like to explore how to differentiate ulcerative colitis from Crohn's colitis when both present with colonic involvement?

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Question 264

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?

A. Actin filament assembly
B. T-cell receptor signaling
C. Microtubule polymerization
D. B-cell maturation

https://openevidence.com/ask/655edabb-58ce-48b4-9807-c5e133f6ea29

The correct answer is **B. T-cell receptor signaling**.

This presentation — a 6-month-old male with **decreased IgG, IgA, and IgE**, **enlarged tonsils/lymph nodes**, recurrent infections, and **Pneumocystis jirovecii pneumonia** (disc-shaped cysts on methenamine silver stain with bilateral interstitial infiltrates) — is classic for **X-linked hyper-IgM syndrome (XHIGM)**.[1][2][3]

XHIGM results from mutations in the **CD40 ligand (CD154) gene** on T cells.[1][4] CD40L on activated T cells normally engages CD40 on B cells, triggering immunoglobulin class-switch recombination from IgM to IgG, IgA, and IgE. When this T-cell costimulatory signal is absent, B cells cannot class-switch, resulting in **very low IgG, IgA, and IgE with normal or elevated IgM**.[1][5] Critically, CD40L signaling also activates macrophages; its absence impairs cell-mediated antimicrobial responses, accounting for the characteristic susceptibility to opportunistic infections such as *Pneumocystis jirovecii* (present in ~40% of cases at diagnosis).[1][3]

> "Paradoxically, the X-linked hyper-IgM syndrome is a T-cell defect rather than a B-cell defect. Until the T-cell defect was discovered, coexistent neutropenia had been considered the explanation for the susceptibility to P. carinii infection."

—Rebecca H. Buckley, M.D., Duke University School of Medicine. Primary Immunodeficiency Diseases Due to Defects in Lymphocytes. N Engl J Med. November 02, 2000.

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Why not the other options:

- **A. Actin filament assembly** — Wiskott-Aldrich syndrome (WASP mutation), which presents with the triad of eczema, thrombocytopenia with small platelets, and recurrent infections.
- **C. Microtubule polymerization** — Chédiak-Higashi syndrome, characterized by partial oculocutaneous albinism and giant cytoplasmic granules in leukocytes.
- **D. B-cell maturation** — X-linked agammaglobulinemia (Bruton's, BTK deficiency). This would cause **absent or markedly reduced tonsils and lymph nodes** due to lack of B cells, the opposite of what is seen here. All immunoglobulin isotypes, including IgM, would be severely reduced.[5]

The key distinguishing feature in this case is the **presence of enlarged lymphoid tissue** with selectively decreased IgG/IgA/IgE, pointing to a T-cell signaling defect (CD40L) that prevents class switching rather than an intrinsic B-cell maturation defect.

Would you like to explore treatment options and long-term prognosis for X-linked hyper-IgM syndrome?

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Question 265

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?

A. Ammonium chloride
B. Mannitol
C. Sodium bicarbonate
D. Thiazide diuretics

https://openevidence.com/ask/cc2b39b9-4d05-4fb4-b4cc-d6e957b5def8

The answer is **C. Sodium bicarbonate**.

The clinical presentation — **somnolence, ataxia, and nystagmus** after ingestion of a grandson's seizure medication — is consistent with **phenobarbital toxicity**. The concern that the INR will trend down confirms the identity of the drug: phenobarbital is a potent **inducer of CYP2C9 and CYP1A2**, which accelerates warfarin metabolism and reduces its anticoagulant effect.[1][2] A case report illustrates this directly: a patient on stable warfarin developed recurrent mesenteric vein thrombosis (INR fell to 1.0) after phenobarbital was started.[3]

Phenobarbital is a weak acid (pKa ~7.24).[4] Urinary alkalinization with **sodium bicarbonate** ionizes the drug within the renal tubular lumen, trapping it in a charged, non-lipid-soluble form that cannot be passively reabsorbed. This "ion trapping" enhances renal clearance.[4][5] The FDA label for sodium bicarbonate specifically lists **barbiturate poisoning** as an indication for urinary alkalinization.[6][7]

Why the other options are incorrect:

- **Ammonium chloride** (A) — Acidifies the urine, which would keep phenobarbital in its non-ionized, lipid-soluble form, thereby **increasing** tubular reabsorption and worsening toxicity.
- **Mannitol** (B) — An osmotic diuretic that increases urine volume but does not alter urinary pH; forced diuresis alone is far less effective than alkalinization for weak acid elimination.
- **Thiazide diuretics** (D) — Do not meaningfully alkalinize urine and are not used for enhanced drug elimination in overdose settings.

Would you like to explore how multiple-dose activated charcoal compares to urinary alkalinization for managing phenobarbital overdose?

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Question 266

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?

A. Thick and thin blood smear
B. Direct antiglobulin test
C. Sickle cell test
D. Ultrasound of the abdomen

https://openevidence.com/ask/e810479c-992d-42e7-bc90-8e2bb6381dd7

A. Thick and thin blood smear. This is malaria — most likely *P. vivax* or *P. falciparum* acquired in the Brazilian Amazon — and Giemsa-stained thick and thin peripheral blood smear microscopy is the reference-standard confirmatory test.[1][2][3][4] Chemoprophylaxis does not exclude the diagnosis: breakthrough infection occurs with imperfect adherence, and prior prophylaxis can blunt or alter the presentation.[5]

Why malaria fits

- **Epidemiology**: Nearly all Brazilian malaria occurs in the Amazon (North Region plus Maranhão and Mato Grosso), with *P. vivax* ~85% and *P. falciparum* ~15%; chloroquine

resistance is widespread. Incubation is compatible — most returning US travelers with *P. vivax* become symptomatic within a month, and non-immune vivax infection manifests around 10–15 days after inoculation.[4][6][7][8]

- **Clinical syndrome**: High-grade fever, myalgia, malaise, splenomegaly, and jaundice with an unconjugated hyperbilirubinemia (total 4.7, direct 0.9) reflecting intravascular/extravascular hemolysis of parasitized erythrocytes, plus normocytic anemia.[7][8]
- **Hypoglycemia (56 mg/dL)** is a recognized hallmark of malaria and is more frequent in children; it is driven in part by heme-mediated suppression of hepatic glucose production and, when treatment includes quinine/quinidine, by hyperinsulinemia.[9][10][11]

Test specifics

- **Thick smear** maximizes sensitivity for detecting parasites; **thin smear** provides speciation and parasite density quantification — both are needed because management differs by species and parasitemia.[3][4][5]
- A single negative smear does not exclude malaria; obtain **three sets 12–24 hours apart** before ruling it out.[3][4][5]
- A rapid diagnostic test may be run concurrently for speed, but positive and negative RDTs must be confirmed by microscopy, and *pfhrp2/3* gene deletions reported in Acre and Amazonas make HRP2-based RDTs (BinaxNOW) unreliable in Brazil. PCR is used for species confirmation, not initial rapid diagnosis.[1][2][6]

Why the other options fail

- **Direct antiglobulin test** would identify autoimmune hemolytic anemia, which does not explain the travel exposure, high-grade fever with rigors, or hypoglycemia; the LDH here is normal (212 U/L), arguing against brisk immune hemolysis as the primary process.
- **Sickle cell test** — sickle cell disease presents earlier in childhood with a known history, would not be newly unmasked by travel, and typically produces autosplenectomy rather than new splenomegaly by age 10.
- **Abdominal ultrasound** would only confirm the already-palpable splenomegaly and exclude biliary obstruction, which is not suggested by a predominantly indirect hyperbilirubinemia and nontender abdomen.

Clinical caveat: Assess immediately for severe malaria criteria — jaundice, hypoglycemia, hemoglobin <7 g/dL, parasitemia ≥5% in a non-immune traveler, acidosis, impaired consciousness, or shock — since severe disease occurs with *P. vivax* as well as *P. falciparum* and

mandates IV artesunate.[2][4][5] This patient's tachycardia and low-normal blood pressure warrant close monitoring, and treatment should not be delayed while awaiting smears if severe malaria is strongly suspected.[5]

Would you like to explore the treatment regimen for malaria acquired in the Brazilian Amazon, including radical cure options?

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Question 267

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?

A. Azithromycin
B. Imipenem
C. Streptomycin
D. No pharmacotherapy

https://openevidence.com/ask/413f7ea6-82a7-4a26-a8d7-7de9c1a87d73

The answer is **C. Streptomycin**.

This presentation is classic **bubonic plague** caused by *Yersinia pestis*: travel to Madagascar (one of the most plague-endemic countries), an initial painless papule at the flea-bite inoculation site on the thigh, followed by painful inguinal lymphadenopathy (bubo) with fever and malaise, gram-negative coccobacilli on microscopy, and a confirmatory **4-fold rise in serum anti-F1 titers** — the F1 capsular antigen being specific to *Y. pestis*.[1][2]

Why streptomycin: CDC guidelines recommend **streptomycin and gentamicin as first-line agents** for bubonic plague treatment.[3] The IDSA similarly identifies **streptomycin (15 mg/kg every 12 hours, adjusted for renal function) as the treatment of choice**.[4] A systematic review of 762 published plague cases found the lowest case-fatality rate among patients treated with aminoglycosides (13%).[5]

Why not the other options:

- **Azithromycin** — not among recommended agents for plague treatment. Effective drug classes include aminoglycosides, fluoroquinolones, tetracyclines, and sulfonamides, but macrolides are notably absent from all guidelines.[3][4]
- **Imipenem** — carbapenems are not recommended for plague treatment.
- **No pharmacotherapy** — untreated bubonic plague carries an extremely high mortality rate (~50–60%) and can progress to secondary septicemic or pneumonic plague. Treatment is essential.

A recent landmark NEJM trial (IMASOY, 2025) demonstrated that oral ciprofloxacin monotherapy was noninferior to aminoglycoside-ciprofloxacin sequential therapy for bubonic plague, which may shift future practice toward fluoroquinolones as first-line therapy.[2] However, streptomycin remains the traditional and guideline-endorsed first-line choice.

Would you like to explore post-exposure prophylaxis recommendations for plague contacts?

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Question 268

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?

A. Lisinopril
B. Fluphenazine
C. Levothyroxine
D. Atorvastatin

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The answer is **B. Fluphenazine**.

This case illustrates **antipsychotic-induced hypothermia**, a potentially life-threatening adverse effect of neuroleptic medications. Fluphenazine, a phenothiazine antipsychotic appropriate for this patient's schizoaffective disorder, is the drug most likely started 10 days ago.

Why fluphenazine fits this presentation:

- **Hypothermia (32°C):** Antipsychotics impair central thermoregulation through disruption of hypothalamic circuits, particularly via dopamine receptor blockade in the preoptic anterior hypothalamic region. The risk is **highest in the first 7–10 days after initiation** or dose escalation, matching this patient's timeline exactly.[1][2][3][4]
- **Paradoxical undressing** (attempting to remove clothing): A classic feature of **moderate hypothermia** (28–32°C), caused by paradoxical vasodilation as thermoregulatory mechanisms fail.[2]

- **Bradycardia, bradypnea, altered mental status, and absent lower extremity DTRs:** All consistent with moderate hypothermia, in which respiratory depression, cardiac conduction slowing, impaired mental function, and areflexia are expected.[2]
- **Dilated, poorly reactive pupils:** Attributable to hypothermia itself, though fluphenazine's anticholinergic properties (the FDA label notes it potentiates atropine effects) may contribute.[5]

Contributing risk factors compound the antipsychotic's thermoregulatory impairment: **underlying hypothyroidism** (a recognized high-risk condition for APD-induced hypothermia due to reduced basal metabolic rate) and **cold exposure** (windows open overnight).[2][3] Patients with schizophrenia-spectrum disorders also carry independently higher risk.[1]

Why not the other options:

- **Lisinopril (A):** ACE inhibitors do not impair thermoregulation or cause anticholinergic effects.
- **Levothyroxine (C):** Would treat hypothyroidism, not worsen it. While myxedema coma shares features (hypothermia, bradycardia, altered mental status), it is not caused by starting levothyroxine; if anything, inadequate dosing over a prolonged period would be the concern, not initiation 10 days prior.
- **Atorvastatin (D):** Statins have no mechanism for hypothermia or the neurological findings seen here.

Would you like to explore the recommended monitoring and management of antipsychotic-induced hypothermia?

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Question 269

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?

A. Periportal hepatocytes
B. Hepatic sinusoidal endothelial cells
C. Hepatic Kupffer cells
D. Centrilobular hepatocytes

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The answer is **D. Centrilobular hepatocytes**.

This patient developed **ischemic hepatitis ("shock liver")** following hemorrhagic shock from diverticular bleeding. The clinical picture is classic: hemodynamic compromise (BP 86/60, HR 115) followed by a **massive but transient rise in serum transaminases** (ALT 2,674, AST 2,254) with concurrent acute kidney injury (BUN 60, creatinine 2.1), reflecting systemic hypoperfusion.[1]

Why centrilobular (zone 3) hepatocytes are damaged first:

The liver acinus is organized into three zones based on proximity to the portal triad blood supply. **Zone 3 (centrilobular) hepatocytes** surround the central vein and are the **farthest from the oxygen-rich blood** entering via the hepatic artery and portal vein at zone 1. This makes them the most vulnerable to hypoxic injury during states of reduced perfusion.[2] The histopathological hallmark of ischemic hepatitis is **centrilobular coagulative necrosis in zone 3**, which may extend to mid-zonal hepatocytes in more severe cases.[2][3]

The other answer choices are incorrect because:

- **Periportal hepatocytes (zone 1)** receive the highest oxygen tension and are the last to be affected by ischemia (though they are preferentially damaged in toxic injuries such as phosphorus poisoning).
- **Kupffer cells** and **sinusoidal endothelial cells** play roles in ischemia-reperfusion injury (Kupffer cells are activated early during reperfusion), but the primary cells damaged first during warm ischemia/hypoperfusion are the hepatocytes themselves — specifically those in zone 3.[4][5]

Would you like to explore how to differentiate ischemic hepatitis from other causes of acute severe transaminase elevation?

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Question 270

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?

A. Inhibits cell wall synthesis
B. Binds D-ala D-ala in the cell wall
C. Inhibits initiation complex
D. Inhibits sterol synthesis

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The answer is **A. Inhibits cell wall synthesis**.

This vignette describes **uncomplicated cystitis** caused by **E. coli** — the gram-negative rods forming pink (lactose-fermenting) colonies on MacConkey agar are classic. The key constraint is the **sulfa allergy**, which eliminates **TMP-SMX**, otherwise a first-line agent.[1]

First-line alternatives per IDSA guidelines include **nitrofurantoin** and **fosfomycin**.[1][2] Nitrofurantoin works by damaging bacterial DNA via reactive intermediates — a mechanism not represented among the answer choices.[3] **Fosfomycin**, by contrast, **inhibits MurA** (UDP-N-acetylglucosamine enolpyruvyl transferase), the first committed step of **peptidoglycan (cell wall) synthesis**, corresponding to option A.[1][4] Beta-lactam antibiotics (e.g., cephalexin, pivmecillinam), which are also appropriate second-line alternatives for uncomplicated UTI, similarly inhibit cell wall synthesis by targeting penicillin-binding proteins.[2][5]

Why the other options are incorrect:

- **B. Binds D-ala D-ala** — This is the mechanism of **vancomycin**, which is not effective against gram-negative organisms and is not used for UTI.
- **C. Inhibits initiation complex** — This describes **aminoglycosides** (bind 30S ribosomal subunit), which are not first-line oral therapy for uncomplicated cystitis.

- **D. Inhibits sterol synthesis** — This describes **azole antifungals** (e.g., fluconazole), which target ergosterol synthesis in fungal cell membranes and are irrelevant to a bacterial UTI.

Would you like to explore the comparative efficacy and pharmacology of nitrofurantoin versus fosfomycin for uncomplicated UTI?

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Question 271

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?

A. Chronic airway inflammation
B. Bronchial hyperresponsiveness and obstruction
C. Pleural scarring
D. Excess collagen deposition in the extracellular matrix of the lung

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The correct answer is **D. Excess collagen deposition in the extracellular matrix of the lung**.

This patient's presentation — **digital clubbing**, progressive dyspnea, dry cough, and CT showing **clustered air spaces (honeycombing) with basal reticular opacities** — constitutes a **usual interstitial pneumonia (UIP) pattern**, the hallmark of **pulmonary fibrosis**.[1][2][3] The ATS/ERS guidelines define the UIP pattern as subpleural, basal-predominant honeycombing with reticular abnormalities.[1][4]

The underlying mechanism of pulmonary fibrosis is **excessive deposition of collagen and other extracellular matrix proteins** by activated fibroblasts and myofibroblasts, leading to progressive stiffening of the lung parenchyma, restrictive physiology, and impaired gas exchange.[5][6][7] This patient's use of **amiodarone** is notable, as it is a well-established cause of pulmonary fibrosis; amiodarone promotes TGF-β production from alveolar macrophages, stimulates fibroblast proliferation, and drives collagen secretion.[6][7][8] However, **idiopathic pulmonary fibrosis (IPF)** is also strongly in the differential given the patient's age, sex, and heavy smoking history.[2][3]

Why the other options are incorrect:

- **A. Chronic airway inflammation** — This describes the mechanism of COPD/chronic bronchitis. The CT findings here show a fibrotic pattern, not emphysema or airway-predominant disease.
- **B. Bronchial hyperresponsiveness and obstruction** — This is the mechanism of asthma, which does not produce honeycombing or basal reticular opacities.
- **C. Pleural scarring** — The imaging findings localize to the lung parenchyma (honeycombing, reticulation), not the pleura.

Would you like to explore monitoring and management strategies for amiodarone-induced pulmonary toxicity?

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Question 272

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?

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.

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The correct 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 0.9–9.7** for the odds ratio. Because this CI **crosses 1.0** (the null value for an odds ratio), the association between low educational status and young-age MI is **not statistically significant**.[1][2][3]

An odds ratio of 1.0 indicates no association between exposure and outcome. As noted in JAMA, "if the 95% CI for an odds ratio does not include 1.0, then the odds ratio is considered to be statistically significant at the 5% level".[1] Conversely, when the CI includes 1.0 — as it does here (0.9 to 9.7) — the result is not significant, meaning the null hypothesis (no association) cannot be rejected.[3][4]

While the point estimate of the OR is 2.1 (suggesting a possible increased odds), the CI indicates this finding could be due to chance. Therefore, **low education cannot be established as a risk factor** for MI in this study. A p-value is not needed to make this determination — the CI provides equivalent information about statistical significance.[5]

Option D is incorrect because the relationship between the CI and the null value (1.0) directly indicates significance without needing a separate p-value. Option C is incorrect because a factor cannot be designated a "risk factor" from a study that fails to demonstrate a statistically significant association.

Would you like to explore the differences between odds ratios and relative risk and when each should be used?

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Question 273

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?

A. Partial molar pregnancy
B. Neural tube defect
C. Trisomy 18
D. Trisomy 21

https://openevidence.com/ask/01d9ad91-2e69-4d60-8bac-f22f2c38ef18

The answer is **B. Neural tube defect**.

An **isolated elevation of maternal serum AFP at 3 times the median**, with normal β-hCG, estriol, and inhibin A, is the classic second-trimester quadruple screen pattern for an **open neural tube defect** (NTD). AFP is a glycoprotein produced by the fetal yolk sac and liver; in open NTDs (anencephaly, open spina bifida), AFP leaks from exposed fetal tissues into the amniotic fluid and then into maternal serum. MSAFP ≥2.5 MoM has a detection rate >95% for anencephaly and 65–80% for open spina bifida.[1]

The other answer choices are excluded by the analyte pattern:

- **Trisomy 21 (Down syndrome):** Associated with **elevated** hCG and inhibin A and **low** AFP and estriol — the opposite AFP direction from what is seen here.[2]
- **Trisomy 18 (Edwards syndrome):** All four markers tend to be **low** (low AFP, low hCG, low estriol), again inconsistent with a markedly elevated AFP.[2]
- **Partial molar pregnancy:** Characterized by **markedly elevated β-hCG**, which is normal in this case.

The isolated AFP elevation with otherwise normal analytes points specifically toward an open neural tube defect as the most likely explanation.

Would you like to explore the recommended next steps for evaluating an elevated MSAFP, including ultrasound and amniocentesis?

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Question 274

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?

A. ECG
B. V/Q scan
C. D-dimer
D. CT pulmonary angiogram with IV contrast

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The answer is **C. D-dimer**.

In patients with **low pretest probability for PE**, the standard diagnostic algorithm recommends **D-dimer testing as the initial step** to determine whether imaging is needed.[1][2] D-dimer has a high negative predictive value (~97–100%) when used within a validated low/intermediate pretest probability pathway, meaning a negative result (typically <500 ng/mL) can **safely exclude PE without chest imaging**.[1] The 2026 AHA/ACC guidelines, ACP best practice advice, and multiple international guidelines all endorse this stepwise approach: clinical probability assessment → D-dimer → imaging only if D-dimer is elevated.[2][3]

> "In patients with low or intermediate clinical probability, a D-dimer of less than 500 ng/mL is associated with a posttest probability of PE that is less than 1.85%. In these patients, PE can be excluded without chest imaging."

—Yonathan Freund, MD, PhD et al., Sorbonne Université, Improving Emergency Care FHU, Paris, France and other institutions. Acute Pulmonary Embolism. JAMA. October 04, 2022.

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Why not the other options:

- **ECG (A):** May show nonspecific findings (sinus tachycardia, right heart strain, S1Q3T3) but **lacks sensitivity and specificity** to rule in or rule out PE. It is part of the general ED workup but does not function as a rule-out test.
- **V/Q scan (B):** An imaging modality appropriate when CTPA is contraindicated (e.g., contrast allergy, renal insufficiency). It is a **downstream test** that follows a positive D-dimer, not the first step in a low-risk patient.[4]
- **CT pulmonary angiogram (D):** The **primary imaging modality** for diagnosing PE, but should be reserved for patients with elevated D-dimer or high pretest probability. Using CTPA as the first test in a low-risk patient exposes the patient to unnecessary radiation and IV contrast.[2][4]

Notably, in a truly low-risk patient, the **PERC rule** could potentially exclude PE without any testing at all — but PERC is not among the answer choices, and this patient's heart rate of 98/min approaches the PERC threshold (≥100), making D-dimer the appropriate next step.[1][3]

Would you like to explore how the Wells score criteria are applied to guide PE diagnostic decisions?

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Question 275

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?

A. Migraine headache
B. Temporal arteritis
C. Temporomandibular joint dysfunction
D. Tension headache

https://openevidence.com/ask/ab80b831-3dc1-49c2-813a-77ccdd2ae410

The answer is **C. Temporomandibular joint dysfunction (TMD)**.

This presentation is classic for TMD: a **young woman** with **dull bilateral pain over the temporal region**, **pain provoked by chewing and jaw movement**, and **tenderness over the mandibular and temporal regions** that worsens with opening and closing the mouth. TMD has a **peak incidence between ages 20 and 40** and is **1.5 to 2 times more common in women**.[1][2]

Key diagnostic features of TMD include pain in the jaw, TMJ, and muscles of mastication that is **triggered by jaw movements or palpation** of the joint or masticatory muscles, often described as **dull**, and localized to the **preauricular or temporal region**.[3][4] The association with chewing and reproducibility on exam with mouth opening/closing is highly characteristic.

Why the other options are incorrect:

- **A. Migraine headache** — Migraine is typically **throbbing, moderate-to-severe**, and aggravated by routine physical activity, with associated **nausea/vomiting, photophobia, and phonophobia**. None of these features are present, and the pain is not specifically triggered by jaw movement.[5]
- **B. Temporal arteritis** — Giant cell arteritis occurs almost exclusively in patients **over age 50**, with an elevated ESR and often visual symptoms. Although jaw claudication can occur,

it is fatigue-related ischemic pain of the masseter, not the reproducible tenderness with jaw movement seen here. This diagnosis is essentially excluded by age alone.

- **D. Tension headache** — Tension-type headache presents as **bilateral, pressure-like ("band-like") pain** of mild-to-moderate intensity, without significant exacerbation by jaw movement or focal tenderness over the mandibular region. It lacks the specific jaw-movement provocation seen in this case.[5]

Would you like to explore the evidence-based management options for TMD?

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Question 276

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?

A. Bladder tumor
B. Renal cell carcinoma
C. Beeturia
D. Urinary tract infection

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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. The most common presenting symptom of bladder cancer is **gross painless hematuria**, occurring in up to 85% of patients.[1][2] The risk of bladder cancer is approximately **16.5% in patients presenting with gross hematuria**, and in adults over age 40 with unexplained visible hematuria, malignancy — most commonly bladder cancer — must be ruled out.[3][4]

The American College of Physicians notes that **painless gross hematuria has a stronger association with cancer** than symptomatic hematuria, while symptomatic gross hematuria with flank pain is more characteristic of urinary stone disease.[5] In the DETECT 1 study of 3,556 adults with hematuria, 10% had cancers, with bladder cancer accounting for the majority (8% of all patients), particularly among **older men**.[4]

Why the other choices are less likely:

- **B. Renal cell carcinoma** — While RCC can cause painless hematuria, it is far less common than bladder cancer as a cause. In the DETECT 1 study, renal parenchymal cancer was found in only 1.0% of patients compared to 8.0% for bladder cancer. The classic triad of RCC (flank pain, hematuria, palpable mass) is present in a minority of cases, and the absence of CVA tenderness further lowers this probability.[4]
- **C. Beeturia** — Beet consumption can cause red-colored urine, but this is transient, not persistent over a month, and would be a diagnosis of exclusion.

- **D. Urinary tract infection** — UTI typically presents with **dysuria, frequency, and urgency**, which this patient explicitly lacks. Additionally, UTI is far more common in women than in men of this age.

Would you like to explore the recommended diagnostic workup for painless gross hematuria in this patient?

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Question 277

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?

A. Decreased glucose uptake by adipocytes
B. Decreased activity of hormone sensitive lipase
C. Decreased proteolysis
D. Increased lipoprotein lipase activity

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The answer is **A. Decreased glucose uptake by adipocytes**.

This patient presents with classic **diabetic ketoacidosis (DKA)** complicating new-onset **type 1 diabetes**: polyuria, polydipsia, weight loss, abdominal pain, vomiting, Kussmaul respirations, altered mental status, pH 7.19, and glucose 754 mg/dL.[1][2] The disease is characterized by **absolute insulin deficiency**.

Why A is correct

Without insulin, **GLUT4 transporters cannot translocate to the cell surface** of adipocytes (and skeletal muscle), so glucose uptake by these tissues is markedly reduced.[1][3] This is a direct and well-established consequence of insulin deficiency and contributes to the hyperglycemia seen in DKA.

Why the other options are incorrect

- **B – Decreased activity of hormone-sensitive lipase (HSL):** Insulin is a **key negative regulator of HSL**; when insulin is present, HSL is inhibited, promoting triglyceride storage. In insulin deficiency, HSL activity **increases**, driving lipolysis, free fatty acid release, and ketogenesis — the exact pathophysiology of DKA.[4][5][6]
- **C – Decreased proteolysis:** Insulin is anabolic and suppresses protein breakdown. Insulin withdrawal leads to **increased proteolysis**, as demonstrated by increased phenylalanine flux and protein oxidation in insulin-withdrawal studies.[7]
- **D – Increased lipoprotein lipase (LPL) activity:** Insulin **stimulates** LPL expression in adipose tissue. In insulin deficiency, LPL activity **decreases**, contributing to hypertriglyceridemia commonly seen in uncontrolled diabetes.[8]

Would you like to explore the management protocol for pediatric DKA, including fluid resuscitation and cerebral edema monitoring?

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Question 278

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?

A. Spironolactone
B. Eplerenone
C. Triamterene
D. Ethacrynic acid

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The answer is **B. Eplerenone**.

Eplerenone is a selective mineralocorticoid receptor antagonist that, unlike spironolactone, has **no significant activity at androgen or progesterone receptors**, making it the preferred choice when antiandrogenic side effects such as gynecomastia and impotence are a concern.[1][2][3]

Why not the other options:

- **A. Spironolactone** is a non-selective MRA that also blocks androgen and progesterone receptors, leading to a **gynecomastia incidence of ~7.9%** in men (OR 8.39 vs. placebo), compared with **~0.5% for eplerenone** (OR 0.77 vs. placebo). The patient's friend likely experienced these side effects on spironolactone.[2][4]
- **C. Triamterene** is a potassium-sparing diuretic that acts by blocking the epithelial sodium channel (ENaC) — it is **not an aldosterone receptor antagonist** and would not fulfill the physician's intent.
- **D. Ethacrynic acid** is a **loop diuretic**, not an aldosterone antagonist, and is irrelevant to the clinical scenario.

Eplerenone is less potent than spironolactone (approximately 50% of MR antagonist potency in vivo), typically requiring doses of **50 mg daily to 50 mg twice daily** for antihypertensive effect,

and has a shorter half-life necessitating twice-daily dosing.[1][2] However, its **superior tolerability profile** — specifically the absence of antiandrogenic effects — makes it the clear choice for this patient.

Would you like to explore the diagnostic workup for primary aldosteronism in resistant hypertension?

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Question 279

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?

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

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The answer is **B. Involuntary hospitalization after informing the parents**.

This adolescent presents with **active suicidal ideation with a specific plan** (using his father's firearm), **a defined timeline** (the upcoming weekend), **access to lethal means**, and **refusal of treatment** — all of which constitute **imminent risk** requiring immediate intervention.[1][2]

Why involuntary hospitalization is indicated:

- The AACAP Practice Parameter states that hospitalization is indicated when a child or adolescent's condition is unstable and behavior is unpredictable, particularly when there is an **inability to form an alliance with the clinician** and refusal to engage in care.[3]
- The AAP guidelines emphasize that when a patient is at **imminent risk and unwilling to engage in care**, emergency hospitalization is warranted, and confidentiality must be breached to protect the minor from harm.[4]

- Inpatient admission should be offered to patients with **specific plans for suicide who have the means to complete their plan**; if a patient refuses treatment, involuntary hospitalization may be required.[2]

- Because this patient is a minor (age 14), parental consent typically suffices for admission. However, the parents must be informed given the imminent danger, which also overrides the usual confidentiality protections afforded to adolescents.[4][5]

Why the other options are incorrect:

- **A (Agree to no treatment):** A minor with active suicidal ideation and a plan cannot autonomously refuse life-saving intervention. The physician has a duty to protect.

- **C (Reassurance):** Reassurance alone is dangerously insufficient for a patient expressing imminent suicidal intent with a specific plan and access to means.

- **D (Outpatient psychotherapy):** Outpatient treatment is appropriate for patients who deny current suicidal intent, have no plan or means, and have good social support. This patient has none of those protective features and has explicitly refused treatment.[2]

Would you like to explore evidence-based approaches to lethal means counseling regarding firearms in suicidal adolescents?

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Question 280

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?

A. Bacillary angiomatosis
B. Condylomata lata
C. Brucellosis
D. Bubonic plague

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The answer is **A. Bacillary angiomatosis**.

This presentation is classic for **cat scratch disease (CSD)** caused by ***Bartonella henselae***. The key features include exposure to animals at a shelter, **linear crusts on an erythematous base** (consistent with cat scratches), **regional lymphadenopathy** developing ~2 weeks post-inoculation, low-grade fever, and **necrotizing granulomas** on lymph node histopathology.[1][2][3]

B. henselae is also the causative organism of **bacillary angiomatosis (BA)**, a vascular proliferative disorder seen almost exclusively in **immunocompromised patients**, particularly those with advanced HIV/AIDS (typically CD4 <50 cells/mm³).[1][4] BA presents as red papules or subcutaneous nodules and can involve skin, bone, brain, and other organs.[1][5] Both *B. henselae* and *B. quintana* can cause BA, though the reservoirs differ — cat exposure for *B. henselae* and body louse infestation for *B. quintana*.[4][5]

The other options are caused by different organisms:

- **Condylomata lata** — *Treponema pallidum* (secondary syphilis)
- **Brucellosis** — *Brucella* species
- **Bubonic plague** — *Yersinia pestis*

Would you like to explore the antibiotic treatment recommendations for cat scratch disease in children?

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Question 281

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?

A. Bed bug bite
B. Molluscum contagiosum
C. Atopic dermatitis
D. Acute urticaria

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The answer is **B. Molluscum contagiosum**.

The presentation is classic: **2–3 mm dome-shaped papules with central umbilication** are the hallmark of molluscum contagiosum, a cutaneous infection caused by a poxvirus.[1][2] The lesions are characteristically **non-pruritic**, flesh-colored, and may extrude a creamy, grey-white material when squeezed.[1] The disease predominantly affects children, sexually active adults, and **immunocompromised individuals**.[1]

This patient's **IV drug use** places him at high risk for HIV, and the combination of **fatigue, malaise, and non-tender cervical lymphadenopathy** raises strong suspicion for underlying HIV infection. Molluscum contagiosum prevalence in HIV-positive individuals ranges from **5% to 18%**, and its presence can indicate advancing immunosuppression.[1][3] HIV testing should be a priority in this patient.

Why the other options are incorrect:

- **A. Bed bug bite** — These cause pruritic, erythematous papules or wheals, often in a linear pattern ("breakfast, lunch, dinner"). They lack central umbilication and dome-shaped morphology.
- **C. Atopic dermatitis** — Presents with pruritic, eczematous, erythematous patches/plaques, not discrete dome-shaped papules with umbilication.
- **D. Acute urticaria** — Characterized by evanescent, pruritic wheals (hives) that typically resolve within 24 hours. Persistent, non-pruritic, umbilicated papules are inconsistent with urticaria.

Would you like to explore the recommended workup and management of molluscum contagiosum in the setting of suspected HIV?

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Question 282

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?

A. Repression
B. Reaction formation
C. Denial
D. Displacement

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The correct answer is **B. Reaction formation**.

Reaction formation is a neurotic-level defense mechanism in which an individual manages an unacceptable impulse or desire by **converting it into its diametrically opposite behavior or expressed attitude**.[1][2] In this vignette, the politician harbors homosexual desires he finds threatening, and rather than acknowledging them, he adopts an exaggerated anti-gay public stance — the precise hallmark of reaction formation.

The other options are distinguishable as follows:

- **Repression (A):** The unconscious exclusion of threatening thoughts or feelings from awareness entirely. If repression alone were operating, the politician would simply be unaware of his desires without actively behaving in an opposite manner.[3]
- **Denial (C):** A refusal to acknowledge an external reality or internal experience — a more primitive defense involving **diminution of perception** rather than transformation into opposite behavior.[3]
- **Displacement (D):** Redirecting an emotion or impulse from its original target onto a **substitute target** (e.g., yelling at a spouse after a bad day at work). The politician is not redirecting his feelings to a different object; he is expressing the **opposite** of his feelings toward the same subject.[1]

The key distinguishing feature is the **transformation into the opposite**: the politician does not merely suppress awareness of his desires or redirect them — he actively and publicly champions

the antithesis of what he privately feels, which is the defining characteristic of reaction formation.[1][3]

Would you like to explore how defense mechanisms are hierarchically classified and their associations with psychopathology?

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Question 283

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?

A. Coagulopathy
B. Gynecomastia
C. Jaundice
D. Caput medusae

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B. Gynecomastia

Gynecomastia is the classic manifestation of hyperestrinism in cirrhosis. Enhanced peripheral conversion of androstenedione to estrone and estradiol, combined with reduced hepatic estradiol degradation, drives benign proliferation of glandular male breast tissue.[1] Reduced hepatic metabolism and clearance of androstenedione underlies this same group of findings — palmar erythema, spider nevi, decreased body hair, and testicular atrophy.[2] Elevated estrogen levels are further amplified by portosystemic shunting, and the resulting suppression of the hypothalamic-pituitary axis contributes to erectile dysfunction, oligospermia, testicular atrophy, and feminization.[3]

Why the other options are incorrect

- **Coagulopathy** — Reflects loss of hepatic synthetic function: reduced production of factors I, II, V, VII, IX, and X, with additional depletion of the vitamin K–dependent factors (II, VII, IX, X) from cholestasis. Factor VII depletes first given its short half-life, which is why the PT rises selectively.[2]
- **Jaundice** — Results from compromised hepatocyte excretory function and loss of functioning hepatocellular mass, becoming clinically apparent when serum bilirubin exceeds ~2 mg/dL.[1][2]

- **Caput medusae** — A purely hemodynamic consequence of portal hypertension, with recanalization of the umbilical vein shunting portal blood into abdominal wall veins radiating from the umbilicus.[1][4]

One nuance worth noting: while spider angiomata and palmar erythema are traditionally attributed to hyperestrogenemia, more recent work suggests some of these vascular findings may relate to increased VEGFA expression rather than impaired estrogen metabolism alone.[4] Gynecomastia remains the most directly estrogen-mediated of the listed signs.

Would you like to explore the workup of gynecomastia in cirrhotic men, including spironolactone as a contributing cause?

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Question 284

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?

A. Clear cell adenocarcinoma
B. Melanoma
C. Botryoid sarcoma
D. Verrucous carcinoma

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The answer is **A. Clear cell adenocarcinoma**.

The defining clinical clue is this patient's **in utero exposure to diethylstilbestrol (DES)**, which her mother received in the 1960s for recurrent miscarriages. DES exposure in utero is strongly and specifically associated with **clear cell adenocarcinoma (CCA) of the vagina and cervix**. DES-exposed women have a standardized incidence ratio approximately **40 times higher** for vaginal/cervical CCA compared with unexposed individuals.[1][2] The mechanism involves DES-mediated interference with normal differentiation and degeneration of müllerian epithelium in the fetal vagina, leading to persistent müllerian-derived cells (vaginal adenosis) that can undergo malignant transformation.[3]

The clinical presentation here — **postcoital bleeding, blood-tinged watery discharge, and a polypoid mass on the anterior vaginal wall** — is consistent with vaginal CCA. Although 80% of DES-associated CCA cases present between ages 15 and 31 (median age 19), a recognized **second peak** occurs around age 42, and the risk remains elevated into the 40s and beyond.[1][4][5]

Why the other options are incorrect:

- **Melanoma** — Primary vaginal melanoma is rare and has no association with DES exposure.

- **Botryoid sarcoma** (sarcoma botryoides/embryonal rhabdomyosarcoma) — This occurs almost exclusively in **children under age 5**, presenting as a grape-like vaginal mass. Age 47 effectively rules this out.
- **Verrucous carcinoma** — A well-differentiated variant of squamous cell carcinoma, not associated with DES exposure. It typically presents as a warty, fungating lesion rather than a polypoid mass.

Would you like to explore current screening recommendations for DES-exposed women as they age?

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Question 285

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?

A. Left anterior descending artery
B. Left circumflex artery
C. Left coronary artery
D. Right marginal artery

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The answer is **B. Left circumflex artery (LCx)**.

The combination of **ST elevation isolated to leads I and aVL** (lateral territory) with autopsy findings of **left atrial and posterior left ventricular ischemia** localizes the culprit to the LCx. The left atrial myocardium is **primarily supplied by branches of the proximal LCx**, and the LCx courses posteriorly in the atrioventricular groove between the left atrium and ventricle, supplying the lateral and posterolateral walls of the left ventricle.[1][2][3]

Why not the other options:

- **Left anterior descending (LAD):** Supplies the anterior wall, anterior septum, and apex. LAD occlusion produces ST elevation in **V1–V4** (with I and aVL only when proximal). The autopsy showed no anterior wall ischemia, and no precordial ST elevations were described.[4]

- **Left coronary artery (left main):** Occlusion would compromise both the LAD and LCx territories simultaneously, producing **extensive anterior and lateral** ischemia with ST elevation across V1–V4 plus I and aVL. The autopsy showed no anterior wall involvement, ruling this out.[5]
- **Right marginal artery:** A branch of the right coronary artery supplying the **right ventricular free wall** — it does not supply the left atrium or posterior left ventricle.[3]

The clinical picture — cardiogenic shock (hypotension, tachycardia, bilateral rales, diaphoresis) progressing to death — is consistent with a large LCx territory infarction with resultant acute heart failure. Notably, LCx occlusions are frequently **electrocardiographically occult** on standard 12-lead ECG because the posterior and lateral walls are relatively "silent" on standard leads.[6][7] In this case, the lateral ST elevation in I and aVL was the surface ECG manifestation, while posterior leads (V7–V9) would have further confirmed the posterior involvement.

Would you like to explore ECG criteria for distinguishing LCx from RCA occlusion in inferior myocardial infarction?

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Question 286

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?

A. Atrioventricular block
B. Mitral valve regurgitation
C. Penile squamous cell carcinoma
D. Thoracic aortic aneurysm

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The answer is **D. Thoracic aortic aneurysm**.

This vignette describes classic **tabes dorsalis**, a late manifestation of **tertiary syphilis**:

- **Painless penile ulcer** 20 years ago → primary syphilis (chancre) that went untreated
- **Argyll Robertson pupils** (accommodate but do not react to light) → pathognomonic for neurosyphilis
- **Lightning (lancinating) pains**, loss of distal sensation, absent patellar reflexes, and **sensory ataxia** with broad-based gait → posterior column and dorsal root degeneration[1][2]

A patient with one tertiary syphilis manifestation (neurosyphilis/tabes dorsalis) is at increased risk for other tertiary complications, most notably **cardiovascular syphilis**. Syphilitic aortitis preferentially involves the **ascending thoracic aorta** and can lead to aortic aneurysm formation, aortic valve insufficiency, and coronary ostial stenosis.[1][3][4] Cardiovascular syphilis develops 15–30 years after untreated infection and occurs in approximately 10% of patients with tertiary disease.[1][3]

Why the other options are incorrect:

- **A. Atrioventricular block** — Not a recognized complication of syphilitic aortitis; the conduction system is not a target of treponemal vascular inflammation.

- **B. Mitral valve regurgitation** — Syphilis classically affects the **aortic** valve (causing insufficiency through aortic root dilation), not the mitral valve.[1][5]
- **C. Penile squamous cell carcinoma** — The primary chancre of syphilis is not a premalignant lesion and does not predispose to squamous cell carcinoma (unlike HPV-related lesions).

Would you like to explore the diagnostic workup and treatment approach for neurosyphilis and cardiovascular syphilis?

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Question 287

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?

A. Primary biliary cirrhosis
B. Hemolytic anemia
C. Hepatitis A
D. Gilbert syndrome

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The answer is **A. Primary biliary cirrhosis** (now termed primary biliary cholangitis, PBC).

This presentation is classic for PBC. The diagnosis requires at least **two of three criteria**: (1) biochemical cholestasis with elevated ALP, (2) positive **anti-mitochondrial antibodies (AMA)**, and (3) histologic evidence of nonsuppurative destructive cholangitis.[1][2][3] This patient satisfies all three.

Key features pointing to PBC:

- **Demographics and symptoms**: PBC predominantly affects **women aged 40–70**, presenting with **pruritus and fatigue** — the hallmark symptoms.[2]
- **Serologic profile**: AMA is detectable in >90% of PBC patients with nearly 100% disease specificity, making it the **serologic hallmark** of the disease. Elevated immunoglobulins (particularly IgM) and cholesterol (including elevated HDL) are characteristic.[2][4][5]
- **Cholestatic biochemistry**: Elevated ALP, GGTP, and bilirubin reflect the cholestatic injury pattern.[6]

- **Histopathology**: Bile duct injury with **granuloma formation** corresponds to the "**florid duct lesion**" — focal duct obliteration with granuloma — which is considered **pathognomonic** for PBC. Cholestasis on biopsy indicates advanced disease.[2][7]

The other choices are excluded:

- **B. Hemolytic anemia** — would not produce AMA positivity, cholestatic liver enzymes, or bile duct injury on biopsy.
- **C. Hepatitis A** — ruled out by the absence of antiviral antibodies.
- **D. Gilbert syndrome** — causes isolated unconjugated hyperbilirubinemia without cholestasis, hepatosplenomegaly, or AMA.

Would you like to explore first-line treatment and response assessment in primary biliary cholangitis?

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Question 288

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?

A. Acetaminophen
B. Dantrolene
C. Intubation
D. Supportive therapy

https://openevidence.com/ask/b75e2af9-57e4-4b70-bb5b-3b5ce8e33ac1

The answer is **B. Dantrolene**.

This scenario describes a young man at a college party with likely **recreational drug-induced hyperthermia** (most likely MDMA/sympathomimetic use) presenting with the classic triad of **hyperthermia, muscle rigidity, and altered mental status**. The initial management with IV fluids, lorazepam, and external cooling has failed to control symptoms, making escalation necessary.

Dantrolene, a direct-acting skeletal muscle relaxant that inhibits calcium release from the sarcoplasmic reticulum, reduces muscle rigidity and thereby decreases muscular thermogenesis — the primary driver of hyperthermia in this setting.[1][2][3] It is a well-established treatment for **refractory hyperthermia with muscle rigidity** when benzodiazepines are insufficient, with particular use in NMS and drug-induced hyperthermic crises.[1][4][5] A meta-analysis of MDMA-induced hyperthermia cases found dantrolene use was associated with improved survival, though data remain limited to case reports and small series.[6]

Why not the other options:

- **A. Acetaminophen** — Antipyretics have no role here. The hyperthermia results from excessive muscular activity, not an alteration in the hypothalamic temperature set point. As noted in a key NEJM review of serotonin syndrome: "There is no role for antipyretic agents…the increase in body temperature is due to muscular activity, not an alteration in the hypothalamic temperature set point".[7]
- **C. Intubation** — Intubation with neuromuscular paralysis (using a nondepolarizing agent such as vecuronium) is reserved for **severe, refractory cases** with temperatures exceeding 41.1°C (106°F) where other measures have failed. This patient's temperature is 39.4°C and oxygenation is maintained, making dantrolene the appropriate next escalation step before proceeding to paralysis and intubation.[7]
- **D. Supportive therapy** — Already being provided (IV fluids, cooling blanket, lorazepam) and has proven insufficient. Continued supportive therapy alone without escalation risks clinical deterioration.

An important clinical nuance: if hyperthermia and rigidity remain refractory to dantrolene as well, the next escalation would be intubation with nondepolarizing neuromuscular blockade (succinylcholine should be avoided due to hyperkalemia risk from rhabdomyolysis).[7] Monitoring should include CK, electrolytes, renal function, coagulation studies, and urine output to detect complications such as rhabdomyolysis and DIC.

Would you like to explore the key differences in management between serotonin syndrome and neuroleptic malignant syndrome?

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Question 289

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?

A. Administration of oral ketorolac
B. Perform joint aspiration
C. Open reduction of the tuberosity
D. Application of a lower leg cast

https://openevidence.com/ask/e10f99fe-e919-423d-a91f-bae56137e350

The answer is **A. Administration of oral ketorolac**.

This presentation is classic for **Osgood-Schlatter disease (OSD)** — a traction apophysitis of the tibial tuberosity seen in active adolescents. The key features include an adolescent male in a high-impact sport (gymnastics), anterior knee pain worsened by activity, tenderness and swelling at the tibial tuberosity, pain with resisted knee extension, and radiographic fragmentation of the tibial tuberosity.[1][2]

Conservative management is the standard of care for OSD, consisting of **activity modification, ice, NSAIDs, and physical therapy**.[1][3] Ketorolac is an NSAID and is appropriate for short-term pain relief in this setting. The American College of Sports Medicine consensus statement recommends treating apophysitis nonoperatively with rest, ice, and NSAIDs.[3] Conservative management is successful in over 90% of patients.[2]

The other options are not appropriate:

- **Joint aspiration (B):** OSD is an extra-articular process involving the tibial tuberosity apophysis, not a joint effusion or septic arthritis. Aspiration is unnecessary and would not be therapeutic.

- **Open reduction (C):** Surgery is rarely indicated for OSD and is reserved only for severe, debilitating pain that persists after physeal closure, typically involving ossicle excision.[1][2]
- **Lower leg cast (D):** Immobilization is not standard first-line management. Activity modification and relative rest are preferred over casting, which would be unnecessarily restrictive for this self-limiting condition.[1][4]

Would you like to explore the indications for surgical intervention in refractory Osgood-Schlatter disease?

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Question 290

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?

A. Pulmonary embolism
B. Subphrenic abscess
C. Pneumonia
D. Pneumothorax

https://openevidence.com/ask/b9507575-2b18-4c60-a804-f09c924ee381

The answer is **C. Pneumonia**.

This presentation is classic for **postoperative pneumonia** following upper abdominal surgery. Several features converge to support this diagnosis:

Risk factors strongly predisposing to postoperative pneumonia:

- **Open cholecystectomy** — patients undergoing open cholecystectomy have a **1.59 times higher risk** of postoperative pneumonia compared to laparoscopic cholecystectomy, due to greater impairment of diaphragmatic function and restrictive pulmonary dysfunction from the upper abdominal incision.[1]
- **Obesity** (BMI ≥27) and **smoking history** are both independently associated with postoperative pulmonary complications after abdominal surgery (adjusted OR 2.82 and 2.27, respectively).[2]
- **Upper abdominal incision site** is itself an independent risk factor (adjusted OR 2.30).[2]

Clinical features consistent with pneumonia:

- **Productive cough**, **fever (39°C)**, **chills**, and **inspiratory crackles at the right lung base** form the hallmark presentation. The right lower lobe is the most common site of postoperative pneumonia after upper abdominal surgery due to basilar atelectasis progressing to infection.[3]
- The **timing (postoperative day 3)** is typical for postoperative pneumonia development.

Why not the other options:

- **Pulmonary embolism** — while this patient has post-surgical risk, PE typically presents with **sudden-onset dyspnea** and pleuritic chest pain but generally lacks a **productive cough** and **inspiratory crackles** localized to one lung base. PE remains in the differential but is less likely given this presentation.[4][5]
- **Subphrenic abscess** — typically occurs **later** (5–10 days postoperatively) and would be expected to cause **abdominal tenderness** or referred shoulder pain; the abdomen here is soft and nontender.
- **Pneumothorax** — would present with **decreased or absent breath sounds**, not inspiratory crackles, and is not a typical post-cholecystectomy complication.

Would you like to explore empiric antibiotic management for postoperative pneumonia?

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Question 291

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?

A. WBC casts in the urine
B. Selective albuminuria
C. Negatively birefringent crystals in the urine
D. Bence-Jones proteinuria

https://openevidence.com/ask/2f95f073-15e3-4393-98ca-35c62af24c61

The 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 children >1 year of age).[1] The key pathophysiologic clue is the **loss of polyanions** (heparan sulfate proteoglycans) in the glomerular basement membrane (GBM), which disrupts the **charge-selective barrier** while leaving the size-selective barrier intact.[2]

As described in the NEJM:

Because the **size barrier remains intact** but the **charge barrier is lost**, only negatively charged, relatively small proteins like **albumin** (which is normally repelled by the GBM polyanions) pass through in large amounts — producing **selective proteinuria**.[3][4][5] Studies of dextran clearance in MCD confirmed that pore size is unchanged (or even reduced), and an approximately 50% reduction in fixed negative charges accounts for the selective albuminuria.[4]

Why the other options are incorrect:

- **A. WBC casts** — Indicate pyelonephritis or interstitial nephritis, not nephrotic syndrome.
- **C. Negatively birefringent crystals** — Indicate monosodium urate crystals (gout), unrelated to glomerular disease.
- **D. Bence-Jones proteinuria** — Represents immunoglobulin light chains in the urine, seen in multiple myeloma — not a charge-barrier defect and exceedingly unlikely in an 11-year-old.

Would you like to explore the recommended steroid regimen for treating minimal change disease in children?

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Question 292

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?

A. Ectopic pregnancy
B. Ovarian torsion
C. Pelvic inflammatory disease
D. Ruptured ovarian cyst

https://openevidence.com/ask/81b5c2e6-4e9c-4f62-a6d2-e675db525137

The correct answer is **D. Ruptured ovarian cyst**.

This presentation — **acute unilateral pelvic pain triggered by vigorous physical activity**, left adnexal tenderness, and a **large amount of free fluid in the rectouterine pouch** (pouch of Douglas) on ultrasound — is classic for a ruptured ovarian cyst.[1][2] Physical activity and trauma are well-recognized precipitants of cyst rupture, and the free pelvic fluid represents hemorrhagic or follicular fluid released into the peritoneal cavity.[1]

Why the other options are less likely:

- **Ectopic pregnancy (A):** The patient's **last menstrual period ended just 2 days ago**, making a pregnancy with a ruptured ectopic exceedingly unlikely in this clinical context. That said, beta-hCG testing remains mandatory in any reproductive-age woman with acute pelvic pain and free fluid, as ectopic pregnancy can cause fatal hemoperitoneum.[3]
- **Ovarian torsion (B):** Torsion typically presents with **nausea/vomiting** and a unilaterally **enlarged, edematous ovary** with peripherally displaced follicles and often a whirlpool sign

on ultrasound. Doppler imaging was performed here and the only reported finding was free fluid — the absence of characteristic morphologic and vascular findings makes torsion less likely, though Doppler flow alone cannot definitively exclude it.[4][5][6][7]

- **Pelvic inflammatory disease (C):** PID typically has a more **insidious onset** with bilateral tenderness, cervical motion tenderness, and often purulent vaginal discharge. The **clear vaginal mucous**, abrupt onset during exercise, and unilateral free fluid pattern are not consistent with PID. The history of chlamydia increases PID risk but does not fit the acute presentation here.

Would you like to explore indications for surgical versus conservative management of ruptured ovarian cysts?

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Question 293

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?

A. Fluoxetine
B. Lamotrigine
C. Buspirone
D. Methylphenidate

https://openevidence.com/ask/1b15e094-86dd-4809-9063-62721b8db151

The answer is **A. Fluoxetine**.

This patient presents with classic **hoarding disorder**: persistent difficulty discarding possessions regardless of their value, resulting in clutter that compromises the use of living spaces, with associated distress and functional impairment. Onset in adolescence and a chronic course are typical.[1]

Why fluoxetine? After an inadequate response to CBT — the first-line treatment for hoarding disorder — the appropriate next step is the addition of an **SSRI**.[1] A meta-analysis of pharmacotherapy for pathological hoarding found that more than half of patients treated with serotonin-reuptake inhibitors responded (ER = 0.58, 95% CI 0.37–0.76).[2] An NEJM clinical practice review on hoarding disorder recommended that an SSRI "may also be helpful" in conjunction with or following CBT, and that the combination of pharmacotherapy and CBT is likely more effective than either alone.[1][3] Fluoxetine is a well-established SSRI used across the obsessive-compulsive spectrum.

Why not the other options?

- **Lamotrigine (B):** A mood stabilizer/anticonvulsant with no established role in hoarding disorder.
- **Buspirone (C):** A 5-HT1A partial agonist used for generalized anxiety disorder; it lacks evidence for hoarding disorder.
- **Methylphenidate (D):** While there is some preliminary (low-level) evidence for stimulants in hoarding disorder based on hypothesized overlap with ADHD neurobiology, this remains investigational with very small uncontrolled studies, and SSRIs are the standard pharmacologic recommendation.[4]

Would you like to explore optimal SSRI dosing strategies and expected timelines for treatment response in hoarding disorder?

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Question 294

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?

A. Brief psychotic disorder
B. Adjustment disorder
C. Schizophrenia
D. Bereavement

https://openevidence.com/ask/f5c2e58f-17b1-4099-86a9-f120c38b7625

The answer is **A. Brief psychotic disorder**.

This presentation is classic for **brief psychotic disorder with marked stressor** (historically termed "brief reactive psychosis"). The key diagnostic features supporting this diagnosis are:

- **Frank psychotic symptoms**: The patient is experiencing **auditory hallucinations** — specifically, voices having conversations about her (third-person auditory hallucinations) and command hallucinations urging self-harm. These are unequivocal positive psychotic symptoms.[1]
- **Clear precipitating stressor**: Symptom onset directly followed her father's death 1 week ago. The DSM-5 specifier "with marked stressor(s)" applies when symptoms occur in response to events that would be markedly stressful to almost anyone.[1]
- **Duration criteria met**: Symptoms have been present for ~1 week, satisfying the requirement of **at least 1 day but less than 1 month**.[1][2]

- **Medical and substance etiologies excluded**: Normal CMP, CBC, TSH, and negative urine toxicology appropriately rule out organic and substance-induced causes.[1]

Why not the other options:

- **B. Adjustment disorder** — Adjustment disorder involves emotional or behavioral symptoms (depressed mood, anxiety, conduct disturbance) disproportionate to a stressor, but **does not include frank psychotic symptoms** such as formed auditory hallucinations. The presence of true hallucinations elevates this beyond adjustment disorder.[1]
- **C. Schizophrenia** — Schizophrenia requires **continuous signs of disturbance for at least 6 months**, including at least 1 month of active-phase symptoms. With only 1 week of symptoms, this diagnosis cannot be made. If symptoms persisted beyond 1 month but less than 6 months, schizophreniform disorder would be considered instead.[1][3]
- **D. Bereavement** — While normal grief can occasionally include brief perceptual experiences (e.g., transiently hearing the deceased's voice), **sustained third-person auditory hallucinations with command features urging suicide are not part of normal bereavement**. The nature and severity of these psychotic symptoms clearly exceed what is attributable to uncomplicated grief.[1]

Notably, although brief psychotic disorder by definition remits within 1 month, **more than 50% of individuals experience a relapse**, and in less than half of cases the diagnosis remains stable long-term — some eventually receive a diagnosis of a schizophrenia spectrum disorder.[1][4] This patient warrants close psychiatric follow-up and safety assessment given the command hallucinations with suicidal content.

Has this patient been assessed for active suicidal ideation or plan, and has a safety plan been established given the command auditory hallucinations?

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Question 295

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?

A. Inappropriate chest tube placement
B. Spontaneous pneumothorax
C. Tension pneumothorax
D. Tracheobronchial rupture

https://openevidence.com/ask/8ab169c9-cd1c-498b-8cbb-563637e4f9e9

The correct answer is **D. Tracheobronchial rupture**.

The combination of a **high-energy blunt mechanism** (unrestrained driver in a head-on collision), **subcutaneous emphysema**, and — most critically — a **recurrent pneumothorax despite a properly positioned chest tube** is the classic presentation of tracheobronchial injury.[1][2] In this scenario, the chest tube initially evacuates the pleural air, but a continuous air leak from the disrupted airway causes reaccumulation that the tube cannot keep pace with. As described in a systematic review by Boutros et al., patients with post-traumatic tracheobronchial injuries "often present with massive subcutaneous emphysema and intractable pneumothorax".[2]

Why the other options are less likely:

- **A. Inappropriate chest tube placement** — The initial chest radiograph confirmed proper tube location and full resolution of the pneumothorax, making malposition an unlikely cause of recurrence.
- **B. Spontaneous pneumothorax** — A spontaneous pneumothorax would not explain the clinical picture in a young trauma patient with subcutaneous emphysema and a high-energy mechanism.

- **C. Tension pneumothorax** — While tension pneumothorax can occur in this setting, a functioning chest tube should decompress any simple tension physiology. Recurrence of pneumothorax with a patent chest tube in place points to a structural airway injury rather than tension alone.

Bronchoscopy is the diagnostic gold standard for confirming tracheobronchial injury, with fiberoptic bronchoscopy achieving approximately 90% sensitivity per the WSES-AAST thoracic trauma guidelines.[3] Early diagnosis is critical, as delayed recognition increases postoperative complications.[4]

Would you like to explore the surgical management and repair strategies for tracheobronchial injuries?

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Question 296

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?

A. Kawasaki disease
B. Rheumatic fever
C. Infective endocarditis
D. Cardiac tamponade

https://openevidence.com/ask/c3c19a54-0acc-4196-80f1-24f4f3165ac2

The answer is **D. Cardiac tamponade**.

This presentation is classic for **cardiac tamponade complicating acute viral pericarditis**. The 5-day prodrome of cough, fever, and malaise suggests a viral etiology, and the pleuritic chest pain with diffuse ST-segment elevation on ECG confirms pericarditis. The hemodynamic compromise and specific physical/ECG findings point to tamponade as the complication.

Beck's triad is present: **hypotension** (85/45 mmHg), **jugular venous distention** (distended neck veins), and **muffled heart sounds** — the hallmark clinical findings of cardiac tamponade.[1][2] Tachycardia is the most sensitive clinical sign, and it is present here (125/min).[1]

ECG findings strongly corroborate the diagnosis:

- **Diffuse ST-segment elevation** — consistent with underlying acute pericarditis
- **Low-voltage QRS complexes** — caused by the insulating effect of pericardial fluid between the heart and chest wall; associated with large effusions and tamponade (OR 4.7 for tamponade)[3][4]

- **Fluctuating R-wave amplitude** — this describes **electrical alternans**, caused by the heart swinging within a large pericardial effusion. In patients with large pericardial effusion, the positive predictive value of electrical alternans for tamponade is **95%**. Electrical alternans associated with pericardial effusion is strongly suggestive of impending or established cardiac tamponade.[3][5]

Why not the other choices:

- **Kawasaki disease (A):** Occurs in children, typically <5 years old; does not present this way in adults.
- **Rheumatic fever (B):** Occurs weeks after streptococcal pharyngitis in children/adolescents; pancarditis can occur but tamponade physiology with this ECG pattern is not the expected presentation.
- **Infective endocarditis (C):** Presents with valvular vegetations, embolic phenomena, and new murmurs — not with diffuse ST elevation, electrical alternans, or muffled heart sounds.

Would you like to explore the emergent management of cardiac tamponade, including pericardiocentesis technique?

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Question 297

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?

A. Support pessary
B. Space-filling pessary
C. Posterior colporrhaphy
D. Sacral colpopexy

https://openevidence.com/ask/57e5b332-3ad0-473c-87ad-9e5012d3e651

The answer is **A. Support pessary**.

This patient has **Stage II pelvic organ prolapse (POP)** based on the POP-Q staging system — at rest the cervix is halfway to the introitus, and on Valsalva it descends to the hymenal plane (leading edge between −1 and +1 cm relative to the hymen).[1] The sensation of a vaginal foreign body worsening on standing is the classic **bulge symptom** of POP.[2]

Why a support pessary is the most reasonable option:

- **Nonsurgical treatment should be offered to all symptomatic POP patients.** The ACOG/AUGS Practice Bulletin recommends that women considering treatment for POP should be offered a **vaginal pessary as an alternative to surgery**. A **ring pessary (support type)** is the most commonly used and the first to be tried.[1][3][4][5]
- **Stage II prolapse responds well to support pessaries.** In one standard fitting protocol, ring pessaries were successfully retained in **100% of Stage II** prolapse cases, compared with 71%

for Stage III. Space-filling pessaries (Gellhorn, donut, cube) are typically reserved for when a support pessary fails or for more advanced stages.[1][3][5]

- **The patient is sexually active**, which further favors a support pessary. Ring pessaries allow continued vaginal intercourse, whereas space-filling pessaries such as the Gellhorn generally do not.[4][5]

Why the other options are less appropriate:

- **B. Space-filling pessary** — Second-line after a support pessary fails; less compatible with sexual activity.[5]
- **C. Posterior colporrhaphy** — A surgical repair of the **posterior vaginal wall** (rectocele), which does not address the **apical/uterine descent** described here.
- **D. Sacral colpopexy** — A major surgical procedure for apical vault prolapse, disproportionate for uncomplicated Stage II uterine prolapse without failed conservative management.[6]

Would you like to explore the management of pessary complications, including erosion and expulsion?

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Question 298

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?

A. Broad ligament
B. Ovarian ligament
C. Cardinal ligament
D. Infundibulopelvic ligament

https://openevidence.com/ask/2b4051ea-6922-4553-b4cf-97cd7d92ce5d

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The answer is **D. Infundibulopelvic ligament**.

This presentation — sudden-onset severe pain, a large ovarian cyst acting as a lead point, and **absent ovarian venous flow with preserved arterial flow** on Doppler — is classic for **ovarian torsion** with partial vascular compromise.[1][2] The **infundibulopelvic ligament** (suspensory ligament of the ovary) is the structure involved because it is the ligament that transmits the **ovarian artery and ovarian vein** from the pelvic sidewall to the ovary.[3]

Why venous flow is lost first

In ovarian torsion, the ovary twists on its ligamentous supports, and **venous and lymphatic flow are compromised before arterial flow** because veins have thinner, more compressible walls.[4][5] The higher-pressure arterial supply is maintained until later stages. This pathophysiology directly explains the Doppler findings here: detectable arterial flow but absent venous flow. Per the Auslender classification, this corresponds to **Class 2 torsion** (arterial flow present, no venous flow), which requires **surgical intervention**.[6] Notably, absent or abnormal ovarian venous flow had **100% sensitivity** for adnexal torsion in one study, and was the only abnormal ultrasound finding in a subset of cases with early torsion.[7]

Why the other ligaments are incorrect

- **Broad ligament (A):** A peritoneal fold draping over the uterus, tubes, and ovaries; it does not directly transmit the main ovarian vessels.
- **Ovarian ligament (B):** Connects the ovary to the uterus; contains only small vessels, not the main ovarian artery and vein.
- **Cardinal ligament (C):** Supports the cervix/upper vagina and contains the uterine artery; unrelated to the ovarian vascular pedicle.

Would you like to explore the ultrasound features and classification systems used to grade the severity of ovarian torsion?

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Question 299

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?

A. Ringed sideroblasts
B. Teardrop cells
C. Smudge cells
D. Hypergammaglobulinemia

https://openevidence.com/ask/90f48205-44ad-4c60-b62c-89ef7fa755a6

The answer is **C. Smudge cells**.

This presentation — an **asymptomatic elderly patient with nontender lymphadenopathy, splenomegaly, and mild leukocytosis** — is classic for **chronic lymphocytic leukemia (CLL)**. The majority of CLL patients are asymptomatic at diagnosis, with the disease often discovered incidentally.[1] Lymphadenopathy is the second most common clinical presentation, and approximately 20–50% of symptomatic patients present with hepatosplenomegaly.[1]

Smudge cells (Gumprecht nuclear shadows), which are fragile lymphocyte remnants created during peripheral blood smear preparation, are a **pathognomonic morphologic feature** of CLL.[2][3][4] As described in a JAMA review:

> "The characteristic presence of smudge cells that result from lymphocyte debris as the peripheral smear is being prepared has been a pathognomonic feature of CLL."
>
> —Chadi Nabhan, MD et al., Section of Hematology and Oncology, Department of Medicine, The University of Chicago Medicine, Chicago, Illinois and other institutions. Chronic Lymphocytic Leukemia. JAMA. December 03, 2014.
>
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Why the other options are incorrect:

- **A. Ringed sideroblasts** — characteristic of myelodysplastic syndrome with ring sideroblasts (MDS-RS), not CLL.

- **B. Teardrop cells** (dacrocytes) — associated with myelofibrosis and other myeloproliferative disorders involving marrow fibrosis.
- **D. Hypergammaglobulinemia** — CLL causes the opposite: progressive **hypogammaglobulinemia** is a well-recognized complication, contributing to infection susceptibility. Hypergammaglobulinemia would be more suggestive of a plasma cell dyscrasia or chronic inflammatory condition.[5]

Would you like to explore current first-line treatment options for CLL and indications for initiating therapy?

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Question 300

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?

A. Candida albicans
B. Neisseria gonorrhoeae
C. Chlamydia trachomatis
D. Haemophilus influenzae

https://openevidence.com/ask/09b0cff5-b5d4-4604-892e-74d6e1565ce0

The answer is **C. Chlamydia trachomatis**.

This presentation — **positive pregnancy test, delayed menses, severe abdominal pain, scant vaginal bleeding, tachycardia, and hypotension with abdominal distension** — is classic for a **ruptured ectopic pregnancy** with hemoperitoneum. The critical risk factor is her history of **untreated pelvic inflammatory disease (PID)**, which causes fallopian tube scarring and predisposes to ectopic implantation.

Why Chlamydia trachomatis?

- **C. trachomatis is the most common pathogen** identified in PID; in one treatment trial it was the most frequently isolated organism (found in 23% of women). Reproductive sequelae of chlamydial PID — infertility, ectopic pregnancy, and chronic pelvic pain — result from **fallopian tube scarring** following upper genital tract infection.[1][2]
- **Nearly 10% of first pregnancies after PID are ectopic**. A meta-analysis of 25 studies (11,960 patients) demonstrated an **OR of 3.03** (95% CI 2.37–3.89) for ectopic pregnancy following C. trachomatis infection. A long-term prospective cohort confirmed an adjusted HR of **1.84** (95% CI 1.14–2.95) for ectopic pregnancy in chlamydia-positive versus chlamydia-negative women.[1][3][4]

- C. trachomatis infection is characteristically **subclinical or mildly symptomatic**, making it more likely to go untreated (as in this patient's case), thereby increasing the risk of chronic tubal damage.[1][5]

Why not the other options?

- **Neisseria gonorrhoeae** (B) also causes PID and ectopic pregnancy, but it typically presents with more acute, symptomatic infection and is less commonly the sole pathogen. Among the answer choices, chlamydia is the **more common cause** of PID and the organism most strongly linked epidemiologically to ectopic pregnancy.[1][6]
- **Candida albicans** (A) causes vulvovaginal candidiasis, not PID or tubal damage.
- **Haemophilus influenzae** (D) is a respiratory pathogen and not a significant cause of PID.

Would you like to explore the emergency management of ruptured ectopic pregnancy in hemodynamically unstable patients?

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Question 301

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?

A. Base excision repair
B. Nucleotide excision repair
C. Mismatch repair
D. Non-homologous end joining

https://openevidence.com/ask/208ef722-f50d-452b-833f-d17b529cd866

The answer is **C. Mismatch repair**. This patient's presentation — early-onset colorectal cancer (age 42) with a strong paternal family history of **colorectal, ovarian, and pancreatic cancers** — is classic for **Lynch syndrome** (hereditary nonpolyposis colorectal cancer, HNPCC), which is caused by germline pathogenic variants in **DNA mismatch repair (MMR) genes** (MLH1, MSH2, MSH6, PMS2, or EPCAM).[1][2][3]

Several features point specifically to Lynch syndrome:

- **Young age at CRC diagnosis**: The estimated average age of colorectal cancer presentation in Lynch syndrome is approximately 44 years, consistent with this patient's age of 42.[4]
- **Right-sided colon cancer**: Lynch syndrome-associated CRCs have a predilection for the **proximal colon** (proximal to the splenic flexure), matching the ascending colon location here.[5]
- **Autosomal dominant pattern of Lynch-associated cancers**: Colorectal cancer in his father and paternal uncle, ovarian cancer in his paternal grandmother, and pancreatic cancer in

his paternal uncle are all well-established Lynch syndrome-associated malignancies.[1][6][7]

- **Iron deficiency anemia** (hemoglobin 9.1 g/dL, conjunctival pallor, hemoccult-positive stool) from chronic occult blood loss from the tumor.

Why not the other answers?

- **Base excision repair (A)**: Defects in base excision repair (e.g., biallelic MUTYH mutations) cause MUTYH-associated polyposis, an autosomal recessive condition characterized by numerous adenomatous polyps — not the pattern seen here.
- **Nucleotide excision repair (B)**: Deficiency leads to xeroderma pigmentosum, a skin photosensitivity and skin cancer syndrome, not hereditary CRC.
- **Non-homologous end joining (D)**: Defects in this double-strand break repair pathway are associated with radiosensitivity syndromes, not hereditary colorectal cancer syndromes.

Lynch syndrome results from loss of MMR function, which leads to the accumulation of replication errors — particularly at microsatellite sequences — producing the hallmark **microsatellite instability (MSI-H)** phenotype that drives tumorigenesis.[3][8]

Would you like to explore the recommended surveillance and risk-reduction strategies for Lynch syndrome?

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Question 302

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?

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

https://openevidence.com/ask/9632fba6-14d6-4469-ae7a-66d2ecb40c14

B. Prevent excess anterior translation of the tibia relative to the femur.

The presentation — non-contact pivoting injury with an audible "pop," rapid hemarthrosis within hours, subjective instability, and positive Lachman and anterior drawer tests — is classic for an **anterior cruciate ligament (ACL) tear**.[1][2][3] The ACL runs from the posteromedial aspect of the lateral femoral condyle to the anterior intercondylar tibia, and its **primary function is restraining anterior translation of the tibia relative to the femur**; it also provides secondary restraint to internal rotation and to varus/valgus angulation near full extension.[2][4][5]

Why the other options are wrong

- **A (posterior translation)** — This is the **posterior cruciate ligament**, tested by the posterior drawer and sag sign. PCL injury typically results from a direct blow to the anterior proximal tibia with the knee flexed (dashboard mechanism), not a pivoting non-contact injury.[6]
- **C (resist valgus force)** — This is the **medial collateral ligament**, assessed by valgus stress testing at 0° and 30°.
- **D (cushion between lateral tibial and femoral condyles)** — This describes the **lateral meniscus**. Meniscal tears produce joint-line tenderness, mechanical locking/catching, and positive McMurray/Thessaly testing; effusion typically develops more slowly over 24–48

hours rather than the rapid hemarthrosis seen here. Notably, the lateral meniscus is concurrently torn in a substantial fraction of acute ACL injuries.[7]

Clinical pearls relevant to the vignette

- Ability to bear weight does not exclude ACL rupture; the giving-way sensation reflects rotatory instability rather than pain.[3]
- Diagnostic accuracy: the Lachman test outperforms the anterior drawer in the acute office setting (Lachman sensitivity 0.81, specificity 0.81 vs. anterior drawer sensitivity 0.38, specificity 0.81 for acute complete rupture), largely because hamstring guarding and effusion limit 90° flexion positioning. A recent bivariate meta-analysis found comparable pooled accuracy across tests and suggests the Lachman has historically been overestimated.[8][9]
- Combining a pivoting mechanism, immediate effusion, and a positive Lachman yields an LR+ of 17.5 for complete ACL tear.[10]
- An acute traumatic hemarthrosis warrants radiographs to exclude fracture (including Segond fracture and tibial eminence avulsion), followed by **MRI**, which has ~97% sensitivity and ~100% specificity for ACL injury and identifies concomitant meniscal, chondral, and collateral ligament pathology.[1]

Would you like to explore surgical versus conservative management and optimal timing of ACL reconstruction in a young competitive athlete?

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Question 303

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?

A. Delusion of pregnancy
B. Pseudocyesis
C. Pregnancy
D. Incomplete abortion

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The answer is **B. Pseudocyesis**.

Pseudocyesis (false pregnancy) is defined as a **false belief of being pregnant accompanied by objective physical signs and symptoms of pregnancy**, in the absence of a confirmed pregnancy.[1][2] This patient presents with the hallmark features: breast tenderness, nausea, weight gain, abdominal enlargement, and urinary frequency — all mimicking pregnancy — yet has a **negative β-hCG and normal transvaginal ultrasound**, definitively excluding true pregnancy. The strong psychosocial context (actively trying to conceive after stopping oral contraceptives) is a classic predisposing factor.[1][3]

Why the other options are incorrect:

- **A. Delusion of pregnancy** — This is a **fixed false belief of pregnancy without accompanying physical signs or symptoms**. This patient has multiple objective physical findings (abdominal enlargement, breast tenderness), which distinguishes pseudocyesis from a pure delusion.[1][4]

- **C. Pregnancy** — Excluded by a negative urine β-hCG and normal transvaginal ultrasound. Even very early pregnancies would produce detectable β-hCG levels by the time physical signs develop.
- **D. Incomplete abortion** — Would require a prior confirmed pregnancy with retained products of conception; β-hCG would still be detectable, and ultrasound would show retained tissue. Neither finding is present here.

Per the DSM-5, pseudocyesis is classified under "**other specified somatic symptom and related disorder**" and involves neuroendocrine mechanisms that can produce genuine physiological changes such as amenorrhea, galactorrhea, abdominal distension, and even apparent fetal movements.[2][5]

Would you like to discuss the recommended management approach for pseudocyesis, including how to sensitively disclose the diagnosis and whether psychiatric referral is indicated?

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Question 304

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?

A. Consumption of undercooked meat
B. Chronic hypertension
C. Alcohol use disorder
D. Spirochete infection

https://openevidence.com/ask/451373c0-a452-4c8f-b916-124c7917578d

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The answer is **C. Alcohol use disorder**.

This vignette describes **Korsakoff syndrome**, the chronic neuropsychiatric sequela of thiamine (vitamin B1) deficiency most commonly caused by **chronic alcohol misuse**.[1][2][3] The clinical and imaging features are classic:

- **Anterograde amnesia** with preserved long-term memory and intact serial sevens — Korsakoff syndrome is defined as a disproportionate impairment in memory relative to other cognitive functions. The patient repeats information and forgets why he is at the office, yet has no long-term memory deficits.[3]
- **Confabulation** — claiming to be a famous published poet is a hallmark of Korsakoff syndrome, in which patients fabricate memories to fill gaps, particularly in early stages.[3][4]
- **Constricted affect** — emotional changes including apathy and blandness are well described.[3]
- **MRI showing atrophy of the anterior thalami and mammillary bodies** — these are the neuroanatomic signatures of Korsakoff syndrome, with structural abnormalities within the

mammillary body–mammillothalamic tract–anterior thalamus circuit accounting for the anterograde amnesia.[3][5][6]

Alcohol use disorder is the most common predisposing factor because chronic alcohol use impairs thiamine absorption, reduces hepatic thiamine stores, increases renal thiamine losses, and raises metabolic demand for thiamine.[1][3] Up to 90% of Wernicke-Korsakoff syndrome cases in Western populations are alcohol-related.[7] The patient's residence in a group home is consistent with the chronic, irreversible functional impairment typical of established Korsakoff syndrome.[8]

Why not the other choices?

- **A (undercooked meat)** — could lead to neurocysticercosis or toxoplasmosis, which present with focal lesions, not symmetric mammillary body/thalamic atrophy with isolated amnesia.
- **B (chronic hypertension)** — causes vascular dementia with multi-domain cognitive decline and white matter disease, not the selective amnesia and mammillary body atrophy seen here.
- **D (spirochete infection)** — neurosyphilis can cause dementia but presents with broader cognitive and neurologic deficits, not this pattern of selective anterograde amnesia with confabulation and mammillary body atrophy.

Would you like to explore the recommended thiamine dosing regimen for prevention and treatment of Wernicke-Korsakoff syndrome?

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Question 305

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?

A. Coronary artery aneurysm
B. Rapidly progressive glomerulonephritis
C. Hearing loss
D. Retinopathy

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The answer is **A. Coronary artery aneurysm**.

This presentation — fever ≥5 days, bilateral conjunctival injection, oral mucosal changes (strawberry tongue, lip erythema), maculopapular rash involving hands/feet/perineum/trunk, and unilateral cervical lymphadenopathy in a child under 5 — is classic **Kawasaki disease** (KD).

Coronary artery aneurysms are the most common and most clinically significant complication of KD, developing in **20–25% of untreated children**.[1][2][3] With timely treatment (high-dose IVIG within 10 days of fever onset), this risk is reduced to **<5%**.[4] KD is the **leading cause of acquired heart disease in children** in developed countries.[1]

The other answer choices are not associated with KD:

- **Rapidly progressive glomerulonephritis** — associated with conditions such as ANCA-associated vasculitis or post-streptococcal disease, not KD.
- **Hearing loss** — a complication of conditions like meningitis or congenital infections, not KD.
- **Retinopathy** — not a recognized complication of KD (though anterior uveitis can occur, it is self-limited and does not cause retinopathy).

Would you like to explore the treatment protocol for Kawasaki disease, including management of IVIG-refractory cases?

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Question 306

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?

A. Median sacral artery
B. Inferior mesenteric artery
C. Celiac artery
D. Superior mesenteric artery

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The answer is **D. Superior mesenteric artery (SMA)**.

The **hepatic flexure and transverse colon** are supplied by branches of the SMA — specifically the **right colic artery** and the **middle colic artery**.[1][2] The SMA supplies the midgut derivatives, which include the jejunum, ileum, ascending colon, and transverse colon up to approximately the splenic flexure.[2][3]

This patient's presentation — acute severe abdominal pain with dusky discoloration (ischemic infarction) of the hepatic flexure and adjacent transverse colon — is consistent with **acute mesenteric ischemia** from an **arterial embolism** to a branch of the SMA. His **atrial fibrillation** is the classic risk factor for cardiogenic embolism, and the SMA is preferentially affected because of its **nearly vertical takeoff from the aorta**, which allows emboli to travel directly into it.[4]

Why not the other options:

- **A. Median sacral artery** — supplies only the sacrum and coccyx, with minor contribution to the anal canal.[5]
- **B. Inferior mesenteric artery (IMA)** — supplies the hindgut (descending colon, sigmoid, and proximal rectum), not the hepatic flexure or right transverse colon.[3]
- **C. Celiac artery** — supplies the foregut (stomach, duodenum, liver, spleen, pancreas) and does not supply the colon.[2]

Would you like to explore the differences between occlusive and non-occlusive acute mesenteric ischemia?

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Question 307

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?

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

https://openevidence.com/ask/c37d319e-8db8-4a29-802e-b04365d7ddb3

The answer is **C. Hypoxanthine-guanine phosphoribosyl transferase of the purine metabolism pathway**.

This presentation is classic for **Lesch-Nyhan syndrome** **(LNS)**: an X-linked disorder caused by deficiency of **hypoxanthine-guanine phosphoribosyltransferase (HGPRT)**, a key enzyme in the **purine salvage pathway**.[1][2] HGPRT catalyzes the conversion of hypoxanthine to inosine monophosphate (IMP) and guanine to guanosine monophosphate (GMP), recycling purines that would otherwise be degraded.[3] Loss of this enzyme leads to uric acid overproduction and severe neurological dysfunction.

Key clinical features supporting the diagnosis:

- **Self-injurious behavior** — the hallmark of LNS; compulsive self-mutilation (especially biting) is the most distinctive behavioral feature[1][4]

- **Absent teeth since age 2** — a consequence of severe self-biting, often necessitating early extraction to prevent tissue destruction[5]
- **Dystonia, choreoathetosis, and facial grimacing** — the involuntary movements described (irregular contractions, writhing) correspond to the generalized dystonia, chorea, and ballismus characteristic of LNS[2]
- **Allopurinol use** — standard treatment for the hyperuricemia/uric acid overproduction seen in all HGPRT-deficient patients[2]
- **Diazepam use** — benzodiazepines are used to manage spasticity and dystonia in LNS[2]
- **Symptom exacerbation after medication discontinuation** — stopping allopurinol and diazepam after the parents' death likely worsened his uric acid levels and movement disorder

Why the other options are incorrect:

- **A** — Names the correct enzyme (HGPRT) but assigns it to **pyrimidine** metabolism, which is wrong; HGPRT is part of the purine salvage pathway[3][6]
- **B** — Aminolevulinic acid synthetase deficiency relates to **porphyria**, not this presentation
- **D** — Thymidylate synthetase is involved in pyrimidine (thymidine) synthesis and is unrelated to this clinical picture

Would you like to explore current and emerging treatment strategies for Lesch-Nyhan syndrome?

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Question 308

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?

A. Niacin
B. Cobalamin
C. Iron
D. Zinc

https://openevidence.com/ask/138484e1-0ef0-4f7e-83a7-c034cc9099ad

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The answer is **D. Zinc**.

This patient's constellation of **perioral bullous plaques, alopecia, and dysgeusia** (bland taste) in the setting of **Crohn's disease with multiple small bowel resections** is classic for **acquired zinc deficiency**, mimicking the presentation of acrodermatitis enteropathica.

Why zinc deficiency fits:

- **Dermatitis**: Zinc deficiency characteristically causes erythematous, bullous-pustular plaques in **periorificial** (perioral, perinasal, perianal) and **acral** distributions.[1][2][3]
- **Alopecia**: A well-recognized cutaneous manifestation of moderate-to-severe zinc deficiency.[1][4]
- **Taste abnormalities (dysgeusia)**: Zinc is essential for gustatory function; deficiency commonly results in hypogeusia or dysgeusia.[4]
- **Crohn's disease with bowel resections**: Zinc absorption is considerably impaired in Crohn's disease, and patients with extensive small bowel resections are at particularly high risk. Zinc deficiency prevalence in IBD ranges from **40–50%**. Multiple resections further reduce absorptive surface area, compounding the risk.[5][6][7]

Why the other options are less likely:

- **A. Niacin** — Deficiency (pellagra) causes the triad of **dermatitis, diarrhea, and dementia**, with photosensitive dermatitis in sun-exposed areas rather than periorificial bullous plaques.
- **B. Cobalamin (B12)** — Deficiency causes **megaloblastic anemia and neurologic symptoms** (peripheral neuropathy, subacute combined degeneration), not this dermatologic pattern.
- **C. Iron** — Deficiency causes **microcytic anemia**, fatigue, and sometimes koilonychia or angular cheilitis, but not bullous perioral plaques or alopecia of this type.

Would you like to explore zinc supplementation dosing and monitoring in Crohn's disease patients with extensive bowel resections?

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Question 309

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?

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

https://openevidence.com/ask/31c810e5-d919-46a3-b870-0979135c111a

The best 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**.

This patient is an **unsensitized Rh(D)-negative** woman (negative anti-D antibody screen) with known risk factors for alloimmunization: a prior Rh(D)-positive delivery and a history of blood transfusion. Despite these exposures, she has not yet developed anti-D antibodies, making her a candidate for the full Rh(D) prophylaxis protocol.

ACOG recommends a three-step approach for unsensitized Rh(D)-negative pregnant women:[1]

1. **Repeat antibody screening at 24–28 weeks** — The USPSTF (Grade B) and ACOG recommend repeating the Rh(D) antibody screen before administering anti-D immunoglobulin, primarily to identify the small proportion of women who become alloimmunized before 28 weeks and require a different management pathway.[1][2]

2. **Administer anti-D immunoglobulin at 28 weeks** — Routine antenatal prophylaxis at 28 weeks is recommended because transplacental hemorrhages large enough to cause sensitization typically occur in the third trimester.[1][3]

3. **Postpartum anti-D immunoglobulin within 72 hours if the newborn is Rh(D)-positive** — This is essential to prevent sensitization from the fetomaternal hemorrhage that occurs at delivery.[1][4]

Why the other options are incorrect:

- **B** omits the critical postpartum dose of anti-D immunoglobulin. Without it, the risk of alloimmunization from delivery-related fetomaternal hemorrhage is 12–16%.[4]

- **C** omits the 28-week antenatal prophylaxis, which addresses the risk of occult sensitizing events in the third trimester. Postpartum prophylaxis alone reduces but does not eliminate alloimmunization risk.[3]

- **D** is incorrect because this unsensitized Rh(D)-negative woman clearly requires Rh(D) prophylaxis.

An additional notable finding: this patient is **rubella non-immune** (negative IgG and IgM), which would warrant **postpartum MMR vaccination** before discharge, as MMR is contraindicated during pregnancy.[5][6] This is not among the answer choices but is an important clinical consideration.

Would you like to explore the management of Rh(D) alloimmunization when the antibody screen is positive?

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Question 310

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?

A. Alcohol abuse
B. Hypertensive changes
C. Parasitic infection
D. Bacterial infection

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C. Parasitic infection — chronic Chagas disease (Trypanosoma cruzi) in its **cardiodigestive form**, acquired through repeated exposure in an endemic region.[1][2]

Why this fits

- **Epidemiology:** Emigration from Mexico with twice-yearly return visits gives ongoing exposure to triatomine vector-borne transmission. An estimated 200,000–300,000 infected persons live in the US, and among Latin America–born patients presenting with new nonischemic cardiomyopathy (LVEF ≤40%) in Los Angeles, **19% had Chagas disease**.[1][3]
- **Cardiac findings:** Chronic Chagas cardiomyopathy develops in **20–40%** of infected persons years to decades after infection and manifests as a **progressive dilated cardiomyopathy** with biventricular failure — orthopnea, JVD, peripheral edema, basilar crackles, and S3 — plus arrhythmias producing palpitations. Chest X-ray would be expected to show **cardiomegaly with pulmonary congestion**.[1][3][4]

- **Digestive findings:** Dysphagia, regurgitation, and dyspepsia reflect **megaesophagus** from destruction of the esophageal myenteric plexus, producing a secondary achalasia with loss of peristalsis and impaired LES relaxation. Gastrointestinal involvement occurs in roughly **10–21%** of symptomatic patients and, when combined with cardiac disease, defines the cardiodigestive form. A widened mediastinum from the dilated esophagus may be visible on chest film.[2][3][5][6]

One caveat worth noting: the normal ECG is atypical. The earliest and most characteristic cardiac abnormality in Chagas disease is a conduction defect — **RBBB, left anterior fascicular block, or their combination** — and electrocardiographic abnormalities are essentially universal once heart failure symptoms develop.[2][4] In real practice, overt Chagas heart failure with a completely normal ECG should prompt reconsideration of alternative etiologies; for the purposes of this question, the epidemiologic exposure plus the combination of dilated cardiomyopathy and esophageal dysmotility is the intended discriminator.

Why the alternatives fail

- **Alcohol abuse (A):** can produce dilated cardiomyopathy, but does not cause megaesophagus with dysphagia and regurgitation.
- **Hypertensive changes (B):** BP is 120/75, and hypertensive heart disease does not explain the esophageal symptoms.
- **Bacterial infection (D):** no fever or acute infectious signs; no bacterial pathogen produces this chronic cardiodigestive syndrome.

Confirmatory workup: two serologic assays using different antigens/formats for anti–T. cruzi IgG (a single positive test is insufficient), echocardiography to assess LVEF, wall motion abnormalities, and apical aneurysm, and barium esophagram with manometry for the digestive form.[3][7] Management includes guideline-directed heart failure therapy and arrhythmia/device evaluation; antitrypanosomal therapy with benznidazole or nifurtimox is directed at early chronic infection and has not been shown to reverse established cardiomyopathy.[7]

Would you like to explore risk stratification for sudden death and anticoagulation thresholds in Chagas cardiomyopathy?

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Question 311

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?

A. Decreased complement levels
B. Increased anti-centromere antibodies
C. Increased anti-cyclic citrullinated peptide antibodies
D. Increased anti-topoisomerase antibodies

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The answer is **A. Decreased complement levels**.

This presentation — a **young woman with bilateral joint pain, fatigue, subjective fever, and bilateral malar erythema** (over the maxillary prominences) that she attributes to sunburn — is highly consistent with **systemic lupus erythematosus (SLE)**. The "sunburn" is characteristic of the SLE malar rash, which tends to occur in a photosensitive distribution and can be mistaken for sun exposure.

Hypocomplementemia (low C3 and C4) is a classic laboratory finding in SLE, resulting from complement consumption through immune complex–mediated classical pathway activation.[1][2] Typical laboratory abnormalities in SLE include **anemia, thrombocytopenia, leukopenia, hypocomplementemia, and characteristic autoantibodies** (ANA, anti-dsDNA, anti-Smith).[1] Low complement levels are included in the **2019 EULAR/ACR classification criteria** for SLE: low C3 or C4 contributes 3 points, while low C3 and C4 together contributes 4 points toward classification.[3] C3 and C4 levels are also routinely used to **monitor disease activity** in established SLE.[1]

Why not the other options:

- **B. Anti-centromere antibodies** — associated with **limited cutaneous systemic sclerosis** (CREST syndrome), which presents with calcinosis, Raynaud phenomenon, esophageal dysmotility, sclerodactyly, and telangiectasias — not malar rash.
- **C. Anti-CCP antibodies** — specific for **rheumatoid arthritis**, which typically presents with symmetric small-joint synovitis and morning stiffness, not malar erythema.
- **D. Anti-topoisomerase (anti-Scl-70) antibodies** — associated with **diffuse cutaneous systemic sclerosis**, characterized by widespread skin thickening and pulmonary fibrosis.

Would you like to explore the recommended initial workup and treatment approach for newly diagnosed SLE?

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Question 312

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?

A. Replacement of D-alanine
B. Mutation of DNA gyrase
C. Inactivation by bacterial transferase
D. Modification of surface binding proteins

https://openevidence.com/ask/ba350f2a-9604-44ba-8e81-0f95c8afb267

The answer is **B. Mutation of DNA gyrase**.

Ciprofloxacin is a fluoroquinolone that exerts its bactericidal effect by **inhibiting DNA gyrase** (topoisomerase II), an essential enzyme that maintains chromosomal DNA in a negatively supercoiled state during replication.[1][2] The **dominant mechanism of ciprofloxacin resistance in *E. coli*** is point mutations in the **quinolone resistance-determining region (QRDR)** of the **gyrA** gene, most commonly at codons **Ser-83** and **Asp-87**, which reduce the drug's binding affinity for the gyrase–DNA complex.[3][4][5] In studies of fluoroquinolone-resistant *E. coli* clinical isolates, **all resistant isolates harbored gyrA mutations**, and these target-site mutations had the **highest impact** on ciprofloxacin resistance compared to other mechanisms.[5][6]

The other answer choices refer to resistance mechanisms for different drug classes:

- **A. Replacement of D-alanine** — mechanism of vancomycin resistance (e.g., VanA/VanB in enterococci), where the terminal D-Ala-D-Ala peptidoglycan target is replaced with D-Ala-D-Lac.
- **C. Inactivation by bacterial transferase** — describes enzymatic drug inactivation, as seen with aminoglycoside acetyltransferases or beta-lactamases.
- **D. Modification of surface binding proteins** — refers to altered penicillin-binding proteins (PBPs), a mechanism of beta-lactam resistance (e.g., MRSA).

Would you like to explore how stepwise accumulation of gyrA and parC mutations leads to progressively higher levels of fluoroquinolone resistance?

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Question 313

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?

A. Chlorpromazine
B. Clonidine
C. Diazepam
D. Haloperidol

https://openevidence.com/ask/fbc59627-b38f-49f5-825f-f2ce3232508f

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The answer is **C. Diazepam**.

This presentation is classic for **delirium tremens (DT)** — the most severe form of alcohol withdrawal syndrome, typically occurring **48–96 hours after cessation** of alcohol use. Key features here include high fever (40.0°C), tachycardia, hypertension, agitation, confusion with complete disorientation, and **tactile hallucinations** (formication — bugs crawling on the skin), all 5 days after abrupt cessation of heavy alcohol use.[1]

Benzodiazepines are the first-line treatment for alcohol withdrawal delirium. The ASAM Clinical Practice Guideline explicitly recommends benzodiazepines as first-line agents, with the goal of achieving and maintaining light somnolence.[2][3] **Diazepam** is preferred among benzodiazepines for its long half-life and active metabolites, which provide a smoother taper of withdrawal symptoms; symptom-triggered front-loading with diazepam has been shown to reduce the duration of delirium.[2]

Why not the other choices:

- **A. Chlorpromazine** — A first-generation antipsychotic that **lowers the seizure threshold**, making it 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**.[2] [3]
- **D. Haloperidol** — While haloperidol can be used as an **adjunct** to benzodiazepines for refractory hallucinations or agitation, antipsychotics are **not recommended as monotherapy** for DT because they lower the seizure threshold and do not address the underlying GABAergic pathology of withdrawal.[2]

Would you like to explore the specific diazepam dosing protocols and front-loading strategies used in delirium tremens?

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Question 314

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?

A. Stimulation of monoamine neurotransmitter release
B. Inhibition of serotonin reuptake
C. Stimulation of norepinephrine release
D. Inhibition of lipase

https://openevidence.com/ask/936c52f4-74a4-45d1-aeb3-f2491a83c867

The correct answer is **D. Inhibition of lipase**.

This patient's presentation — **greasy diarrhea (steatorrhea), flatulence, and belching** after starting a weight-loss medication — is classic for **orlistat**, which works by **inhibiting pancreatic and gastric lipases**, reducing dietary fat absorption by approximately 30%.[1][2] The unabsorbed fat passes into the stool, producing the characteristic GI side effects: oily/fatty stools, fecal urgency, flatulence, and oily spotting.[3]

The key additional findings — **night blindness and dry, scaly skin** — point to **vitamin A deficiency**, a consequence of fat-soluble vitamin malabsorption caused by orlistat. Because fat-soluble vitamins (A, D, E, K) require dietary fat for absorption, orlistat's lipase inhibition impairs their uptake.[1][4] Vitamin A deficiency specifically causes nyctalopia (night blindness) and xerosis (dry, scaly skin). The FDA label for orlistat warns that it reduces absorption of fat-soluble vitamins and beta-carotene, and patients should take a multivitamin supplement at least 2 hours before or after the dose.[4]

Why not the other options:

- **A (Stimulation of monoamine release)** and **C (Stimulation of norepinephrine release)** — These describe sympathomimetic agents like phentermine, which cause anorexigenic effects centrally but do not produce steatorrhea or fat-soluble vitamin deficiency.

- **B (Inhibition of serotonin reuptake)** — This would describe agents like lorcaserin (withdrawn) or SSRIs, which also would not cause fat malabsorption.

Would you like to explore the comparative efficacy and safety of current anti-obesity medications?

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Question 315

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?

A. Naloxone
B. Cyproheptadine
C. Ammonium chloride
D. Sodium bicarbonate

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D. Sodium bicarbonate. This is nortriptyline (TCA) overdose with cardiotoxicity — sinus tachycardia, hypotension, and QRS 130 ms from fast sodium channel blockade — plus an antimuscarinic toxidrome (mydriasis, dry skin, ileus with distention, urinary retention producing suprapubic dullness). Hypertonic sodium bicarbonate is the therapy of choice for symptomatic TCA poisoning, indicated for QRS >100 ms, fluid-unresponsive hypotension, seizures, or ventricular dysrhythmia.[1][2]

Why bicarbonate works

- Combines **sodium loading** and **serum alkalinization**, which act additively to reverse sodium channel blockade, narrow the QRS, and improve hypotension. Alkalemia also increases protein binding, reducing free drug.[1][2][3]
- Degree of QRS widening (and terminal R in aVR) predicts seizures, PEA, and death; serum drug levels do not guide management.[4][5]

Practical dosing and limits

- Bolus **1–2 mmol/kg IV**, repeated if the patient remains unstable, up to a **maximum of ~6 mmol/kg**; exceeding this risks hypernatremia, fluid overload, metabolic alkalosis, and cerebral edema.[6][7]

- Target **pH ~7.45–7.55** and **serum Na^+ ≤150–155 mEq/L**; the endpoint is the alkalinization target and hemodynamic/ECG improvement, not forcing QRS <100 ms.[3][6]
- In intubated patients, **hyperventilation (PCO_2 ~30–35 mm Hg)** works synergistically and reduces the bicarbonate dose needed; combined therapy narrows the QRS roughly twice as fast.[6][7]
- **Monitor for hypokalemia and hypocalcemia** during alkalinization.[1][3]
- Second line if refractory: **lidocaine** (class Ib) for wide-complex dysrhythmia, then vasopressors, with VA-ECMO for refractory cardiogenic shock; intravenous lipid emulsion only as last resort.[3]
- Adjuncts: activated charcoal for early presentation with a protected airway, benzodiazepines for seizures. Avoid class Ia/Ic antiarrhythmics and physostigmine.[4][5]

Why the other options are wrong

- **Naloxone** — reverses opioid toxicity; the pupils here are dilated, not pinpoint, and there is no respiratory depression described.
- **Cyproheptadine** — 5-HT_2A antagonist for serotonin syndrome, which would show hyperthermia, clonus, and hyperreflexia rather than QRS widening.
- **Ammonium chloride** — acidifies serum, which would worsen sodium channel blockade and increase free drug; contraindicated in this setting.

Would you like to explore the observation period and criteria for medical clearance after TCA overdose?

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Question 316

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?

A. Low serum potassium
B. Low blood urea nitrogen
C. Elevated serum calcium
D. Elevated serum creatine kinase

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The answer is **D. Elevated serum creatine kinase**.

This presentation is classic for **rhabdomyolysis**. The key diagnostic clue is **tea-colored urine that is dipstick-positive for blood (3+) but shows no RBCs on microscopy** — this pattern indicates **myoglobinuria**, as the urine dipstick cannot distinguish myoglobin from hemoglobin.[1][2] Serum creatine kinase (CK), the most reliable biochemical marker of rhabdomyolysis, would be markedly elevated (typically >5 times the upper limit of normal).[3][4][5]

Multiple etiologies converge in this patient:

- **Cocaine** causes direct myotoxicity, vasoconstriction-mediated muscle ischemia, and hyperthermia — all established triggers of rhabdomyolysis[4][6]
- **Prolonged immobilization** while unconscious (opiate overdose) leads to compression-induced muscle necrosis
- **Trauma**, evidenced by large contusions and oral bleeding (possible seizure with tongue bite), contributes to direct muscle injury

Why the other options are incorrect:

- **A. Low serum potassium** — Rhabdomyolysis causes **hyperkalemia**, not hypokalemia, due to massive release of intracellular potassium from damaged myocytes.[4][5]
- **B. Low BUN** — BUN would be **elevated**, not low, given dehydration (specific gravity 1.045) and evolving acute kidney injury from myoglobin nephrotoxicity. Between 13% and 50% of patients with rhabdomyolysis develop AKI.[1][4]
- **C. Elevated serum calcium** — Rhabdomyolysis characteristically causes **hypocalcemia**, as calcium deposits in damaged muscle tissue. Hypercalcemia may occur later during the recovery phase but not acutely.[4]

Would you like to explore the optimal fluid resuscitation and urine alkalinization strategy for preventing AKI in rhabdomyolysis?

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Question 317

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?

A. Autoimmune liver damage
B. Congestive hepatopathy
C. Insulin resistance
D. Acetaminophen use

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C. Insulin resistance. The constellation of BMI 36.3 kg/m², HbA1c 6.3% (prediabetes), hepatomegaly, a diffusely hyperechoic liver on ultrasound, and ALT-predominant transaminitis with negative viral and autoimmune serologies is **metabolic dysfunction–associated steatotic liver disease (MASLD, formerly NAFLD)**, in which insulin resistance is the central pathogenic driver.[1][2][3] Insulin resistance is nearly universal in MASLD and operates at the level of liver, adipose tissue, and muscle — adipose insulin resistance drives unrestrained lipolysis and free fatty acid flux to the liver, while hyperinsulinemia and carbohydrate excess drive de novo lipogenesis, overwhelming hepatic disposal capacity and generating lipotoxic intermediates.[1][4][5]

Features that fit MASLD in this patient

- **AST/ALT ratio 0.64** (92/144). ALT > AST is typical of MASLD; a ratio ≥1.5–2 would point to alcohol-related liver disease.[3][6][7]
- **Alcohol intake ~2–4 drinks/week**, far below the diagnostic threshold of <210 g/wk (<3 standard drinks/day) for men.[2]
- **Diffusely hyperechoic, mildly enlarged liver** — the classic sonographic appearance of steatosis; 50–60% of patients with MASLD have mild-to-moderate hepatomegaly.[2][3]
- **Diagnosis requires steatosis plus ≥1 cardiometabolic criterion** (obesity, prediabetes/diabetes, hypertension, hypertriglyceridemia, low HDL) with exclusion of competing causes — satisfied here by obesity and prediabetes. Elevated aminotransferases raise concern for steatohepatitis (MASH), but that distinction cannot be made without histology or further risk stratification.[2][3]

Why the other options are less likely

- **A. Autoimmune liver damage** — ANA 1:20 is below the 1:60 reference cutoff, with negative anti–smooth muscle and anti-LKM1 antibodies, and the imaging shows steatosis rather than an autoimmune hepatitis pattern.
- **B. Congestive hepatopathy** — no clinical evidence of right-sided heart failure; congestive hepatopathy typically produces a cholestatic-predominant pattern with hyperbilirubinemia and hepatic venous congestion on imaging, not diffuse hyperechogenicity.
- **D. Acetaminophen use** — 650 mg every other day is a trivial cumulative exposure. Acetaminophen hepatotoxicity presents as marked, AST-predominant elevations, often in the thousands, rather than chronic ALT-predominant elevation in the 100s.[6]

Risk stratification

The next step is fibrosis assessment, since fibrosis stage drives prognosis and transaminase levels correlate poorly with histologic severity.[2][8]

Computed value for FIB-4 Score: 0.89

Low risk of advanced fibrosis. An FIB-4 score between 0 and 1.3 indicates a low probability of advanced hepatic fibrosis (F3-F4) and can be used to exclude advanced fibrosis in patients with NAFLD, with a strong negative predictive value (NPV) of ≥90%.[9][10][11] Patients with scores in this range generally do not require further evaluation for advanced fibrosis but should be considered for repeat testing in 2-3 years.[10]

FIB-4 of 0.89 falls below the 1.3 low-risk threshold, with sensitivity 85% and negative predictive value 95% for advanced fibrosis, so elastography is not immediately required.[8] Management centers on **7–10% weight loss**, treatment of the prediabetes, lipid assessment, smoking cessation, and minimizing alcohol; hepatitis B surface antibody positivity indicates existing immunity.

Would you like to explore pharmacologic options such as GLP-1 receptor agonists or resmetirom for MASLD in this setting?

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Question 318

A 64-year-old male with a past medical history of two myocardial infarctions presents to the emergency room with shortness of breath. He notes that he stopped taking his furosemide two weeks prior, because he ran out of pills. On exam, his oxygen saturation is 78%, his lungs have crackles throughout, and jugular venous pulsation is located at the earlobe. EKG and troponin levels are normal. Which of the following is consistent with this man's pulmonary physiology?

A. Decreased Aa gradient, decreased surface area for diffusion, normal diffusion distance
B. Decreased Aa gradient, increased surface area for diffusion, decreased diffusion distance
C. Increased Aa gradient, normal surface area for diffusion, increased diffusion distance
D. Increased Aa gradient, decreased surface area for diffusion, increased diffusion distance

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The answer is **D: Increased A-a gradient, decreased surface area for diffusion, increased diffusion distance**.

This patient presents with **acute decompensated heart failure with cardiogenic pulmonary edema** — a history of two MIs, medication non-adherence (furosemide cessation), severe hypoxemia (SpO_2 78%), diffuse crackles, and JVD to the earlobe, with a normal EKG and troponin ruling out acute MI.

Pulmonary physiology in cardiogenic pulmonary edema is best understood through Fick's law of diffusion, which states that gas transfer is proportional to surface area and the pressure gradient, and inversely proportional to diffusion distance (membrane thickness):

- **Increased A-a gradient:** Flooding of alveoli with edema fluid impairs gas exchange, producing hypoxemia that is not explained by hypoventilation alone. In a cardiogenic pulmonary edema model, the A-a gradient increased from 23 ± 4 to 56 ± 6 mmHg, demonstrating significant impairment of oxygen transfer.[1]
- **Decreased surface area for diffusion:** Fluid-filled alveoli are effectively excluded from gas exchange, reducing the total alveolar surface area available for diffusion. Studies in heart failure show that alveolar-capillary membrane conductance (Dm) — which reflects both membrane thickness and effective surface area — is significantly reduced.[2][3][4]

- **Increased diffusion distance:** Edema fluid accumulates in the interstitium and alveolar spaces, thickening the alveolar-capillary barrier. Morphometric studies confirm that even mild interstitial edema increases the arithmetic mean barrier thickness from 1.06 to 1.33 μm, directly increasing resistance to gas diffusion. In severe pulmonary edema, alveolar flooding further extends the diffusion path between alveolar gas and capillary blood.[5][6]

The other answer choices can be excluded because they include a **decreased or normal A-a gradient**, which is inconsistent with the impaired gas exchange seen in pulmonary edema.

Would you like to explore the acute management of decompensated heart failure with pulmonary edema?

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Question 319

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?

A. Rheumatic fever
B. Innocent murmur
C. Non-bacterial thrombotic endocarditis
D. Atrial myxoma

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The correct answer 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 is the hallmark finding. Cardiac myxomas are the most common primary cardiac tumor in adults, with ~75% located in the left atrium, and >90% attached by a stalk to the **fossa ovalis** of the interatrial septum.[1][2]
- **Positional symptoms** (dyspnea worse when lying on the left side) occur because the pedunculated tumor shifts with gravity, intermittently obstructing the mitral valve orifice and mimicking **mitral stenosis**. The extent of valvular obstruction varies with body position.[3]
- **Diastolic murmur accentuated in the left lateral decubitus position** results from this intermittent mitral valve obstruction. Approximately two-thirds of patients have an auscultatory abnormality, with 15% demonstrating a low-frequency diastolic murmur ("tumor plop").[4]
- **Syncope** (the unexplained loss of consciousness 10 days prior) can occur when the tumor temporarily causes complete obstruction of the mitral orifice.[3][5]

- **Pulmonary congestion, JVD, and fine crackles** reflect left-sided heart failure from chronic obstruction of mitral inflow, with secondary pulmonary hypertension.[6]

Why the other answers are incorrect:

- **A. Rheumatic fever** — Would not produce an intracardiac mass on echocardiography. Though left atrial myxoma can mimic rheumatic mitral stenosis hemodynamically, the echocardiographic mass attached to the atrial septum distinguishes the two.[6][7]
- **B. Innocent murmur** — Innocent murmurs are systolic (not diastolic), do not produce hemodynamic compromise, and are not associated with intracardiac masses, syncope, or heart failure.
- **C. Non-bacterial thrombotic endocarditis (NBTE)** — 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 risk of cardiac myxoma?

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Question 320

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?

A. Chlorine-based solution
B. Iodine-based solution
C. Isopropanol-based solution
D. Quaternary amine-based solution

https://openevidence.com/ask/bd166411-f622-43e2-99f4-0d607dad5e16

The answer is **A. Chlorine-based solution**.

This clinical scenario describes **Clostridioides difficile infection (CDI)** — a hospitalized patient on broad-spectrum antibiotics (ceftriaxone, azithromycin) who develops foul-smelling, watery diarrhea, with stool cultures growing **gram-positive anaerobic rods**. The key to this question is understanding the unique resistance properties of C. difficile **spores**.

Why chlorine-based solutions (sodium hypochlorite/bleach)?

C. difficile spores are highly resistant to most common hospital disinfectants. The 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.[1] Sodium hypochlorite was the only chemical reagent that **consistently reduced both vegetative cells and spores** across multiple C. difficile strains.[2]

Why the other options are incorrect:

- **B. Iodine-based solution** — Not established as a reliable sporicidal environmental disinfectant for C. difficile and not recommended in guidelines.
- **C. Isopropanol-based solution** — C. difficile spores are **resistant to the bactericidal effects of alcohol**. As noted in an NEJM review, "using alcohol-based hand sanitizers does not reduce the number of viable C. difficile spores".[1][3]

- **D. Quaternary amine-based solution** — C. difficile spores are specifically resistant to **quaternary ammonium compounds**, which are among the "commonly used hospital disinfectants" that lack sporicidal activity.[1]

The spore coat of C. difficile renders it impervious to alcohol and quaternary ammonium compounds, which is a fundamental differentiator from other healthcare-associated pathogens like MRSA and VRE that do not form spores.[1]

Would you like to explore the current treatment guidelines for C. difficile infection, including management of recurrences?

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Question 321

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?

A. Trientine
B. Calcium disodium edetate (EDTA)
C. Penicillamine
D. Dimercaptosuccinic acid (DMSA), also known as succimer

https://openevidence.com/ask/de1122d2-6fe8-48f0-a1f1-7e9fff2ecb78

The best treatment is **D. Dimercaptosuccinic acid (DMSA), also known as succimer**.

This child presents with classic **symptomatic lead poisoning**: abdominal cramps, myalgias, decreased activity, and **microcytic anemia** (Hb 7 g/dL, MCV 72) in the setting of residence in a **pre-1960 home** (lead paint exposure). The **venous blood lead level of 60 mcg/dL** confirms significant toxicity. The peripheral blood smear would characteristically show **basophilic stippling**, a hallmark of lead poisoning.

Chelation therapy is indicated for children with blood lead levels ≥45 mcg/dL.[1][2] For levels in the **45–69 mcg/dL range without encephalopathy**, **oral DMSA (succimer) is the first-line chelation agent**.[2][3] It is FDA-approved for lead poisoning in pediatric patients aged ≥1 year with blood lead levels >45 mcg/dL, dosed at **10 mg/kg every 8 hours for 5 days, then every 12 hours for an additional 14 days** (19-day course).[3] DMSA was shown to reduce blood lead levels

by 78% over a 5-day course at this dose and was significantly more effective than CaNa2EDTA in a controlled study.[3]

Why not the other options:

- **Trientine (A):** A copper chelator used in **Wilson disease**, with no role in lead poisoning.
- **CaNa2EDTA (B):** An effective lead chelator but requires **parenteral administration** (IV or IM) and carries greater risk of **nephrotoxicity** and essential metal depletion. It is primarily reserved for **BLL ≥70 mcg/dL** or **lead encephalopathy**, where it is combined with dimercaprol (BAL). With a BLL of 60 mcg/dL and no encephalopathy, oral DMSA is preferred.[2][4][5][6]
- **Penicillamine (C):** A less commonly used chelator with a **more significant adverse effect profile** (leukopenia, thrombocytopenia, rashes); it is not first-line for lead poisoning.[1][7]

This child has no signs of encephalopathy (no headaches, seizures, or altered mentation), making outpatient oral DMSA with close follow-up the appropriate choice rather than the more aggressive parenteral BAL + CaNa2EDTA regimen.

Would you like to explore the stepwise management algorithm for pediatric lead poisoning across different blood lead level thresholds?

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Question 322

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?

A. Femoral neck fracture
B. Femoral shaft fracture
C. Osgood-Schlatter disease
D. Proximal phalanx fracture

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The answer is **A. Femoral neck fracture**.

Long-term prednisone use causes **glucocorticoid-induced osteoporosis (GIOP)**, the most common form of secondary osteoporosis, which predominantly affects skeletal regions rich in **cancellous (trabecular) bone** — the lumbar spine, proximal femur (including the femoral neck), and distal radius.[1][2] Even low-dose glucocorticoids (≥2.5 mg/day of prednisone) increase fracture risk at these sites.[3][4] The risk of **hip fracture increases by approximately 50%** among patients receiving 2.5–7.5 mg of prednisolone daily, escalating further at higher doses.[1][5] Bone loss occurs most rapidly in the first 3–6 months of treatment, and fracture risk can rise within 3 months of initiation.[1][2]

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 fractures. Atypical femoral shaft fractures are classically associated with prolonged bisphosphonate use, not glucocorticoids.
- **C. Osgood-Schlatter disease** — This is a traction apophysitis of the tibial tubercle occurring in adolescents during growth spurts, unrelated to glucocorticoid therapy.
- **D. Proximal phalanx fracture** — The proximal phalanx is not a recognized site of osteoporotic fragility fracture.

Patients with SLE have an approximately **2-fold increased risk of osteoporosis and fracture** compared with healthy controls, driven both by the disease itself and by glucocorticoid exposure.[6] The ACR recommends fracture risk assessment soon after initiating glucocorticoid therapy, with calcium and vitamin D supplementation and consideration of bisphosphonates based on individual risk.[1][4]

Would you like to explore the prevention and treatment guidelines for glucocorticoid-induced osteoporosis in premenopausal women?

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Question 323

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?

A. Defect in ATM gene
B. Adenosine deaminase deficiency
C. NADPH oxidase deficiency
D. Defect in BTK gene

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The answer is **B. Adenosine deaminase deficiency**.

This infant's presentation — **failure to thrive, chronic diarrhea, recurrent bacterial and viral infections, absent thymic shadow, and absent lymph node germinal centers** — is the classic phenotype of **severe combined immunodeficiency (SCID)**.[1][2] ADA deficiency is an **autosomal recessive** cause of SCID, accounting for approximately **15% of cases**, and produces a **T−B−NK− phenotype** through toxic accumulation of purine metabolites (adenosine, 2'-deoxyadenosine) that cause lymphocyte apoptosis.[3][4]

Several features narrow the differential among the answer choices:

- **The patient is female**, which excludes **BTK deficiency** (option D), an X-linked disorder causing Bruton agammaglobulinemia. BTK deficiency also typically presents later (after ~6 months, when maternal IgG wanes), affects only B cells, and does not cause thymic aplasia.[5]
- **ATM gene defect** (option A) causes **ataxia-telangiectasia**, a DNA repair disorder presenting with cerebellar ataxia, oculocutaneous telangiectasias, and selective IgA deficiency — not SCID.
- **NADPH oxidase deficiency** (option C) causes **chronic granulomatous disease**, a phagocyte disorder with recurrent catalase-positive bacterial and fungal infections but intact lymphocyte development and a normal thymus.

ADA-SCID characteristically presents in the **first weeks to months of life** with opportunistic infections, persistent diarrhea, growth failure, and absence of lymphoid tissue including an undetectable thymic shadow on chest radiograph.[1][6] The absent germinal centers reflect the profound loss of both T- and B-cell compartments. Additional findings relatively specific to ADA deficiency include **chondro-osseous dysplasia** (e.g., rib cupping, scapular spurring) and pulmonary alveolar proteinosis.[1][4]

Would you like to explore the current treatment options and outcomes for ADA-SCID, including gene therapy?

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Question 324

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?

A. ATP7A
B. COL5A1
C. FBN1
D. ATP7B

https://openevidence.com/ask/cbb8314e-5491-4e4b-a7df-5fb6bf25ea46

A. ATP7A. The presentation — a male infant with failure to thrive, microcephaly, and sparse, kinky, brittle hair in the setting of impaired copper absorption and transport with connective tissue involvement — is classic Menkes disease, an X-linked recessive disorder caused by pathogenic variants in **ATP7A** (Xq21.1), which encodes a copper-transporting P-type ATPase.[1][2][3]

Why ATP7A explains the findings

Loss of ATP7A function impairs copper efflux from enterocytes into portal circulation and blocks delivery of copper to cuproenzymes in the secretory pathway. Copper accumulates in the intestine and kidney while the brain, hair, bone, and vasculature remain copper-deficient.[1][4] Reduced activity of lysyl oxidase produces the connective tissue weakness (vascular tortuosity, bladder diverticula, wormian bones, metaphyseal spurring); reduced tyrosinase causes hypopigmentation; reduced cytochrome c oxidase and dopamine β-hydroxylase drive the neurodegeneration.[4][5]

Classic Menkes presents after 6–12 weeks of apparent good health with feeding difficulty, seizures, hypotonia, and failure to thrive.[2][5] Hair shaft microscopy shows pili torti, trichorrhexis nodosa, and monilethrix; serum copper and ceruloplasmin are low.[3][6] Untreated, death typically occurs between 7 months and 3.5 years; early subcutaneous copper histidine may attenuate neurologic progression.[5]

Why the other options are wrong

- **ATP7B (D)** — Wilson disease, autosomal recessive, chromosome 13q14. The defect is in **biliary copper excretion and ceruloplasmin loading**, causing hepatic copper overload rather than systemic copper deficiency. It presents later (typically after age 3–5, more often in adolescence/adulthood) with liver disease, Kayser–Fleischer rings, and neuropsychiatric findings — not kinky hair.[7][8]
- **COL5A1 (B)** — classic Ehlers-Danlos syndrome: skin hyperextensibility, atrophic scarring, joint hypermobility. No copper abnormality.
- **FBN1 (C)** — Marfan syndrome: tall stature with long limbs (opposite of this child's growth pattern), ectopia lentis, aortic root dilation.

A useful mnemonic: **Menkes = Minus copper (ATP7A, A for Absorption)**; **Wilson = ATP7B, copper Building up**.

Would you like to explore the evidence on copper histidine therapy timing and outcomes in Menkes disease?

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Question 325

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?

A. Gonadectomy
B. Testosterone therapy
C. Vaginal dilatory therapy
D. Prednisolone therapy

https://openevidence.com/ask/bf5dcf3e-96ca-41a7-8dae-34b25968ab54

The correct answer is **A. Gonadectomy**.

This presentation is classic for **complete androgen insensitivity syndrome (CAIS)**: primary amenorrhea in a phenotypically female adolescent with breast development (Tanner 4), sparse pubic hair, bilateral inguinal masses (undescended testes), a blind-ended vaginal pouch, and absent uterus/ovaries on ultrasound. These individuals have a **46,XY karyotype** with nonfunctional androgen receptors; anti-Müllerian hormone from the testes causes Müllerian regression (no uterus), while androgen insensitivity prevents virilization and Wolffian duct development.[1][2][3]

Prophylactic gonadectomy is recommended because the retained testes carry a significant risk of **germ cell tumor (GCT)** development. The prepubertal risk is low (0.8–2%), but postpubertally it increases to an estimated **15% (range 0–22%)**, with some data suggesting risk exceeding 30% in late adulthood if gonads are not removed.[1][2] Gonadectomy is typically delayed until after puberty (around age 15–16) to allow spontaneous feminization through aromatization of testicular androgens to estrogens, and this patient — at age 15 with Tanner 4 breast development — is at an appropriate stage.[2] Following gonadectomy, **estrogen replacement therapy** is required lifelong to maintain secondary sexual characteristics and bone health.[1][4]

Why the other options are incorrect:

- **B. Testosterone therapy** — Ineffective, as these patients have complete androgen receptor insensitivity; exogenous testosterone would not produce a clinical response.[3]
- **C. Vaginal dilatory therapy** — May be appropriate as an adjunct for vaginal lengthening if needed for sexual function, but it does not address the primary concern of **gonadal malignancy risk**, which takes precedence.[4]
- **D. Prednisolone therapy** — Has no role in CAIS management; this would be relevant in conditions like congenital adrenal hyperplasia, not androgen insensitivity.

Would you like to explore the estrogen replacement protocol following gonadectomy in CAIS?

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Question 326

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?

A. ECG changes
B. Hypercholesterolemia
C. Gastritis
D. Increased pulse rate

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C. Gastritis.

Aspirin, even at low dose, injures the gastroduodenal mucosa through COX-1 inhibition and impairs platelet-mediated hemostasis, so pre-existing gastric mucosal disease is the relevant precaution in this patient. Low-dose aspirin (75–325 mg/d) raises upper GI bleeding risk **2- to 4-fold**, with a point prevalence of dyspepsia around 31% and gastroduodenal erosions around 60%. [1][2][3] In primary-prevention trials, low-dose aspirin (≤100 mg/d) increased major GI bleeding by 58% (Peto OR 1.58, 95% CI 1.38–1.80) and intracranial bleeding (Peto OR 1.31, 95% CI 1.11–1.54). [4][5]

Why the other options are not contraindications

- **ECG changes** — an indication, not a contraindication; ischemic ECG findings favor antiplatelet therapy.
- **Hypercholesterolemia** — a cardiovascular risk factor that raises the potential benefit of aspirin; no pharmacologic interaction.

- **Tachycardia (pulse 110)** — nonspecific, plausibly anxiety- or pain-related, and unrelated to aspirin safety.

Practical qualifications

- Strictly, gastritis is a **relative** contraindication. Absolute contraindications are aspirin/NSAID hypersensitivity (including aspirin-exacerbated respiratory disease), active GI bleeding or active peptic ulcer, and severe bleeding disorders. Among the options offered, gastritis is the only one bearing on aspirin safety.
- Enteric-coated or buffered formulations do **not** reduce GI bleeding risk.[2][3]
- If aspirin is judged necessary, **co-prescribe a PPI**, which is superior to an H2RA for preventing aspirin-associated ulcers and bleeding. **H. pylori testing and eradication** is recommended for patients starting long-term low-dose aspirin who have prior ulcer or GI bleeding.[1][2][6]
- The risk-benefit balance differs by indication: if a peptic ulcer develops on aspirin taken for **primary** prevention, aspirin is generally stopped; if taken for **secondary** prevention, it is usually continued with acid suppression.[7]

Separately, this presentation — hours of chest pain radiating to the left neck and shoulder with dyspnea, tachycardia, and "slight ECG changes" — warrants ACS evaluation with serial troponins and serial ECGs before it is framed as an outpatient primary-prevention aspirin discussion.

Would you like to explore which aspirin users warrant PPI co-therapy and at what dose?

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Question 327

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?

A. Perform hemodialysis
B. Perform C. difficile toxin assay
C. Measure serum drug concentration
D. Administer oral activated charcoal

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The correct answer is **C. Measure serum drug concentration** (digoxin level).[1][2][3]

This presentation is highly consistent with **chronic digoxin toxicity**. The classic triad includes **GI symptoms** (nausea, vomiting, diarrhea — present in 30–70% of overdosed patients), **visual disturbances** (blurry vision), and **cardiac manifestations** (relative bradycardia at 61/min in a patient with atrial fibrillation).[1][2] The **mild hyperkalemia** (K^+ 5.2 mEq/L) is also expected, as digoxin inhibits the Na^+ /K^+ ATPase pump.[4][5] Multiple risk factors predispose this patient to toxicity: **advanced age, female sex, chronic renal failure** (creatinine 1.3 mg/dL represents

significant impairment in an 89-year-old woman), and **concomitant spironolactone**, which may increase digoxin's half-life.[6][7]

Measuring the serum digoxin concentration, interpreted alongside the clinical picture and electrolytes, is the appropriate next diagnostic step. Toxicity is commonly associated with levels **>2 ng/mL**, though chronic toxicity can occur at lower levels, particularly in elderly patients with renal impairment.[1][2][4]

Why the other options are incorrect:

- **A. Hemodialysis** — Digoxin has a **large volume of distribution** and is **not effectively removed by dialysis**. The 2018 ACC/AHA/HRS bradycardia guidelines assign a **Class III (No Benefit)** recommendation to dialysis for digoxin removal.[2][8]
- **B. C. difficile toxin assay** — While the travel history and diarrhea could raise concern for an infectious etiology, C. difficile would not explain the visual disturbances, headache, or hyperkalemia pattern. The full constellation of symptoms is best unified by digoxin toxicity.
- **D. Activated charcoal** — Indicated for **acute massive ingestion** of digoxin (to interrupt enterohepatic recirculation), not for chronic toxicity developing over days in the setting of predisposing factors.[2][5]

Would you like to explore the indications and dosing for digoxin immune Fab in managing confirmed digoxin toxicity?

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Question 328

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?

A. Acute calculous cholecystitis
B. Acute acalculous cholecystitis
C. Acute pancreatitis
D. Ascending cholangitis

https://openevidence.com/ask/a3735c68-0a83-40b4-8cb8-b0c7e7e821f2

The answer is **A. Acute calculous cholecystitis**.

This presentation is a textbook case of acute calculous cholecystitis, supported by the following:

- **Positive Murphy sign**: The arrest of inspiration during deep palpation of the RUQ is **pathognomonic** for acute cholecystitis, with a sensitivity of 62% and specificity of 96%.[1][2]
- **Positive sonographic Murphy sign**: Tenderness elicited when the ultrasound probe presses over the gallbladder carries a **positive predictive value of 92%** for acute cholecystitis when gallstones are also present.[3][4]

- **Classic history**: Recurrent upper abdominal pain precipitated by food suggests prior biliary colic from gallstones, with this episode representing progression to acute cholecystitis (biliary colic typically resolves within 5 hours, whereas cholecystitis pain persists beyond 6 hours).[2]

- **Supportive labs**: **Leukocytosis** (18,000 with 79% neutrophils) and **low-grade fever** (38.3°C) are typical. The mildly elevated AST/ALT can occur from surrounding inflammation or direct compression of the biliary tree by the inflamed gallbladder.[1]

Why not the other options:

- **B. Acute acalculous cholecystitis** — Accounts for only 5–10% of cholecystitis cases and occurs predominantly in **critically ill, hospitalized patients** (ICU, post-surgical, sepsis), not in an otherwise healthy ambulatory patient with recurrent food-related episodes.[1]

- **C. Acute pancreatitis** — Effectively excluded by **normal serum amylase (46 U/L) and lipase (55 U/L)**. Lipase elevation ≥3 times the upper limit of normal is expected in acute pancreatitis.[1]

- **D. Ascending cholangitis** — Requires **Charcot's triad** (fever, jaundice, RUQ pain) and typically presents with a more prominent obstructive pattern (markedly elevated bilirubin, alkaline phosphatase, and GGT). The lab pattern here does not suggest biliary obstruction.[5]

Would you like to explore the optimal timing and surgical approach for cholecystectomy in acute cholecystitis?

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Question 329

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?

A. Phrenoesophageal ligament
B. Gastrohepatic ligament
C. Phrenicocolic ligament
D. Ligamentum venosum

https://openevidence.com/ask/9f94f7e7-64b4-41ab-ae26-40b78348ee2f

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The correct answer is **B. Gastrohepatic ligament**.

The space posterior to the stomach is the **lesser sac (omental bursa)**, and the pancreas forms part of its posterior wall. The **gastrohepatic ligament** — the thin, membranous portion of the lesser omentum connecting the lesser curvature of the stomach to the liver — can be divided to enter the lesser sac and expose the pancreas.

Multiple surgical descriptions confirm that **transecting the gastrohepatic ligament gains access to the lesser sac**, allowing inspection of the superior border of the pancreas and visualization of the splenic artery and vein.[1][2][3] This has been specifically described as a named approach ("gastrohepatic ligament approach") in minimally invasive distal pancreatectomy, where dividing the gastrohepatic ligament provides direct pancreatic access without needing to dissect the gastrocolic ligament or retract the stomach.[4][5] An important anatomic consideration during this approach is identifying and preserving an **accessory or replaced left hepatic artery** arising from the left gastric artery, which traverses the gastrohepatic ligament.[1][6]

Why the other choices are incorrect:

- **A. Phrenoesophageal ligament** — attaches the esophagus to the diaphragm at the hiatus; dividing it does not enter the lesser sac.
- **C. Phrenicocolic ligament** — connects the splenic flexure of the colon to the diaphragm; it defines the boundary of the left paracolic space, not the lesser sac.

- **D. Ligamentum venosum** — the fibrous remnant of the fetal ductus venosus on the posterior surface of the liver; it is not a peritoneal ligament that would be divided for surgical access.

Would you like to explore the technique and outcomes of laparoscopic enucleation versus formal resection for pancreatic insulinomas?

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Question 330

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?

A. Duodenal peptic ulcer
B. Gastric peptic ulcer
C. Pancreatitis
D. Perforated gastric peptic ulcer

https://openevidence.com/ask/935e9352-ccf7-4ff5-a833-903bd6869697

The answer is **D. Perforated gastric peptic ulcer**.

This presentation is classic for **peptic ulcer perforation** — the combination of a known history of poorly treated peptic ulcer disease, **sudden severe abdominal pain**, hematemesis, and critically, **board-like rigidity with rebound tenderness** (signs of diffuse peritonitis) points to perforation rather than an uncomplicated ulcer or pancreatitis.[1][2]

Why perforation, not uncomplicated ulcer (options A and B):

Uncomplicated gastric or duodenal ulcers present with dyspepsia, epigastric pain, and potentially bleeding (hematemesis/melena), but they **do not cause peritoneal signs** such as board-like rigidity and rebound tenderness.[2][3] The peritonitis in this case results from leakage of acidic gastric contents into the peritoneal cavity, which is pathognomonic of perforation.[1]

Why gastric rather than duodenal:

The brown/red vomitus (hematemesis) and the clinical context of a gastric-pattern presentation (nausea, vomiting, poor response to antacids) favor a **gastric** source. Gastric ulcers are more commonly associated with postprandial pain, nausea, and vomiting, whereas duodenal ulcers more typically cause hunger pain, nocturnal pain, and pain relief with eating.[4]

Why not pancreatitis (option C):

While pancreatitis can cause severe abdominal pain, it typically does not produce **board-like rigidity** — a hallmark of peritoneal irritation from viscus perforation. As noted in major reviews, pancreatitis is an important differential to exclude in perforated peptic ulcer because its management is primarily non-operative, unlike perforation.[1]

The **erect abdominal X-ray** is ordered to detect **pneumoperitoneum** (free air under the diaphragm), which is present in 30–85% of perforations and, in the appropriate clinical context, is sufficient to justify surgical exploration.[5][6] CT scanning has 98% diagnostic accuracy and is the gold standard when available.[7]

Would you like to explore the surgical management options for perforated peptic ulcer, including laparoscopic versus open repair?

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Question 331

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?

A. Meta-analysis
B. Cross-sectional
C. Case-control
D. Genome-wide association study

https://openevidence.com/ask/5d8ee050-a089-4017-bab8-90384703fbe4

The answer is **C. Case-control**.

This study has all the defining features of a **case-control design**: participants were classified by **outcome** (breast cancer = cases vs. no breast cancer = controls), and the investigators then **retrospectively** compared the prevalence of an **exposure** (bilateral salpingo-oophorectomy) between the two groups.[1][2] The reported measure of association — an **odds ratio** — is the characteristic statistic of case-control studies, as this design does not permit direct calculation of incidence rates or relative risk.[1]

As described in JAMA, a case-control study "works backward from outcome to exposure," comparing the odds of prior exposure among those with and without the outcome of interest.[1] That is precisely what occurred here: the researchers started with breast cancer status and looked back to determine surgical history.

Why the other options are incorrect:

- **A. Meta-analysis** — A meta-analysis statistically combines results from multiple independent studies. This scenario describes a single study.

- **B. Cross-sectional** — A cross-sectional study measures exposure and outcome at a single point in time in a population, providing a "snapshot." Here, the investigators specifically selected groups based on outcome and looked backward at exposure history, which is the retrospective directionality characteristic of a case-control design.[3]
- **D. Genome-wide association study (GWAS)** — A GWAS scans the genome for genetic variants associated with a trait. This study examined a surgical exposure, not genetic polymorphisms.

Would you like to explore the key biases in case-control studies and strategies to mitigate them?

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Question 332

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?

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

https://openevidence.com/ask/48786645-e534-46f5-b3bc-c1183235ec14

The answer is **A. Systolic murmur that increases with hand clenching**.

This child has a **membranous ventricular septal defect (VSD)** with signs of hemodynamic significance (failure to thrive, diaphoresis and dyspnea with feeding, decreased LVEF). A VSD produces a **pansystolic murmur** best heard at the left lower sternal border.[1] The murmur reflects left-to-right shunting driven by the pressure gradient between the ventricles.

Hand clenching (isometric handgrip) increases systemic vascular resistance (afterload), which widens the LV-to-RV pressure gradient and augments flow across the defect, making the VSD murmur louder.[2][3] Per ACC/AHA guidelines, murmurs of MR, VSD, and AR all increase with handgrip exercise.[3] A landmark NEJM study confirmed that the VSD murmur is augmented by handgrip with **68% sensitivity and 92% specificity**.[4]

Why the other options are incorrect:

- **B (increases with Valsalva):** The Valsalva maneuver decreases LV preload, which reduces most murmurs including VSD. The only systolic murmurs that increase with Valsalva are **HCM** and **MVP**.[2][3]
- **C (diastolic murmur with opening snap):** This describes **mitral stenosis**, not VSD. While a large VSD can produce an apical diastolic rumble from increased mitral inflow, it would not be accompanied by an opening snap.[5]

- **D (continuous murmur loudest at S2):** This describes a **patent ductus arteriosus (PDA)**, which produces a continuous "machinery" murmur peaking around S2 — a different lesion entirely.

Would you like to explore the indications for surgical closure of VSD in children with heart failure symptoms?

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Question 333

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?

A. Emergent fasciotomy
B. Venous doppler
C. Arteriogram
D. External fixation

https://openevidence.com/ask/d5db5a07-4f63-4687-9e46-608cca7e2d20

The correct answer is **A. Emergent fasciotomy**.

This patient presents with a **crush mechanism** (pinned under motorcycle for 30 minutes) and a clinical picture consistent with **acute compartment syndrome (ACS)**: asymmetric limb swelling, pain, paresthesias, paralysis, absent distal pulses, and pallor with coolness. The **measured compartment pressure of 35 mmHg exceeds the absolute threshold of 30 mmHg** traditionally considered indicative of impaired tissue perfusion requiring emergency surgical fasciotomy.[1][2] The American College of Surgeons best practice guidelines additionally recommend using the **delta pressure (ΔP = diastolic BP − compartment pressure)**, with fasciotomy indicated when ΔP < 30 mmHg.[3] In this clinical scenario, the unequivocal exam findings alone are sufficient to mandate decompression.

Why not the other options?

- **Arteriogram (C):** The absent pulses and pallor could raise concern for concomitant arterial injury. However, in confirmed ACS, **elevated intracompartmental pressure can externally compress vessels and cause pulselessness**, and delaying fasciotomy for additional vascular imaging risks irreversible tissue necrosis. Animal studies suggest **tissue necrosis can begin within 6 hours** of hypoxemia onset. An arteriogram may be appropriate after fasciotomy if

pulses do not return following decompression, but it should not precede fasciotomy. Notably, the EAST guidelines state that in the setting of hard signs of arterial injury, **surgical exploration** — not arteriography — is indicated, and fasciotomy would still be performed first or concurrently.[1][4]

- **Venous Doppler (B):** This presentation is not consistent with venous thromboembolism, and venous imaging would not address the surgical emergency.
- **External fixation (D):** This is used for fracture stabilization but is not the priority when ACS is present. Fracture management follows compartment decompression.

Key management considerations: Definitive treatment of ACS is **four-compartment fasciotomy** of the lower leg, typically via two incisions, with wounds left open.[1] Crush injuries carry additional risk of **rhabdomyolysis and reperfusion syndrome**, necessitating aggressive fluid resuscitation and monitoring for metabolic derangements including hyperkalemia, acidosis, and acute renal failure.[1]

Would you like to explore the management of rhabdomyolysis and crush syndrome following fasciotomy?

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Question 334

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?

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

https://openevidence.com/ask/11110d01-7ad2-4a04-a19e-6b9c39809978

The answer is **B. Conservative management with IV fluid hydration and observation**.

This presentation is a classic **Mallory-Weiss tear** — a longitudinal mucosal laceration at the gastroesophageal junction caused by forceful vomiting in the setting of alcohol intoxication. The critical detail is that **EGD shows no active bleeding**, which dictates the management approach.

Why conservative management is correct:

Mallory-Weiss tears are **self-limiting in over 90% of cases**.[1] Endoscopic hemostatic therapy (injection, clips, electrocoagulation, banding) is reserved for tears with **active bleeding or hemodynamic instability**.[2][3] In non-bleeding Mallory-Weiss tears, the rebleeding risk is very low — a study of 66 patients with non-bleeding tears managed without endoscopic therapy found only 1 rebleeding episode, which itself did not require intervention.[3] Both U.S. (ASGE) and European guidelines recommend that **only patients with ongoing or severe bleeding require endoscopic therapy**.[2][3]

Why the other options are incorrect:

- **A (Cyanoacrylate injection and banding):** Cyanoacrylate is used for **gastric variceal bleeding**, not Mallory-Weiss tears. Banding could be used for actively bleeding tears, but there is no active bleeding here.

- **C (Esophageal manometry and impedance studies):** These are motility diagnostic tests used in the workup of conditions such as achalasia or GERD; they have no role in the acute management of a Mallory-Weiss tear.
- **D (Calcium channel blockers and Botox injection of the LES):** This is a treatment strategy for **achalasia**, not Mallory-Weiss syndrome.

Would you like to explore the risk factors for rebleeding in Mallory-Weiss syndrome and thresholds for endoscopic intervention?

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Question 335

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?

A. Tinea corporis
B. Tinea cruris
C. Candidal balanitis
D. Tinea unguium

https://openevidence.com/ask/e1c85904-5041-4390-a877-b0992b0cc91b

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The answer is **B. Tinea cruris**.

This presentation is classic for **tinea cruris** ("jock itch") — a dermatophyte infection of the **groin, perineal, and perianal area**, most common in adolescent and adult males.[1][2] Several features in this vignette point specifically to this diagnosis:

- **Distribution**: The erythematous, well-demarcated patch involves the thigh, pubic region, and perineum — the characteristic sites for tinea cruris.[1][3]
- **Scrotal sparing**: This is a hallmark distinguishing feature of tinea cruris, helping differentiate it from candidal infections and other groin dermatoses, which tend to involve the scrotum.[1]
- **Pruritis**: Itch is the predominant complaint in tinea cruris.[1]
- **Wrestling participation**: Direct skin-to-skin contact in wrestling is a well-recognized transmission route for dermatophyte infections.[1][3]

Why not the other choices?

- **A. Tinea corporis** — By definition, tinea corporis refers to dermatophyte infection of the body **excluding** the groin, scalp, beard area, hands, and feet. The groin-specific location makes tinea cruris the correct classification.[1]

- **C. Candidal balanitis** — This involves the glans penis and would not present as an inguinal/perineal rash with scrotal sparing.
- **D. Tinea unguium** — This is onychomycosis (nail fungal infection), which is not consistent with the described skin findings.[4]

Would you like to explore first-line treatment options for tinea cruris in athletes?

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Question 336

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?

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

https://openevidence.com/ask/fec5be27-9700-4305-b3b9-8e72f473cf3a

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The 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, and diplotene). By the end of fetal life, all primary oocytes have reached the **diplotene/dictyate stage of prophase I**, where they arrest.[1][2] At birth, a newborn female has approximately **1–2 million primary oocytes** already formed and arrested at this stage.[3][4] These oocytes remain in prophase I arrest from birth until puberty, when the preovulatory LH surge triggers meiotic resumption in individual oocytes during each ovulatory cycle.[5][6]

Why the other options are incorrect:

- **A (oocytes not yet developed):** Oocytes form during fetal life; by 20 weeks' gestation, there are 6–7 million oogonia, and by birth all have differentiated into primary oocytes.[3][4]
- **C (arrested in interphase):** Interphase is not part of meiotic prophase. The arrest occurs specifically at the **diplotene substage of prophase I** (also called the dictyate stage), not interphase.[1][7]
- **D (fully matured):** Full maturation (to metaphase II) does not occur until after puberty, triggered by the LH surge, and completion of meiosis II only occurs upon fertilization.[7][8]

Would you like to explore the molecular mechanisms maintaining oocyte meiotic arrest and triggering resumption?

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Question 337

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?

A. Red blood cell transfusions
B. Gluten-free diet
C. Vitamin B12 injections
D. Folic acid supplementation

https://openevidence.com/ask/67f63a78-6739-4340-a66e-8e594558cc56

The answer is **D. Folic acid supplementation**.

This child has **hereditary spherocytosis (HS)** complicated by **folate deficiency**. The underlying diagnosis is established by erythrocytes without central pallor (spherocytes) on peripheral smear, a family history of early cholecystectomy for gallstones (father at age 26), splenomegaly, and scleral icterus.[1] The chronic hemolysis in HS drives accelerated erythropoiesis, which markedly increases folate demand; without supplementation, this leads to folate depletion — particularly in **growing children**, who already have higher baseline requirements.[1]

The superimposed folate deficiency explains the current presentation: **glossitis** (swollen, red tongue), **oral ulcers**, and a **burning mouth sensation** are classic mucosal manifestations of folate (or B12) deficiency, resulting from impaired DNA synthesis in the rapidly turning over oral epithelium.[2][3] The **macrocytic anemia** (MCV 104 fL) layered on top of the underlying hemolytic anemia (reticulocyte count 9%) further supports megaloblastic change from folate deficiency.[1][4] The hyperpigmentation over dorsal surfaces and skin creases is also a recognized feature of folate/B12 deficiency.

Why not the other options:

- **A (RBC transfusions)** — Transfusions treat acute anemia but do not address the underlying folate deficiency causing the oral symptoms.
- **B (Gluten-free diet)** — Relevant to celiac disease, which is not supported by this clinical picture.
- **C (Vitamin B12 injections)** — While B12 deficiency produces similar oral findings, it is **not** a recognized complication of HS. Folate deficiency is the expected nutritional consequence of chronic hemolysis due to the increased erythropoietic demand for folate. B12 deficiency more characteristically produces neurological findings (paresthesias, subacute combined degeneration), though their absence does not exclude it.[1][5]

Preventive folic acid supplementation is specifically recommended for unsplenectomized patients with HS to prevent megaloblastic crises — guidelines suggest **1 mg daily for children under 5 years and 5 mg daily thereafter**.[1][6][7]

Would you like to explore the indications and timing for splenectomy in pediatric hereditary spherocytosis?

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Question 338

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?

A. Sitagliptin
B. Glimepiride
C. Canagliflozin
D. Pioglitazone

https://openevidence.com/ask/0b33ed16-4931-4521-8c8c-52bfbfb8d666

The answer is **A. Sitagliptin**.

The experimental drug described — one that **increases incretin levels by preventing their degradation**, thereby enhancing **glucose-dependent insulin secretion** — mirrors the mechanism of **DPP-4 inhibitors**. Sitagliptin is a DPP-4 inhibitor that slows the inactivation of the incretin hormones GLP-1 and GIP by inhibiting the enzyme dipeptidyl peptidase-4 (DPP-4), which is expressed on endothelial and other cell surfaces.[1][2] This increases circulating intact incretin levels, which in turn stimulates insulin secretion and suppresses glucagon in a **glucose-dependent** manner.[1][3]

The phrase "preventing their degradation at the endothelium" is the key clue — DPP-4 is an enzyme prominently expressed on endothelial cell surfaces, where it cleaves and inactivates circulating incretins.[2][4]

The other options have distinct mechanisms:

- **Glimepiride** — a sulfonylurea that directly stimulates insulin release from pancreatic beta cells by closing K-ATP channels, independent of incretins or glucose levels.
- **Canagliflozin** — an SGLT2 inhibitor that lowers glucose by blocking renal glucose reabsorption in the proximal tubule.
- **Pioglitazone** — a thiazolidinedione that acts as a PPARγ agonist, improving insulin sensitivity in peripheral tissues.

Would you like to explore the clinical differences between DPP-4 inhibitors and GLP-1 receptor agonists?

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Question 339

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?

A. Airway epithelial shedding
B. Airway smooth muscle atrophy
C. Airway remodeling
D. Airway hyperresponsiveness

https://openevidence.com/ask/3ecf86f5-1757-4b03-aee0-e26be50930f8

The answer is **C. Airway remodeling**.

This patient has had **severe persistent asthma for ~46 years** and now demonstrates **partial irreversible airway obstruction** on spirometry with loss of control despite good compliance with high-dose inhaled corticosteroids — a clinical picture characteristic of cumulative airway remodeling.

Airway remodeling refers to the progressive structural changes that occur in chronically inflamed asthmatic airways, including subepithelial fibrosis, airway smooth muscle **hypertrophy and hyperplasia**, goblet cell hyperplasia, basement membrane thickening, and increased vascularity.[1][2] These changes result in **fixed airflow limitation and reduced treatment reversibility**.[1] Asthmatic patients experience an accelerated decline in lung function proportional to the **duration and severity** of their disease, which is directly relevant to this patient's decades-long disease course.[3] Airway smooth muscle mass is the **strongest predictor of airflow limitation**, and the structural thickening and fibrosis diminish bronchodilator responsiveness.[1][2]

Why not the other choices:

- **A. Airway epithelial shedding** — A component of the remodeling process but alone does not explain the progressive, partially irreversible obstruction or loss of control despite therapy.
- **B. Airway smooth muscle atrophy** — The opposite occurs in chronic asthma; smooth muscle undergoes **hypertrophy and hyperplasia**, not atrophy.[1][2][4]
- **D. Airway hyperresponsiveness** — Present from early in the disease and is a hallmark of asthma in general. It does not specifically explain the new development of **irreversible** obstruction and treatment failure after decades of disease. In fact, airway remodeling itself can contribute to a persistent component of hyperresponsiveness, making remodeling the upstream driver.[1][5]

The spirometry finding of partial irreversibility is the critical clue — it reflects **permanent structural change** rather than purely functional bronchospasm, pointing squarely to remodeling as the mechanism behind this patient's deterioration.

Would you like to explore current and emerging therapies targeting airway remodeling in severe asthma?

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Question 340

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?

A. Past hepatitis B infection
B. Acute hepatitis A
C. Acute hepatitis D superinfection
D. Acute hepatitis B

https://openevidence.com/ask/d4668ac8-2b19-4269-827c-6607c7ff27c8

The correct answer is **D. Acute hepatitis B**.

The serologic pattern in this case is diagnostic of **acute HBV infection**: **HBsAg positive** (indicating current infection) combined with **IgM anti-HBc positive** (the hallmark of acute or recently acquired infection).[1][2][3] As the CDC STI Treatment Guidelines state, "presence of IgM antibody to hepatitis B core antigen (IgM anti-HBc) is diagnostic of acute or recently acquired HBV infection".[2] The markedly elevated ALT (2,000 IU/L), jaundice, and fatigue further support an acute hepatitis presentation.

The other options are ruled out by this serologic panel:

- **A. Past hepatitis B infection** — Would show **HBsAg negative**, **anti-HBs positive**, and **IgG anti-HBc positive** (not IgM). This patient has active HBsAg and IgM anti-HBc, inconsistent with resolved infection.[1][4]
- **B. Acute hepatitis A** — Ruled out by the **negative anti-HAV IgM**.
- **C. Acute hepatitis D superinfection** — Ruled out by the **negative anti-HDV**. HDV requires co-infection with HBV, but no HDV serologic evidence is present.

The clinical context is also informative: the patient has risk factors for HBV acquisition including **IV drug use** and **emigration from an endemic region (Africa) without documented immunization**.[1] In acute HBV infection in immunocompetent adults, approximately 30% develop symptomatic hepatitis with fatigue, jaundice, and abdominal discomfort, as seen here, while about 95% of adults will spontaneously clear the infection.[1]

Would you like to explore the management of acute hepatitis B, including indications for antiviral therapy?

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Question 341

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?

A. Antibodies directed against platelet glycoprotein IIb/IIIa
B. Antibodies directed against phospholipids
C. Antibodies directed against endothelial cells
D. Vitamin K deficiency

https://openevidence.com/ask/d10c7705-1ba5-4ea6-98a2-cb67285d2af0

The answer is **B. Antibodies directed against phospholipids**.

This presentation is classic for **antiphospholipid syndrome (APS)** in the setting of SLE. The clinical triad here — **venous thrombosis** (popliteal DVT), **pregnancy loss at 12 weeks**, and a **markedly prolonged PTT that fails to correct on mixing study** — points directly to antiphospholipid antibodies (lupus anticoagulant).[1]

Key lab interpretation: The PTT is severely prolonged at 90 seconds with a normal PT (14 seconds). The mixing study remains prolonged at 89 seconds, indicating an **inhibitor** rather than a factor deficiency. A factor deficiency would correct upon mixing with normal plasma (which supplies the missing factor), whereas an inhibitor — in this case, lupus anticoagulant — continues to interfere with phospholipid-dependent coagulation steps even after mixing.[2][3][4]

> "When combined with thrombosis or obstetrical complications, the following clinical findings may be a clue that a patient has the antiphospholipid syndrome: livedo, signs or symptoms of another systemic autoimmune disease, unexplained prolongation of the aPTT, or mild thrombocytopenia."
>
> —David Garcia, M.D. et al., University of Washington and other institutions. Diagnosis and Management of the Antiphospholipid Syndrome. N Engl J Med. May 24, 2018.
>
> Used under license from The New England Journal of Medicine.

Antiphospholipid antibodies are found in approximately **30–40% of patients with SLE** and are the main triggers of thrombosis in this population.[5][6] Paradoxically, the lupus anticoagulant prolongs clotting times in vitro while promoting a hypercoagulable state in vivo. Pregnancy complications in APS typically develop **after 10 weeks of gestation**, consistent with this patient's 12-week loss.[1]

Why not the other options:

- **A. Anti-GPIIb/IIIa antibodies** — These cause immune thrombocytopenic purpura (ITP), presenting with low platelets and bleeding, not thrombosis or a prolonged PTT. This patient's platelets are normal.
- **C. Anti-endothelial cell antibodies** — Not the mechanism underlying APS and not associated with a prolonged, noncorrecting PTT.
- **D. Vitamin K deficiency** — Would prolong **both** PT and PTT and would **correct** on mixing study, since the issue is factor deficiency, not an inhibitor.

Would you like to explore the recommended anticoagulation approach for secondary thromboprophylaxis in antiphospholipid syndrome?

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Question 342

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?

A. Staphylococcus aureus
B. Streptococcus pyogene
C. Streptococcus pneumoniae
D. Non-typeable H. influenzae

https://openevidence.com/ask/fbd005ac-aa16-41e5-9732-35ff8d6bed07

C. Streptococcus pneumoniae

This is overwhelming post-splenectomy infection (OPSI). The teenage motor vehicle accident requiring surgery points to traumatic splenectomy, and the peripheral smear in an asplenic patient characteristically shows **Howell-Jolly bodies** — and in fulminant pneumococcal sepsis the bacteremia can be dense enough that gram-positive diplococci are visible within neutrophils or free in the plasma on the buffy coat/blood smear.[1] The autopsy Gram stain description — **gram-positive, lancet-shaped diplococci** — is the classic morphology of S. *pneumoniae*.[2][3]

Why the presentation fits

- **Pathogen frequency:** S. *pneumoniae* is the most common cause of post-splenectomy sepsis, accounting for >50% of infections in asplenic patients. In a prospective multicenter

ICU cohort, pneumococcus was identified in 42% of OPSI patients vs 12% of non-asplenic septic patients ($P < .001$), and asplenia was the only independent predictor of pneumococcal sepsis (aRR 2.53, 95% CI 1.06–6.08).[1][4][5]

- **Tempo and features:** OPSI has a brief nonspecific prodrome (fever, chills, myalgias, vomiting, **diarrhea**), often with no localizing focus, followed by abrupt deterioration within hours, shock, DIC, and profound hypoglycemia; mortality reaches 50% despite maximal care.[1][4]
- **DIC/purpura fulminans:** Purpura fulminans complicated 19% of OPSI cases vs 5% of non-asplenic sepsis, and in adults pneumococcus is the organism most often implicated in infectious purpura fulminans. Non-meningococcal Waterhouse–Friderichsen syndrome in asplenic/hyposplenic patients is most often pneumococcal.[5][6][7]
- **Timing:** Decades-long latency is typical — half of pneumococcal purpura fulminans episodes in asplenic patients occurred a median 20 years after splenectomy, consistent with splenectomy in adolescence and presentation at age 30.[8]
- **Absent immunization:** Recent immigration makes lack of post-splenectomy pneumococcal vaccination likely; vaccine coverage in these cohorts was only 35–42%.[5][8]

Why not the others

- **S. aureus** — gram-positive cocci in grape-like clusters, not lancet-shaped diplococci; accounts for only a small fraction of asplenic bloodstream isolates and asplenia is not an established risk factor.[1]
- **S. pyogenes** — gram-positive cocci in chains, but not lancet-shaped/encapsulated diplococci; causes toxic shock with erythroderma and usually a soft-tissue or pharyngeal portal of entry. It is a reported but uncommon cause of purpura fulminans.[6]
- **Non-typeable H. influenzae** — gram-negative pleomorphic coccobacilli, and being unencapsulated it is not the organism of encapsulated-organism sepsis in asplenia (that risk applies to Hib).[9]

Practical corollary: any asplenic patient with fever of any severity warrants immediate empiric coverage (e.g., ceftriaxone, with vancomycin if resistant pneumococcus or meningitis is a concern) and blood cultures, before deterioration.[1] Lifelong pneumococcal, meningococcal, and Hib vaccination plus a patient-held emergency antibiotic supply are the preventive standard.[9][10]

Would you like to explore the current vaccination and antibiotic prophylaxis regimens recommended for asplenic adults?

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Question 343

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?

A. Autoantibody-mediated tissue damage
B. Complement inhibitor deficiency
C. Drug-induced bradykinin excess
D. Mast-cell activation

https://openevidence.com/ask/a94c23ba-922b-47d4-a7a5-9886ebb14990

B. Complement inhibitor deficiency — C1 esterase inhibitor deficiency (hereditary angioedema type I/II from SERPING1 mutation), in which loss of C1-INH regulation of factor XIIa and plasma kallikrein produces unchecked bradykinin generation and B2-receptor–mediated vascular leak.[1][2][3]

Why the vignette fits HAE

- **Nonpruritic, nonpitting, non-urticarial facial/lip/tongue swelling** is the hallmark of bradykinin-mediated angioedema; absence of itching, hives, and hypotension argues against a mast-cell process.[1][4][5]
- **Trauma as trigger:** dental extraction and the prior bicycle accident are classic physical triggers; mechanical trauma to the oropharynx is a well-recognized precipitant.[3][6]
- **Abdominal attack with segmental bowel wall thickening:** submucosal intestinal edema causes colicky pain, vomiting, and imaging findings of segmental wall edema ± ascites, often mimicking an acute abdomen and leading to unnecessary surgery.[1][6][7]

- **Age and course:** onset typically in childhood (mean 8–12 years), with attacks that worsen over ~24 h and remit over 48–72 h without treatment, as in her prior self-resolving episode.[1][6]

Why the others are wrong

- **A. Autoantibody-mediated tissue damage** — describes acquired C1-INH deficiency (anti-C1-INH antibodies), which occurs in older adults with lymphoproliferative or autoimmune disease, not a 12-year-old with recurrent trauma-triggered attacks.[5]
- **C. Drug-induced bradykinin excess** — ACE-inhibitor angioedema is bradykinin-mediated but requires ACE-inhibitor exposure and is a disease of adults; no such drug here.[4][5]
- **D. Mast-cell activation** — would produce pruritus, urticaria, flushing, and often bronchospasm/hypotension, and responds to antihistamines/epinephrine; isolated angioedema without wheals plus recurrent GI attacks points away.[8][9]

Clinically actionable corollaries

- **Confirmatory testing:** C4 (low during and usually between attacks, a practical screen), then C1-INH antigen and functional levels; C1q distinguishes hereditary from acquired deficiency.[7][9][10]
- **Treatment:** epinephrine, antihistamines, and glucocorticoids are ineffective; on-demand therapy is plasma-derived/recombinant C1-INH, icatibant, or ecallantide, and short-term prophylaxis should be given before future dental or surgical procedures. Airway involvement (tongue enlargement here) warrants close monitoring, since laryngeal attacks occur in >50% of patients over a lifetime and can be fatal.[1][3]

Would you like to explore short-term prophylaxis regimens before dental or surgical procedures in pediatric HAE?

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Question 344

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?

A. Aspirin
B. Isosorbide dinitrate
C. Heparin
D. Propranolol

https://openevidence.com/ask/6dedfd7f-526d-47c3-9ec6-a84feabe6304

The answer is **B. Isosorbide dinitrate**.

This presentation is classic for **Prinzmetal (vasospastic) angina**: recurrent rest angina in a young patient without cardiovascular risk factors, episodes occurring nocturnally and at random times unrelated to exertion, lasting minutes and resolving spontaneously.[1]

Why isosorbide dinitrate is correct: Coronary vasospasm is highly responsive to nitrates and calcium channel blockers. The ACC/AHA guidelines identify long-acting nitrates and CCBs as first-line therapies for vasospastic angina.[2] A randomized crossover trial directly comparing isosorbide dinitrate with nifedipine in patients with coronary artery spasm found both drugs equally efficacious.[3] Among the available answer choices, isosorbide dinitrate is the only agent with established benefit.

Why the other options are incorrect:

- **A. Aspirin** — A meta-analysis found aspirin did not reduce major adverse cardiovascular events in vasospastic angina without significant coronary artery disease. Aspirin may even contribute to vasospasm via **prostacyclin inhibition**.[4]

- **C. Heparin** — Anticoagulation has no role in the management of vasospastic angina, which is driven by smooth muscle hyperreactivity rather than thrombosis.
- **D. Propranolol** — Beta-blockers should be **avoided** in vasospastic angina. Propranolol potentiates coronary vasoconstriction through **unopposed alpha-adrenergic activity**, which can worsen spasm. Guidelines explicitly note their potential detrimental effect in this condition.[2][5][6]

Would you like to explore the diagnostic workup and provocative testing for vasospastic angina?

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Question 345

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?

A. Bed rest and activity limitation
B. Ganciclovir
C. Amoxicillin
D. Prednisone

https://openevidence.com/ask/dbc181c0-4783-4c25-8775-25ca3e244b00

The answer is **A. Bed rest and activity limitation**.

This presentation is classic for **EBV infectious mononucleosis**: an adolescent with fever, pharyngitis, tonsillar exudate, posterior auricular lymphadenopathy, splenomegaly, atypical lymphocytes, and a positive heterophile antibody test. IM is a **self-limited illness managed with supportive care**.[1][2] Given the presence of **splenomegaly**, activity restriction — particularly avoidance of contact sports and heavy exertion — is recommended for **at least 3 weeks** from symptom onset to reduce the risk of splenic rupture.[1][2][3]

Notably, while strict bed rest is not required per the NEJM review,[2] **activity limitation is the critical intervention** among the answer choices and reflects the standard of care for uncomplicated IM with splenomegaly.

Why the other options are incorrect:

- **B. Ganciclovir** — Antiviral therapy has **not been shown to diminish the severity or duration** of IM symptoms, as the clinical syndrome is driven by the immune response rather than direct viral cytopathology. Routine antiviral use is not recommended.[1][3][4]
- **C. Amoxicillin** — Penicillin-class antibiotics should be **specifically avoided** in IM because they trigger a characteristic **diffuse maculopapular rash** in a high proportion of patients. If

coexisting streptococcal pharyngitis requires treatment, a non-penicillin antibiotic should be used.[3]

- **D. Prednisone** — Corticosteroids are **not recommended for uncomplicated IM** (SORT A recommendation). They are reserved for severe complications such as **impending airway obstruction, hemolytic anemia, severe thrombocytopenia, or myocarditis**. This patient's tonsils are not notably enlarged, so there is no indication.[1][4][5]

Would you like to explore the latest return-to-play guidelines for athletes recovering from infectious mononucleosis?

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Question 346

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?

A. Catecholamines
B. Glucagon
C. Glucocorticoids
D. Peroxisome proliferator-activated receptor gamma

https://openevidence.com/ask/693052f5-d4f6-4e0a-bf1d-11e8959acd42

The answer is **D. Peroxisome proliferator-activated receptor gamma (PPARγ)**.

PPARγ is a nuclear receptor and master regulator of adipogenesis, lipid metabolism, and insulin sensitivity.[1][2] Activation of PPARγ improves glucose tolerance and whole-body insulin sensitivity, which is the basis for the thiazolidinedione (TZD) class of antidiabetic drugs.[3][4] PPARγ enhances insulin sensitivity through multiple mechanisms, including promoting appropriate lipid storage in adipose tissue (protecting muscle and liver from lipid overload), stimulating adiponectin secretion, and upregulating glucose transporter translocation.[4][5][6]

The other three options are all **counter-regulatory hormones that induce insulin resistance**:[7][8]

- **Catecholamines** antagonize insulin by stimulating gluconeogenesis, glycogenolysis, and lipolysis, and by inhibiting peripheral glucose uptake via β-adrenergic mechanisms — epinephrine reduces insulin-mediated glucose metabolism by ~41%.[7][9]
- **Glucagon** opposes insulin action primarily in the liver by stimulating glycogenolysis and gluconeogenesis.[7]
- **Glucocorticoids** impair insulin sensitivity by reducing the number or efficacy of glucose transporters, increasing hepatic insulin resistance, and elevating circulating free fatty acids

— up to 70% of patients with Cushing syndrome develop impaired glucose tolerance or diabetes.[7][10]

This patient's presentation — obesity (BMI 34), impaired fasting glucose (120 mg/dL), and impaired glucose tolerance (2-hour glucose 190 mg/dL) — is consistent with **prediabetes driven by insulin resistance**, making PPARγ activation clinically relevant as a pathway that would improve her insulin sensitivity.

Would you like to explore current ADA guidelines on prediabetes diagnosis and management?

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Question 347

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?

A. Anti-Smith antibodies
B. Anti-neutrophil antibodies
C. Anti-mitochondrial antibodies
D. Anti-glomerular basement membrane antibodies

https://openevidence.com/ask/0be9c30c-cd62-41a7-91b6-9ed89c02155b

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The answer is **D. Anti-glomerular basement membrane antibodies**.

This presentation — a **young male with hemoptysis, bilateral pulmonary consolidation, hematuria with RBC casts, and oliguria (400 mL/24 hours)** — is the classic **pulmonary-renal syndrome of Goodpasture disease (anti-GBM disease)**. It is caused by autoantibodies directed against the **α3 chain of type IV collagen** found in glomerular and alveolar basement membranes. [1][2]

Why the other options are incorrect:

- **A. Anti-Smith antibodies** — Associated with **systemic lupus erythematosus (SLE)**. While SLE can cause renal disease (lupus nephritis), it does not typically present as an isolated pulmonary-renal syndrome with diffuse alveolar hemorrhage and rapidly progressive GN in this classic fashion.
- **B. Anti-neutrophil antibodies (ANCA)** — ANCA-associated vasculitis (e.g., GPA, MPA) can cause a pulmonary-renal syndrome, but the classic triad of hemoptysis from diffuse alveolar hemorrhage, RBC casts, and oliguria in a young male is most characteristic of anti-GBM disease. Additionally, ANCA-associated vasculitis typically involves additional features such as ENT involvement, skin vasculitis, or neuropathy.[2][3]
- **C. Anti-mitochondrial antibodies** — Associated with **primary biliary cholangitis**, a hepatic condition with no relevance to a pulmonary-renal syndrome.

Key supporting features for anti-GBM disease in this case:

- **Male sex and young age** — Anti-GBM disease with pulmonary involvement is more frequent in men (~80%) and typically occurs in the second to third decade of life.[1][2]
- **Oliguria** — Patients are frequently oliguric or anuric at presentation, reflecting the severity and rapidity of glomerular injury.[2]
- **RBC casts** — Indicate glomerulonephritis, consistent with the crescentic necrotizing GN seen in anti-GBM disease.[4]
- **Bilateral pulmonary consolidation with hemoptysis** — Reflects diffuse alveolar hemorrhage, present in 40–60% of anti-GBM disease cases.[1][4]

Would you like to explore the treatment protocol for anti-GBM disease, including plasmapheresis and immunosuppressive regimens?

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Question 348

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?

A. Pyridostigmine
B. Physostigmine
C. Hydrocortisone
D. Azathioprine

https://openevidence.com/ask/7080adac-e523-4b21-9324-7065f5f6cb45

A. Pyridostigmine.

This is ocular myasthenia gravis — fatigable, diurnally worsening diplopia and asymmetric bilateral ptosis with spared pupils and normal visual acuity, plus generalized fatigue, in a young woman with a personal/family history of autoimmunity (type 1 diabetes, maternal Sjögren's). Ocular symptoms are the presenting feature in ~85% of MG patients, with asymmetric ptosis that fatigues on sustained upgaze and fluctuating diplopia; pupillary function is always spared, which distinguishes MG from a compressive third nerve palsy.[1][2] Note that "extraocular movements intact" does not exclude ocular MG — ptosis alone with fatigability is sufficient, and subtle ophthalmoparesis is often missed on brief exam.

Why pyridostigmine

- Acetylcholinesterase inhibition is the first-line symptomatic therapy across all MG subgroups, and pyridostigmine is the preferred agent. The 2020 International Consensus Guidance states pyridostigmine should be part of the initial treatment in most patients with MG, with dose titrated to symptoms.[3][4][5]

- For purely ocular or mild generalized disease, pyridostigmine alone is often sufficient. Typical starting dose is 30–60 mg PO every 4–6 hours while awake, titrated to effect; dose-limiting side effects are muscarinic (cramping, diarrhea, salivation, urinary urgency).[3][4][6]
- Ptosis tends to respond better than ophthalmoparesis, so residual diplopia is common and may later require escalation.

Why not the others

- **Physostigmine (B)** is a tertiary-amine cholinesterase inhibitor that crosses the blood-brain barrier; it is used for central anticholinergic toxicity, not MG. Pyridostigmine's quaternary structure keeps it peripherally restricted.
- **Hydrocortisone (C)** — corticosteroids are the initial immunosuppressant in ocular MG, but only when symptoms remain functionally limiting after an adequate anticholinesterase trial. Prednisone (typically low-dose, ~10–20 mg/d in ocular disease) rather than hydrocortisone would be the agent, and steroids carry particular risk here given type 1 diabetes and predictable glycemic destabilization.[4][7]
- **Azathioprine (D)** is a second-line, steroid-sparing agent used when corticosteroids fail, are contraindicated, or cannot be tapered; its effect is delayed 6–15 months, making it inappropriate as initial therapy.[4][5][8]

Concurrent workup (not a substitute for starting pyridostigmine): AChR-binding antibodies (and MuSK if negative), chest CT for thymoma, and single-fiber EMG if serology is negative. Screen for coexisting thyroid disease given the autoimmune background. Counsel on generalization risk — roughly 50–80% of ocular-onset patients generalize, most within 2 years — and on warning symptoms of bulbar or respiratory involvement.[1][9]

Would you like to explore whether early immunosuppression reduces the risk of generalization in ocular myasthenia gravis?

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Question 349

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?

A. Echocardiogram
B. International normalized ratio
C. Partial thromboplastin time
D. Serum drug levels

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The answer is **B. International normalized ratio (INR)**.

INR is the standard monitoring parameter for warfarin therapy, used to assess both adherence and therapeutic efficacy.[1][2] This patient has atrial fibrillation with a prior ischemic stroke and is on warfarin for secondary stroke prevention. The **target INR is 2.0–3.0** (aiming for 2.5) for nonvalvular AF, as recommended by the 2023 ACC/AHA/ACCP/HRS AF guidelines and the FDA label.[2][3] Warfarin has a **narrow therapeutic index** with high interpatient dosing variability, making routine INR monitoring critical — a subtherapeutic INR indicates either nonadherence or underdosing (risking recurrent thromboembolism), while a supratherapeutic INR increases bleeding risk.[1][3]

Why the other options are incorrect:

- **A. Echocardiogram** — Evaluates cardiac structure and function. The patient has no significant structural, valvular, or ischemic heart disease, and an echocardiogram does not assess anticoagulant adherence or efficacy.

- **C. Partial thromboplastin time (PTT)** — Monitors **heparin** therapy, not warfarin. Warfarin primarily affects the extrinsic pathway (factors II, VII, IX, X), which is reflected by the **prothrombin time/INR**, not the PTT.[1]
- **D. Serum drug levels** — Warfarin is not monitored by serum drug concentrations. Its pharmacologic effect is assessed functionally via the INR, because the clinical response depends on clotting factor depletion rather than plasma drug level.[2]

Would you like to explore whether switching to a DOAC might be preferable over continued warfarin for this patient?

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Question 350

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?

A. Convergent validity
B. Discriminant validity
C. Negative predictive value
D. Test specificity

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The answer is **C. Negative predictive value**.

Lowering the cut-off from 5 mm to 4 mm classifies more individuals as test-positive, which **increases sensitivity** (capturing more true positives) at the expense of **decreased specificity** (more false positives).[1][2] This inverse relationship between sensitivity and specificity when adjusting a continuous threshold is well established. Data from a JAMA systematic review of TST performance illustrate this directly: as the induration threshold decreases from 15 mm to 10 mm to 5 mm, pooled sensitivity rises (0.60 → 0.81 → 0.80) while specificity falls (0.99 → 0.98 → 0.95).[3] Similarly, a study in non-U.S.-born persons showed sensitivity/specificity of 55.6%/88.0% at 15 mm, 81.7%/71.3% at 10 mm, and 86.5%/61.6% at 5 mm.[4]

The key consequence for **negative predictive value (NPV)** is that higher sensitivity means **fewer false negatives**. Since NPV = true negatives / (true negatives + false negatives), reducing false negatives increases NPV — among those who screen negative, a greater proportion truly lack disease.[2][5]

The other options are incorrect:

- **Specificity (D)** decreases with a lower threshold, as more healthy individuals are misclassified as positive.[1]
- **Convergent validity (A)** and **discriminant validity (B)** are psychometric constructs related to how well a test correlates with related or unrelated measures, respectively; they are not directly altered by adjusting a diagnostic threshold.

Would you like to explore how ROC curves are used to select optimal cut-off thresholds for TB screening tests?

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Question 351

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?

A. Phenobarbital administration
B. Plasma exchange
C. Switch from breast milk to formula
D. Continue normal breast feeding

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The answer is **D. Continue normal breastfeeding**.

This vignette describes **breast milk jaundice**, a benign, self-limited unconjugated hyperbilirubinemia occurring in a healthy, thriving, breastfed infant at one week of age. Per the AAP, breast milk jaundice occurs with adequate human milk intake and weight gain, can persist up to 3 months, and **no treatment is necessary**.[1][2]

Key distinctions among the answer choices:

- **Phenobarbital** (A) is not part of standard management of neonatal jaundice. It has been used historically as an enzyme inducer in rare conditions (e.g., Crigler-Najjar type II) but has no role in breast milk jaundice.
- **Plasma exchange** (B) is reserved for severe hemolytic disease (e.g., refractory hemolysis); it is not indicated here.
- **Switching to formula** (C) is incorrect. While discontinuing breastfeeding can accelerate bilirubin decline, the AAP explicitly discourages interrupting breastfeeding because it increases the risk of early breastfeeding discontinuation and is not warranted in an otherwise well infant with breast milk jaundice. Breastfeeding interruption is also no longer recommended as a diagnostic maneuver.[3][4]

- **Continuing breastfeeding** (D) is correct. The AAP states that breast milk jaundice in a healthy, thriving infant with appropriate weight gain "is almost always nonpathologic" and requires continued breastfeeding with reassurance.[1][2]

One important clinical note: this infant is sleeping 7–8 hours uninterrupted at night, which means fewer than the recommended 8+ feedings per 24 hours. While the question frames this as a well-feeding infant (pointing toward breast milk jaundice rather than suboptimal intake jaundice), in practice one would counsel the mother to increase feeding frequency, as breastfeeding fewer than 8 times per day is associated with higher bilirubin concentrations.[2]

Would you like to explore the specific phototherapy thresholds and escalation criteria for neonatal hyperbilirubinemia?

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Question 352

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?

A. Diabetic polyuria
B. Primary polydipsia
C. Urethral hypermobility
D. Vescicovaginal fistula

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The answer is **C. Urethral hypermobility**.

This patient presents with classic **stress urinary incontinence (SUI)**: progressive leakage initially with exercise, now occurring with coughing and laughing, and objectively confirmed by urine leakage on Valsalva during examination.[1][2] **Urethral hypermobility** is the most common mechanism of SUI, resulting from loss of pelvic-floor musculature or vaginal connective tissue support such that the urethra and bladder neck do not close sufficiently in response to increases in intraabdominal pressure.[1][3]

Key risk factors present in this patient include **prior vaginal delivery**, which is associated with approximately double the risk of SUI compared to cesarean delivery, and[1] **high-impact exercise** (running), which repetitively increases intra-abdominal pressure.[2]

Why the other options are incorrect:

- **A. Diabetic polyuria** — The urinalysis is normal (no glucosuria), and the leakage pattern is provoked by increased abdominal pressure, not driven by volume overload.
- **B. Primary polydipsia** — Fluid intake of ~6 glasses of water plus 2 coffees daily is within a normal range. The normal urinalysis with normal specific gravity further argues against a dilutional or volume-mediated process. Lithium can cause nephrogenic diabetes insipidus, but a low specific gravity would be expected if this were the cause.
- **D. Vesicovaginal fistula** — A fistula typically produces **continuous** urinary leakage unrelated to activity, and both pelvic and speculum examinations were unremarkable in this patient.[1]

  "Urethral hypermobility occurs because of 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."

  —Jennifer M. Wu, M.D., M.P.H., University of North Carolina at Chapel Hill. Stress Incontinence in Women. N Engl J Med. June 24, 2021.

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The positive **cough stress test** (Valsalva-provoked leakage) is a standard clinical method for objectively confirming SUI before initiating treatment.[1]

Would you like to explore first-line nonsurgical management options for stress urinary incontinence?

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Question 353

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?

A. Distal tubule
B. Descending limb of loop of Henle
C. Proximal tubule
D. Ascending limb of loop of Henle

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The answer is **C. Proximal tubule**.

The **proximal tubule reabsorbs approximately 60–70% of filtered sodium**, making it by far the largest site of sodium reabsorption in the nephron.[1][2][3] This process is isotonic (water follows sodium), driven primarily by the basolateral Na^+/K^+-ATPase and apical Na^+/H^+ exchange (NHE3).[2] In hypovolemic states — as in this patient with volume depletion from vomiting and diarrhea — angiotensin II and catecholamines can increase proximal tubular sodium reabsorption to as high as 80%.[4]

For context, the remaining nephron segments reabsorb substantially less:

- **Thick ascending limb of the loop of Henle**: ~20–25% via the Na-K-2Cl cotransporter (NKCC2)[1][5]
- **Distal convoluted tubule**: ~5–10% via the NaCl cotransporter (NCC)[1]
- **Collecting duct**: ~1–2% via ENaC, regulated by aldosterone[4]

The **descending limb** (option B) is permeable to water but has minimal sodium reabsorption, so it is not a significant site for sodium handling.

Would you like to explore how angiotensin II and aldosterone regulate sodium reabsorption along different nephron segments during volume depletion?

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Question 354

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?

A. Absence of UDP-glucuronosyltransferase-1A1
B. Alteration in the ankyrin protein
C. Reduction in UDP-glucuronosyltransferase-1A1 activity
D. Deficiency in glucocerebrosidase

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The answer is **A. Absence of UDP-glucuronosyltransferase-1A1**, consistent with **Crigler-Najjar syndrome type I (CN1)**.

This neonate presents with the hallmarks of CN1: **severe unconjugated hyperbilirubinemia** (29.2 mg/dL of 29.4 mg/dL total) apparent from the first days of life, progressively worsening, with **neurological signs** (lethargy, hypotonia) indicating acute bilirubin encephalopathy. Critically, all other liver biochemistry is normal — a characteristic finding in CN1.[1]

CN1 results from **complete absence of UGT1A1 enzyme function**, leading to total inability to conjugate bilirubin. Serum bilirubin typically reaches **20–50 mg/dL** without treatment, and the risk of kernicterus is high.[2] Treatment consists of **exchange transfusion and intensive phototherapy**.[1][3]

Why not the other options:

- **C (Reduction in UGT1A1 activity)** — This describes **Crigler-Najjar type II**, where residual enzyme activity (<10–20% of normal) produces milder hyperbilirubinemia, typically **6–20 mg/dL**. Type II responds to phenobarbital (which induces residual enzyme activity) and carries a much lower risk of kernicterus. The severity here — bilirubin >29 mg/dL with neurological compromise in the first week — far exceeds a type II presentation.[1][2]
- **B (Alteration in ankyrin protein)** — This causes **hereditary spherocytosis**, a hemolytic anemia that can produce unconjugated hyperbilirubinemia but would be accompanied by anemia, reticulocytosis, and spherocytes on smear. The question states labs are otherwise within normal limits.
- **D (Deficiency in glucocerebrosidase)** — This causes **Gaucher disease**, a lysosomal storage disorder presenting with hepatosplenomegaly and cytopenias, not isolated unconjugated hyperbilirubinemia.

Would you like to explore the current treatment landscape for Crigler-Najjar type 1, including emerging gene therapy approaches?

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Question 355

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?

A. Parathyroid gland adenoma
B. Excess vitamin D
C. Malabsorption of fatty acids
D. High urine pH

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The answer is **C. Malabsorption of fatty acids**.

The **envelope-shaped crystals** are pathognomonic for **calcium oxalate dihydrate**, and in the setting of **Crohn disease with prior small bowel resection**, the unifying mechanism is **enteric hyperoxaluria** driven by fat malabsorption.[1][2]

Mechanism of enteric hyperoxaluria: Small bowel resection in Crohn disease causes steatorrhea. Excess unabsorbed fatty acids in the intestinal lumen **bind intraluminal calcium**, reducing the free calcium available to complex with dietary oxalate. Normally, calcium precipitates oxalate as insoluble CaOx in stool; when calcium is sequestered by fatty acids, oxalate remains soluble and is hyperabsorbed across the colonic mucosa.[2][3] Additionally, unabsorbed bile salts and fatty acids **increase colonic mucosal permeability**, further enhancing passive oxalate absorption.[1][4] The net result is markedly elevated urinary oxalate excretion — often exceeding 100 mg/day — leading to calcium oxalate supersaturation and recurrent stone formation.[1][2]

Why not the other options:

- **A (Parathyroid adenoma):** Could cause hypercalciuria and calcium-based stones, but no clinical evidence of hypercalcemia is provided, and this would not explain the specific clinical context of Crohn disease with bowel resection.
- **B (Excess vitamin D):** Standard multivitamin doses do not provide sufficient vitamin D to cause clinically significant hypercalciuria. No features of vitamin D toxicity are described.
- **D (High urine pH):** High urine pH favors **calcium phosphate** stone formation, not calcium oxalate. Calcium oxalate crystallization is relatively pH-independent.[3]

Would you like to explore current management strategies for enteric hyperoxaluria in patients with IBD and bowel resection?

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Question 356

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?

A. Pedunculated cervical growth
B. Inflammation of the cervix
C. Cervical trauma
D. Premature separation of the placenta

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The correct answer is **C. Cervical trauma**.

The pivotal finding is the speculum examination revealing a **tender, bruised cervix** in a patient who recently resumed sexual intercourse at 22 weeks' gestation. Cervical bruising is a direct sign of mechanical injury, and the temporal association with resumption of coitus makes **postcoital cervical trauma** the most likely explanation for the antepartum bleeding.[1][2]

Why the other options are less likely:

- **A. Pedunculated cervical growth** — No polyp or mass was identified on speculum examination; a pedunculated growth would typically be visible on direct inspection.

- **B. Inflammation of the cervix (cervicitis)** — Although the patient has a history of HPV and abnormal Pap smears, HPV is associated with **cervical dysplasia**, not cervicitis (which is more typically caused by infections such as chlamydia or gonorrhea). Moreover, the speculum finding describes **bruising**, not the erythema, friability, or mucopurulent discharge characteristic of cervicitis.

- **D. Premature separation of the placenta (abruption)** — The abdomen is **nontender** with no uterine hypertonicity, the CTG is reassuring, and the ultrasound shows a normally positioned fundal-posterior placenta without evidence of separation. While abruption can be sonographically occult, the absence of abdominal pain, tenderness, and uterine irritability makes this diagnosis unlikely in this presentation.[1]

Non-emergent lower genital tract lesions, including cervical trauma, are recognized among the common etiologies of antepartum bleeding, particularly when major obstetric causes (placenta previa, abruption, vasa previa) have been excluded by clinical and ultrasound assessment.[1][3]

Would you like to explore the recommended workup and management of postcoital bleeding during pregnancy?

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Question 357

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?

A. Administer IV fluids and insulin
B. Administer IV antibiotics
C. Administer IV fluids with oral antidiabetic medications
D. Administer potassium and magnesium

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The answer is **A. Administer IV fluids and insulin**.

This patient has **diabetic ketoacidosis (DKA)**, evidenced by marked hyperglycemia (691 mg/dL), metabolic acidosis (pH 7.21, HCO3 15.2), ketonuria, Kussmaul respirations, fruity breath, and severe dehydration — precipitated by insulin omission. The **cornerstones of DKA management are IV fluid resuscitation and insulin therapy**.[1][2]

Why IV fluids and insulin (A) is correct:

- **IV fluid resuscitation** is the first intervention, using 0.9% normal saline to restore circulatory volume and tissue perfusion. For pediatric patients not in shock, 10 mL/kg of 0.9% saline is initially administered over 30 minutes.[1]

- **Insulin therapy** (continuous IV infusion at 0.05–0.1 U/kg/hr) should be started **1–2 hours after initiation of fluid resuscitation** to correct hyperglycemia, suppress ketogenesis, and resolve acidosis.[1]
- The **serum potassium of 5.8 mEq/L** is elevated but reflects a transcellular shift due to insulin deficiency and acidosis — total body potassium is actually depleted. Because potassium is above the upper limit of normal, potassium should **not** be added to initial fluids; it is added only once levels fall below the upper limit of normal and urine output is established. Insulin will drive potassium intracellularly, so frequent monitoring (every 1–2 hours) is essential.[1]

Why the other options are incorrect:

- **B (IV antibiotics):** There is no clinical evidence of infection (afebrile, no infectious source identified). DKA was clearly precipitated by insulin non-adherence.
- **C (Oral antidiabetics):** This patient has **type 1 diabetes** requiring insulin. Oral antidiabetic agents are ineffective in DKA and do not address the acute ketoacidosis.
- **D (Potassium and magnesium):** Administering potassium when serum K is already 5.8 mEq/L risks life-threatening hyperkalemia and cardiac arrhythmias. Potassium replacement is indicated only when levels drop below the upper limit of normal during treatment.[1][3]

Would you like to explore the key complications to monitor for during pediatric DKA treatment, including cerebral edema risk?

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Question 358

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?

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

https://openevidence.com/ask/9bcabb59-4085-49c5-8471-2de5766e0f18

The correct answer is **B. They occur only during non-REM sleep**.

This vignette describes classic **sleep terrors (pavor nocturnus)** — a disorder of arousal characterized by sudden screaming, inconsolability, unresponsiveness to parental comfort, episodes lasting minutes to ~30 minutes, and **complete amnesia** for the event the following morning.[1][2]

Sleep terrors are classified as **NREM parasomnias** and occur almost exclusively during **slow-wave sleep (NREM stage N3)**, typically in the first third of the night when slow-wave sleep predominates.[1][3][4] Children are particularly vulnerable because of their high proportion of slow-wave sleep, which decreases with adolescence.[1]

Why the other choices are incorrect:

- **A. Persistent into adulthood** — Sleep terrors are characteristically **self-limiting**. Remission rates are **50–65%** by adolescence, and the condition is uncommon after puberty due to the developmental decrease in delta sleep. They are not expected to persist.[2][3]
- **C. Associated with child abuse** — The literature explicitly states that in the vast majority of cases, these episodes **do not indicate the presence of a primary underlying psychological problem or trauma**. While stress can be a trigger, sleep terrors should not raise concern for abuse.[1]

- **D. Associated with later development of a mood disorder** — Although some observational data link frequent sleep terrors to internalizing symptoms in early childhood, a **specific causal correlation between sleep terrors and psychiatric disorders has not been demonstrated**. This association is not an established feature of the condition.[3][5]

Would you like to explore the management of sleep terrors in children, including when pharmacologic treatment is warranted?

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Question 359

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?

A. Tertiary hyperparathyroidism
B. Secondary hyperparathyroidism
C. Elder abuse
D. Primary hyperparathyroidism

https://openevidence.com/ask/6c0169dc-be53-4bcc-bd89-8c0cc797faa9

The answer is **B. Secondary hyperparathyroidism**.

This patient has **CKD on dialysis** with a **low serum calcium (8.2 mg/dL)** and a **vertebral compression fracture** — the classic presentation of **renal osteodystrophy** caused by secondary

hyperparathyroidism. In CKD, declining GFR leads to phosphate retention, decreased renal 1-alpha-hydroxylase activity with reduced 1,25-dihydroxyvitamin D production, and consequent hypocalcemia — all of which stimulate PTH secretion.[1][2] Chronic PTH elevation drives excessive osteoclast-mediated bone resorption, resulting in bone loss (particularly cortical bone), increased fracture risk, and the spectrum of renal osteodystrophy.[1][3]

Why not the other options:

- **Primary hyperparathyroidism (D):** Characterized by **hypercalcemia** from autonomous PTH secretion by a parathyroid adenoma. This patient's calcium is low (8.2 mg/dL), which excludes primary disease.[4]
- **Tertiary hyperparathyroidism (A):** Occurs when long-standing secondary hyperparathyroidism leads to autonomous parathyroid hyperplasia, resulting in **hypercalcemia** — typically seen after renal transplantation. Again, the low calcium here is inconsistent.[4][5]
- **Elder abuse (C):** While the patient reports frequent fights with her daughter, a **compression fracture at L2 without bruising, soft-tissue injury, or other signs of trauma** is far better explained by metabolic bone disease in a dialysis patient. The low calcium and CKD context point strongly toward a pathologic fracture.

Supporting clinical clues: The patient is already on **sevelamer** (a non-calcium-based phosphate binder) and **sodium bicarbonate** (for CKD-associated metabolic acidosis), confirming advanced CKD management consistent with secondary hyperparathyroidism.[2][6]

Would you like to explore the management of secondary hyperparathyroidism in dialysis patients?

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Question 360

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?

A. Losartan
B. Spironolactone
C. Hydrochlorothiazide
D. Amlodipine

https://openevidence.com/ask/6c476d7d-4165-4e20-afdf-8b44307482c4

The answer is **D. Amlodipine**.

Amlodipine, a dihydropyridine calcium channel blocker (CCB), is the antihypertensive most associated with **dose-dependent bilateral lower extremity edema**. The timeline in this vignette (onset ~2 months after starting the drug) is classic — one cohort study found a **mean edema onset time of 8.3 weeks** after CCB initiation.[1] The incidence ranges from **2% to 25%** depending on dose and duration, and amlodipine poses the greatest concern among CCBs because it is the most widely prescribed and more likely to cause edema than nondihydropyridine or newer lipophilic dihydropyridine CCBs.[2]

Mechanism: Dihydropyridine CCBs cause **selective precapillary arteriolar dilation** without proportional postcapillary venodilation, leading to increased intracapillary hydrostatic pressure and extravasation of fluid into dependent tissues.[3][4] Critically, this is **not a volume-overload state** — laboratory studies (renal function, albumin) remain normal, as in this patient, and diuretics are generally ineffective.[2][4]

Why not the other options:

- **Losartan** (ARB): Adverse effects include hyperkalemia and rarely AKI, but **not peripheral edema**.[5]
- **Spironolactone** (mineralocorticoid receptor antagonist): A potassium-sparing diuretic — would promote natriuresis, not edema. Its notable side effects are **hyperkalemia and gynecomastia**.[5]

- **Hydrochlorothiazide** (thiazide diuretic): Promotes diuresis; associated with **hyponatremia, hypokalemia, and hyperuricemia**, not peripheral edema.[5]

Would you like to explore management strategies for CCB-induced peripheral edema, including the role of adding an ACE inhibitor or ARB?

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Question 361

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?

A. Group B streptococcus (GBS) infection
B. Hepatitis B infection
C. Thyroid stimulating hormone deficiency
D. Vitamin K deficiency

https://openevidence.com/ask/cec384e7-8ac9-4080-b0a8-f39e585fab21

D. Vitamin K deficiency. A 20-day-old, exclusively breastfed infant born at home with no postnatal care — and therefore almost certainly no vitamin K prophylaxis at birth — presenting with diffuse petechiae and bruising, poor feeding, lethargy, and hypothermia is the classic picture of vitamin K deficiency bleeding (VKDB), with the depressed mental status raising immediate concern for intracranial hemorrhage.[1][2]

Why this fits

- **Timing.** The American Academy of Pediatrics defines late-onset VKDB as occurring between 1 week and 6 months, with **peak incidence between 2 and 8 weeks**, and it is characteristically seen in **exclusively breastfed infants who did not receive vitamin K prophylaxis at birth**. (A parallel AAP report on bleeding conditions places classic VKDB from the first week to the first month, and late VKDB from 1 to 3 months — either classification captures a 20-day-old.)[1][2]
- **Mechanism.** Neonates are near-universally vitamin K deficient at baseline: poor placental transfer, minimal hepatic stores, low breast milk content, and absent gut colonization by menaquinone-producing flora. Functional levels of factors II, VII, IX, X and proteins C/S fall

below the ~30 U/dL threshold at which bleeding occurs, with prolongation of PT (and later aPTT).[2][3]

- **Presentation.** Cutaneous and mucosal bleeding, generalized ecchymoses, intramuscular hematomas, and intracranial hemorrhage. **Intracranial bleeding is the presenting feature in 30–60% of late-onset cases**, and late VKDB carries roughly 20% mortality — consistent with this infant's lethargy and difficulty arousing.[1][2][4]
- **Missed prophylaxis.** A single IM dose of 0.5–1.0 mg vitamin K at birth is recommended for all newborns and virtually eliminates the disease; home birth with no postnatal care is a major risk setting, and nonreceipt is associated with increased infant bleeding, including intracranial hemorrhage.[1][5]

Why not the others

- **A. GBS.** Early-onset GBS presents at or shortly after birth — 94–95% of cases within 48 hours. Late-onset GBS is possible at this age but manifests as bacteremia/meningitis with **fever**, irritability, and poor feeding, not diffuse petechiae and bruising. Purpura in sepsis would reflect DIC, which would typically be accompanied by fever or overt shock rather than a near-normal heart rate and blood pressure.[6][7]
- **B. Hepatitis B.** Perinatally acquired HBV is essentially always asymptomatic in the neonate; fulminant neonatal hepatitis is rare and would present with jaundice, hepatomegaly, and hypoglycemia rather than isolated bruising at 3 weeks.
- **C. TSH deficiency.** Central hypothyroidism (missed because of no newborn screening after a home birth) causes lethargy, poor feeding, hypothermia, prolonged jaundice, constipation, and large fontanelle — **but not petechiae or bruising**.

Immediate management

1. **Vitamin K1 (phytonadione) 1 mg IV/IM now** — do not wait for coagulation results.
2. **PT/INR, aPTT, fibrinogen, CBC with platelets, type and screen**; PT markedly prolonged with normal platelets and fibrinogen supports the diagnosis (correction after vitamin K is confirmatory).
3. **Fresh frozen plasma (10–15 mL/kg)** or 4-factor PCC for active/life-threatening bleeding, since vitamin K takes hours to restore factor levels.
4. **Emergent head imaging** (CT or cranial ultrasound) given altered mental status, with neurosurgical consultation if hemorrhage is found.

5. **Concurrent sepsis evaluation and empiric antibiotics** are reasonable given hypothermia and poor feeding in an unimmunized, unscreened neonate; also obtain glucose, and pursue newborn screening and maternal serologies (HBsAg, HIV, syphilis) that were never performed.

6. Address ongoing prophylaxis and family counseling before discharge.

Would you like to explore the specific treatment regimen for active VKDB with intracranial hemorrhage?

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Question 362

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?

A. Coronary artery aneurysms
B. Encephalitis
C. Mitral valve regurgitation
D. Minimal change disease

https://openevidence.com/ask/f82825c0-9a72-4064-807e-c9595b547cd0

The answer is **C. Mitral valve regurgitation**.

This presentation is classic **scarlet fever** caused by Group A beta-hemolytic streptococcus (GAS): circumoral pallor, diffuse blanching papular ("sandpaper") rash, **strawberry tongue**, pharyngeal erythema, fever, sore throat, and neutrophilic leukocytosis.[1] Without antibiotic treatment, GAS pharyngitis can trigger **acute rheumatic fever (ARF)**, whose hallmark cardiac manifestation is **valvulitis involving the mitral valve**, presenting as mitral regurgitation.[2][3]

Why mitral valve regurgitation:

- Carditis occurs in **50–70% of first ARF episodes** and almost always involves valvulitis.[4][5]
- **Endocarditis (valvulitis) involving regurgitation of the mitral valve, followed by the aortic valve, is the hallmark of rheumatic carditis**.[2]
- Nearly 50% of ARF patients have cardiac involvement, with the **mitral valve most commonly affected**.[6]

Why the other options are incorrect:

- **A. Coronary artery aneurysms** — a complication of **Kawasaki disease**, not GAS infection.

- **B. Encephalitis** — not a recognized sequela of GAS pharyngitis. Sydenham chorea is the CNS manifestation of ARF, but it involves the basal ganglia, not encephalitis.[7][8]
- **D. Minimal change disease** — post-streptococcal glomerulonephritis (PSGN) is a renal complication of GAS but presents as **nephritic syndrome** (hematuria, hypertension, edema), not minimal change disease (which causes nephrotic syndrome and is associated with atopy/viral infections).[6][7]

Would you like to explore the updated Jones Criteria for diagnosing acute rheumatic fever?

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Question 363

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?

A. Lipoteichoic acid
B. K capsule
C. Toxin B
D. Pyoverdine

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The answer is **D. Pyoverdine**.

The clinical and microbiological profile — a **non-lactose-fermenting, oxidase-positive, gram-negative rod** causing a catheter-associated urinary tract infection (CAUTI) complicated by pyelonephritis in a recently hospitalized patient — is classic for **Pseudomonas aeruginosa**.[1][2]

Why Pseudomonas aeruginosa:

- **Non-lactose fermenting** distinguishes it from common Enterobacteriaceae such as *E. coli* and *Klebsiella* (both lactose fermenters).[1]
- **Oxidase-positive** further separates it from most Enterobacteriaceae, which are oxidase-negative.[1]
- **Healthcare exposure** (recent hospitalization) and a **chronic indwelling catheter** are major risk factors for *Pseudomonas* UTI.

Why pyoverdine:

Pyoverdine is a fluorescent yellow-green **siderophore** (iron-chelating compound) produced by *P. aeruginosa* that scavenges iron from host transferrin and lactoferrin, facilitating bacterial growth and survival under iron-limiting conditions.[3][4] Beyond iron acquisition, pyoverdine also

functions as a **signaling molecule** that upregulates the production of other virulence factors, including exotoxin A and endoproteases.[3][5] All clinical isolates of *P. aeruginosa* from CAUTIs have been shown to produce significant amounts of pyoverdine.[3]

Eliminating the other choices:

- **A. Lipoteichoic acid** — a cell wall component of **gram-positive** bacteria; incompatible with a gram-negative rod.
- **B. K capsule** — associated with **Klebsiella pneumoniae**, which is lactose-fermenting and oxidase-negative.
- **C. Toxin B** — produced by **Clostridioides difficile**, an anaerobic gram-positive organism causing colitis, not UTI.

Would you like to explore the recommended empiric antibiotic regimen for Pseudomonas CAUTI?

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Question 364

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?

A. Ratio of head to abdominal circumference
B. Femoral length
C. Crown-rump length
D. Biparietal length

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The answer is **C. Crown-rump length**.

At **6 weeks gestational age** (first trimester), **crown-rump length (CRL)** is the most accurate predictor of gestational age, with a precision of **±5–7 days**.[1][2] Per ACOG and the AIUM-ACR-ACOG-SMFM-SRU practice parameter, first-trimester CRL measurement is the **most accurate means for sonographic dating of pregnancy**, and its accuracy improves the earlier in the first trimester it is performed.[3][4]

The other answer choices are second- and third-trimester parameters:

- **Biparietal diameter (D)**, **femoral length (B)**, and **head-to-abdominal circumference ratio (A)** are used after 14 weeks of gestation. Second-trimester composite biometry (including these measurements) has a wider precision of ±7–10 days, and third-trimester dating is even less precise at ±21–30 days.[5][6]
- **Abdominal circumference** is specifically noted to be the **least reliable** of these later biometric measurements for estimating gestational age.[3][4]
- The **head-to-abdominal circumference ratio** is primarily used for assessing fetal growth (e.g., distinguishing symmetric from asymmetric growth restriction), not for dating.

In this patient with a last menstrual period 6 weeks ago, CRL is the appropriate and most accurate dating parameter.

Would you like to explore guidelines for when to redate a pregnancy based on ultrasound vs. LMP discrepancies?

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Question 365

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?

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

https://openevidence.com/ask/4dd9777b-65a8-46a7-b9ba-d94439d47a60

The answer is **C. Elongated and thickened pylorus on abdominal ultrasound**.

This presentation is classic for **infantile hypertrophic pyloric stenosis (IHPS)**. The key features supporting this diagnosis include:

- **Age and sex**: IHPS typically presents between **3 and 8 weeks of age** with a **4:1 male-to-female predominance**.[1]
- **Nonbilious, postprandial vomiting** with irritability during feeds and feeding refusal — hallmarks of gastric outlet obstruction.
- **Palpable epigastric mass** ("olive sign"): This 2.5-cm mass represents the hypertrophied pylorus. Palpation of a pyloric mass has high specificity (**97.5%**) for the diagnosis.[2]
- **Down syndrome association**: Pyloric stenosis occurs in approximately **0.3% of infants with trisomy 21**, a recognized gastrointestinal association.[3][4]

Abdominal ultrasound is the imaging modality of choice, with **sensitivity ~97–100% and specificity ~94–100%**.[2][5] Diagnostic criteria include **pyloric muscle thickness ≥3–4 mm** and **pyloric channel length >14.5–18 mm**, appearing as an elongated, thickened pylorus with no passage of gastric contents.[5][6]

Why the other options are incorrect:

- **A (Dilated colon segment)** — Would suggest **Hirschsprung disease**. While associated with Down syndrome, Hirschsprung presents with failure to pass meconium, abdominal distension, and constipation — not nonbilious vomiting with a palpable epigastric mass.
- **B (Rotavirus antigen)** — Rotavirus gastroenteritis causes **diarrhea** as the predominant feature, not isolated postprandial vomiting with an abdominal mass.
- **D (Triple bubble sign)** — A "double bubble" sign is associated with **duodenal atresia** (common in Down syndrome), but that presents at birth with **bilious** vomiting, not at 6 weeks with nonbilious vomiting and a palpable mass. A "triple bubble" would suggest jejunal atresia, which also presents in the neonatal period.

The normal ABG is notable — classically IHPS causes **hypochloremic, hypokalemic metabolic alkalosis** from gastric acid losses, but the 2-day history suggests early presentation before significant electrolyte derangement has developed.[1]

Would you like to explore the preoperative resuscitation and surgical management of infantile hypertrophic pyloric stenosis?

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Question 366

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?

A. Respiratory alkalosis
B. Metabolic alkalosis
C. Respiratory acidosis
D. Mixed respiratory and metabolic acidosis

https://openevidence.com/ask/f2d671c1-ac94-4157-942b-d082dc35c006

The answer is **B. Metabolic alkalosis**.

This presentation is classic for **infantile hypertrophic pyloric stenosis (IHPS)**: a 1-month-old with progressive, nonbilious projectile vomiting, hunger immediately after emesis, dehydration, and a palpable **olive-shaped epigastric mass**.[1][2]

The hallmark acid-base disturbance is **hypochloremic, hypokalemic metabolic alkalosis**, resulting from the following pathophysiology:[3][4]

- **Loss of gastric acid**: Persistent vomiting causes loss of gastric secretions rich in **HCl**, leading to depletion of hydrogen and chloride ions and a primary metabolic alkalosis.
- **Hypokalemia**: Potassium is also lost in gastric secretions and through renal wasting.
- **Renal maintenance**: Volume depletion activates the renin-angiotensin-aldosterone system, causing avid sodium and bicarbonate reabsorption. Chloride depletion impairs the kidney's ability to excrete excess bicarbonate. In the distal tubule, potassium is conserved at the

expense of hydrogen excretion (**paradoxical aciduria**), which perpetuates the alkalosis.[3] [4]

Compensatory **hypoventilation** (CO_2 retention) may occur to partially offset the alkalosis, but the primary disturbance remains metabolic alkalosis.[4] Respiratory acidosis, respiratory alkalosis, and mixed respiratory/metabolic acidosis are not expected in this clinical scenario.

Would you like to explore the preoperative electrolyte and fluid correction targets before pyloromyotomy?

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Question 367

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?

A. Reassurance
B. Adding pramlintide
C. Increasing daily insulin dose
D. Reducing daily insulin dose

https://openevidence.com/ask/cb755c75-301e-41f2-801d-111ec468f437

The answer is **D. Reducing daily insulin dose**.

This presentation is classic for the **Somogyi effect (posthypoglycemic hyperglycemia)** — nocturnal hypoglycemia triggering counter-regulatory hormone release (epinephrine, glucagon, cortisol, growth hormone), which causes rebound morning hyperglycemia.[1][2] The nocturnal adrenergic symptoms (sweating, tremors, weakness) that awaken the patient confirm hypoglycemia is occurring during sleep.

Why reducing insulin is correct: The nocturnal hypoglycemia is caused by **excessive insulin action overnight**. Reducing the evening/basal insulin dose prevents the hypoglycemic trigger, thereby eliminating both the dangerous nocturnal episodes and the subsequent rebound morning hyperglycemia.[1][3][4] In clinical trials of basal insulin titration, dose decreases were specifically recommended when symptomatic nocturnal hypoglycemia was present or fasting blood glucose fell below 4.4 mmol/L.[4]

Why the other options are incorrect:

- **A (Reassurance):** Nocturnal hypoglycemia is dangerous — it can cause hypoglycemia unawareness and, in severe cases, dead-in-bed syndrome. Active intervention is required.[5]
- **B (Adding pramlintide):** Pramlintide is an amylin analog that slows gastric emptying and suppresses glucagon; it would further increase hypoglycemia risk rather than address it.

- **C (Increasing insulin):** Although morning glucose is high, this would worsen the underlying nocturnal hypoglycemia, creating a vicious cycle. The morning hyperglycemia is a consequence of the hypoglycemia, not of insufficient insulin.[2]

Key clinical distinction: The Somogyi effect must be differentiated from the **dawn phenomenon**, which also causes morning hyperglycemia but without preceding nocturnal hypoglycemia — the dawn phenomenon is managed by increasing or adjusting the timing of basal insulin, the opposite approach.[1][3]

Would you like to explore how to distinguish and manage the dawn phenomenon versus the Somogyi effect?

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Question 368

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?

A. Syringomyelia
B. Spinal metastasis
C. Herniated disc
D. Spinal hematoma

https://openevidence.com/ask/6348d4a1-f4b9-47ce-817e-1c97c06dad12

The answer is **B. Spinal metastasis**.

This presentation is classic for **metastatic spinal cord compression (MSCC) from prostate cancer**. The key findings that converge on this diagnosis include:

- **Hard nodular mass on rectal exam** — highly suggestive of prostate carcinoma. Prostate cancer is one of the three most common causes of MSCC, alongside breast and lung cancer, with bone being the most common site of metastasis (observed in 82% of metastatic prostate cancer). Spinal cord compression occurs in approximately **7% of men with prostate cancer**.[1][2]
- **Back pain for 2 months, including at night** — back pain is the earliest and most common symptom in 83–95% of MSCC cases, and the median time from pain onset to diagnosis is approximately **2 months**. Characteristically, the pain is **worse when recumbent and at night**, distinguishing it from degenerative disease where lying down typically provides relief.[3][4][5]
- **Bilateral lower limb weakness, sensory deficits (temperature and vibratory sense), fecal incontinence, and decreased rectal sphincter tone** — these reflect progressive spinal cord or cauda equina compression. Weakness is the second most common finding at MSCC

diagnosis (present in 35–75% of patients), and sphincter dysfunction follows the onset of pain and motor deficits.[3][5][6]

Why not the other options:

- **Syringomyelia (A):** Produces a dissociated sensory loss (loss of pain/temperature with preserved dorsal column function), typically in a "cape-like" distribution, and does not explain the rectal mass.
- **Herniated disc (C):** Usually causes unilateral radiculopathy, pain improves with recumbency, and would not account for the hard nodular prostate or the bilateral, progressive cord-level deficits.
- **Spinal hematoma (D):** Presents acutely (minutes to hours), often in the setting of anticoagulation or trauma, and does not explain the rectal mass or the 2-month progressive course.

Would you like to explore the initial management of metastatic spinal cord compression, including steroid dosing and surgical versus radiation therapy indications?

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Question 369

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?

A. Cooling the dialysate
B. Eating heavier meals during dialysis
C. Increasing ultrafiltration
D. Steroid administration

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The correct answer is **A. Cooling the dialysate**.

This patient presents with classic **intradialytic hypotension (IDH)** — a systolic BP drop of 25 mmHg (135 → 110 mmHg) with associated lightheadedness and fall risk. Her 22-year history of diabetes mellitus likely contributes through **autonomic neuropathy**, impairing compensatory vasoconstriction during fluid removal.

Why cooling the dialysate works

Lowering dialysate temperature from the standard 37°C to 35–36°C reduces core body temperature, **promotes peripheral vasoconstriction, increases peripheral vascular resistance, and stabilizes blood pressure** during hemodialysis.[1] A systematic review and meta-analysis found that cooled dialysate **reduces IDH occurrence by approximately 65%** compared to standard-temperature dialysate.[1] A randomized crossover trial confirmed that low dialysate temperature (35°C) resulted in significantly smaller intradialytic systolic BP drops (9.6 vs. 20.3 mmHg) compared to standard temperature.[2] This is a simple, cost-effective, first-line nonpharmacological intervention recommended in clinical guidelines.[3][4]

Why the other options are incorrect

- **B. Eating heavier meals during dialysis** — Food ingestion during dialysis **decreases systemic vascular resistance** via splanchnic vasodilation, worsening hypotension. Guidelines actually recommend **avoiding eating during dialysis** in patients prone to IDH.[5][6][7]
- **C. Increasing ultrafiltration** — Higher ultrafiltration rates **exacerbate** IDH by accelerating intravascular volume depletion. Reducing, not increasing, the ultrafiltration rate is recommended.[4][8]
- **D. Steroid administration** — Steroids have no established role in managing intradialytic hypotension.

Would you like to explore the role of midodrine as a pharmacologic option for preventing intradialytic hypotension?

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Question 370

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?

A. Decreased carbohydrate intake
B. Increased tryptophan intake
C. Medication change
D. Surreptitious opiate abuse

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The answer is **B. Increased tryptophan intake**.[1][2][3]

This patient presents with **serotonin syndrome** precipitated by the combination of **citalopram (an SSRI) and a tryptophan-containing amino acid supplement**. The clinical picture is characteristic: **autonomic instability** (fever, diaphoresis, tachycardia, hypertension), **neuromuscular excitation** (3+ hyperreflexia, increased tone, inducible clonus), and malaise — occurring acutely in a patient on a serotonergic agent.[4][5][6] By the **Hunter criteria**, the presence of **inducible clonus with diaphoresis** in a patient taking a serotonergic drug is sufficient for diagnosis.[5][7]

Tryptophan is an amino acid and the biosynthetic precursor to serotonin. When ingested as a supplement, it raises brain tryptophan levels and stimulates conversion to serotonin in neurons.[1] The **citalopram FDA label explicitly lists tryptophan** as a serotonergic agent that increases the risk of serotonin syndrome when co-administered.[2][3] The "amino acid supplement" she recently started, combined with her SSRI, is the most likely precipitant.

> "No laboratory tests confirm the diagnosis of the serotonin syndrome. Instead, the presence of tremor, clonus, or akathisia without additional extrapyramidal signs should lead clinicians to consider the diagnosis, which must be inferred from the patient's history and physical examination."
>
> —Edward W. Boyer, M.D., Ph.D. et al., University of Massachusetts and other institutions. The Serotonin Syndrome. N Engl J Med. March 17, 2005.
>
> Used under license from The New England Journal of Medicine.

Why the other options are less likely:

- **A. Decreased carbohydrate intake** — Low-carb diets may reduce tryptophan transport into the brain (by increasing competition from other large neutral amino acids), which would theoretically *decrease* serotonin synthesis, not precipitate serotonin syndrome.
- **C. Medication change** — The switch from paroxetine to citalopram occurred **6 months ago**, and her mood has been stable. Serotonin syndrome typically develops within hours to days of a serotonergic change. This is too remote to be the inciting factor.[4][6]
- **D. Surreptitious opiate abuse** — While certain opioids (tramadol, meperidine, fentanyl) have serotonergic properties and can precipitate serotonin syndrome with SSRIs, there is no evidence of recent opioid exposure in the vignette. Her occupation as a nurse is a red herring suggesting drug access, but the recent addition of an amino acid supplement provides a more direct explanation.[2]

Would you like to explore the acute management of serotonin syndrome, including cyproheptadine dosing?

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Question 371

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?

A. Intracellular receptors
B. cAMP pathway
C. cGMP pathway
D. JAK/STAT pathway

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The answer is **A. Intracellular receptors**.

This presentation — **hypertension, hypokalemia, headaches, constipation, polydipsia, polyuria, and a unilateral adrenal mass** — is classic for **primary hyperaldosteronism (Conn syndrome)** caused by an aldosterone-producing adenoma.[1][2] The hyperglycemia can be explained by hypokalemia-induced impairment of pancreatic beta-cell insulin secretion.

Aldosterone signals through intracellular receptors. As a steroid hormone, aldosterone freely crosses the cell membrane and binds to the **mineralocorticoid receptor (MR)**, a cytoplasmic receptor belonging to the **nuclear receptor superfamily of ligand-dependent transcription factors**.[3][4][5] Upon aldosterone binding, the MR dissociates from chaperone proteins (Hsp70, Hsp90), translocates to the nucleus, and binds hormone response elements (HRE) in the promoter regions of target genes — notably those encoding ENaC (epithelial sodium channel) and SGK1 — to promote sodium reabsorption and potassium excretion.[4][6]

Why the other options are incorrect:

- **B. cAMP pathway** — Used by peptide hormones such as ACTH, PTH, and glucagon acting via G-protein–coupled receptors, not steroid hormones.
- **C. cGMP pathway** — Used by natriuretic peptides (ANP, BNP) and nitric oxide signaling.
- **D. JAK/STAT pathway** — Used by cytokines (e.g., interferons, interleukins) and growth hormone/erythropoietin receptors.

Would you like to explore the recommended diagnostic workup and confirmatory testing for suspected primary hyperaldosteronism?

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Question 372

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?

A. Covalently X-links DNA
B. Blocks microtubule formation
C. Intercalates between DNA
D. Modifies DNA transcription and protein synthesis

https://openevidence.com/ask/87816f6c-f896-4747-801e-6e5d9cee1cd3

The answer is **B. Blocks microtubule formation**.

The culprit medication is **vincristine**, a vinca alkaloid with a well-established and strong association with **dose-limiting peripheral neuropathy**. The FDA label for vincristine describes a characteristic sequence: initial sensory impairment and paresthesias, followed by neuritic pain and motor difficulties with continued treatment.[1] This patient's presentation — tingling, numbness, weakness, and difficulty gripping small objects — is classic for vincristine-induced peripheral neuropathy (VIPN).[2][3][4]

Vincristine exerts its antineoplastic effect by **interfering with microtubule formation**, leading to mitotic arrest and cell death.[2][5] This same mechanism underlies its neurotoxicity: disruption of axonal microtubules impairs axonal transport, causing Wallerian degeneration and a length-dependent sensorimotor neuropathy.[6][7]

Mapping the other agents to their mechanisms:

- **Cyclophosphamide** — covalently cross-links DNA (choice A; alkylating agent)
- **Doxorubicin** — intercalates between DNA base pairs (choice C; anthracycline)

- **Dexamethasone** — modifies DNA transcription and protein synthesis (choice D; corticosteroid)
- **Dasatinib** — tyrosine kinase inhibitor (not listed among the choices)

Among the agents in this hyper-CVAD–like regimen, vincristine has been identified as the **dominant driver of grip strength decline** and motor neuropathy, while cyclophosphamide and doxorubicin may contribute to sensory hypersensitivity through different mechanisms, and dexamethasone does not induce sensory neuropathy.[8]

Would you like to explore prevention and management strategies for vincristine-induced peripheral neuropathy?

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Question 373

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?

A. Aldesleukin
B. Interferon beta
C. Filgrastim
D. Romiplostim

https://openevidence.com/ask/4c9962fd-f7e1-40e0-8fa6-595e9dd54eeb

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The answer is **C. Filgrastim**.[1]

The key laboratory finding is the **selective increase in leukocyte count** (800 → 2,000/mm³) with minimal change in hemoglobin (10.4 → 10.6 g/dL) and platelets (50,000 → 56,000/mm³). This pattern is characteristic of **filgrastim (G-CSF)**, a leukocyte growth factor that produces a **dose-dependent increase in circulating neutrophil counts**.[1][2] The monocyte percentage decreased from 5% to 2%, consistent with the FDA-labeled pharmacodynamic profile: filgrastim increases absolute monocyte counts in a dose-dependent manner, but the **percentage of monocytes in the differential remains within the normal range** — diluted by the proportionally greater rise in neutrophils.[1]

Filgrastim is FDA-indicated to **decrease the incidence of infection, as manifested by febrile neutropenia**, in patients with nonmyeloid malignancies receiving myelosuppressive chemotherapy.[1] This patient's WBC of 800/mm³ represents severe leukopenia warranting G-CSF support.

Why not the other options:

- **Aldesleukin (IL-2)** — an immunotherapy used for metastatic melanoma and renal cell carcinoma; it does not selectively raise neutrophil counts and is not used for chemotherapy-induced neutropenia.
- **Interferon beta** — used primarily for multiple sclerosis; it does not stimulate granulopoiesis.
- **Romiplostim** — a thrombopoietin receptor agonist that **stimulates platelet production**. If this drug had been given, the expected change would be a preferential rise in platelet count rather than the leukocyte count.

Would you like to explore the recommended dosing and duration of filgrastim for chemotherapy-induced neutropenia?

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Question 374

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?

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

https://openevidence.com/ask/3334309f-2bd7-4d68-8a63-bc52ff82b597

The answer is **C. Hyaline membranes lining the alveoli on lung biopsy**.

This presentation — a **27-week premature neonate** with rapid-onset respiratory distress (intercostal retractions, nasal flaring), hypoxia, and chest X-ray showing **low lung volumes, air bronchograms, and diffuse ground-glass opacities** — is classic for **neonatal respiratory distress syndrome (RDS)**, previously known as hyaline membrane disease.[1][2] Lack of prenatal care implies the mother did not receive antenatal corticosteroids, further increasing the risk of surfactant deficiency.

Why C is correct: RDS results from surfactant deficiency in the structurally immature lung, leading to alveolar collapse, capillary leak edema, and the formation of **hyaline membranes** — eosinophilic proteinaceous material (composed of plasma proteins and necrotic epithelial cells) lining the alveolar surfaces.[1][2][3] This is the hallmark histopathologic finding and the basis for the disease's original name.

Why the other options are incorrect:

- **A. Bilateral pleural effusions** — more characteristic of hydrops fetalis, chylothorax, or congenital infection, not RDS.
- **B. Corkscrew-shaped organisms on umbilical cord culture** — describes *Treponema pallidum* (congenital syphilis), which can cause neonatal pneumonia but does not present with this classic RDS radiographic pattern in a premature infant.

- **D. Meconium-stained fluid on deep suctioning** — meconium aspiration syndrome occurs in **term or post-term** infants, not at 27 weeks' gestation. Meconium passage in utero is exceedingly rare at this gestational age.

Would you like to explore current guidelines for surfactant replacement therapy in preterm neonates with RDS?

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Question 375

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?

A. Bleomycin
B. Cyclophosphamide
C. Doxorubicin
D. Etoposide

https://openevidence.com/ask/8ee560c2-8ace-4297-af81-ee8f170133c2

The answer is **B. Cyclophosphamide**, which causes **hemorrhagic cystitis** — the classic chemotherapy-associated cause of true hematuria (red urine that tests positive for blood).[1][2][3]

The critical clue is that the urine **tests positive for blood**. Cyclophosphamide is metabolized to **acrolein**, a highly reactive aldehyde that is excreted renally and directly damages the urothelium, causing necrosis, ulceration, and hemorrhage of the bladder mucosa.[1][4] This results in frank hematuria, which will be positive for red blood cells on urinalysis. Hemorrhagic cystitis occurs in **5–10% of patients** receiving cyclophosphamide and can range from microscopic hematuria to life-threatening bladder hemorrhage.[5] Mesna (2-mercaptoethane sulfonate) is the standard uroprotective agent used to neutralize acrolein and prevent this complication.[6]

Why not the other choices:

- **Doxorubicin (C)** — also causes red-appearing urine, but this is due to excretion of the drug's red anthracycline pigment, not blood. The FDA label specifically notes it "can cause urine to appear red for 1 to 2 days after administration". Critically, this discoloration would be **negative for blood** on dipstick, distinguishing it from true hematuria.[7]

- **Bleomycin (A)** — primarily associated with **pulmonary fibrosis**, not bladder toxicity.
- **Etoposide (D)** — associated with **secondary leukemia** (topoisomerase II inhibitor), not hemorrhagic cystitis.

Cyclophosphamide is used in Hodgkin lymphoma regimens such as BEACOPP (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone). The combination of red urine with a positive blood test after chemotherapy initiation is the hallmark presentation of cyclophosphamide-induced hemorrhagic cystitis.

Would you like to explore mesna dosing strategies for preventing cyclophosphamide-induced hemorrhagic cystitis?

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Question 376

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?

A. Recent hiking trip
B. Intravenous heroin abuse
C. Exposure to a patient with mengingococcemia
D. Currently menstruating

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The answer is **D. Currently menstruating**.

This presentation is classic for **staphylococcal toxic shock syndrome (TSS)**, and the history most likely to be elicited is active menstruation (typically with tampon use).

Why TSS is the diagnosis

This patient meets the CDC clinical case definition for staphylococcal TSS:[1]

1. **Fever** ≥38.9°C — present (39.1°C)
2. **Diffuse macular erythroderma** — present (widespread erythematous rash)
3. **Desquamation** — present (skin peeling on palms and soles)
4. **Hypotension** — present (systolic BP 94 mm Hg)
5. **≥3 organ systems involved:**
6. **GI** — nausea and vomiting
7. **Muscular** — myalgia
8. **Renal** — BUN 47, creatinine 1.8 (both elevated)
9. **Hepatic** — bilirubin 2.1, AST 190, ALT 175 (all elevated)
10. **Hematologic** — platelets 98,000 (thrombocytopenia)
11. **CNS** — lightheadedness, lethargy

Why menstruation

Menstrual TSS accounts for the majority of cases in reproductive-age women and is strongly associated with tampon use, particularly prolonged wear. The median age of menstrual TSS patients is approximately **18 years**.[2] Up to **95% of menstrual TSS cases** have onset during menstruation.[1] TSST-1 accounts for over **90%** of menstruation-associated cases.[3]

Why not the other options

- **A (Recent hiking trip)** — would suggest Rocky Mountain spotted fever (RMSF), which can cause rash and multiorgan dysfunction, but the rash in RMSF typically starts on the wrists/ankles and spreads centrally (petechial, not erythroderma with desquamation), and hypotension is less prominent early.
- **B (IV heroin abuse)** — would raise concern for endocarditis or bloodstream infection, but does not explain the diffuse erythroderma with desquamation pattern.
- **C (Meningococcemia exposure)** — typically presents with purpuric/petechial rash, not diffuse erythroderma with desquamation, and would be expected to have positive blood cultures.

Would you like to explore the antibiotic regimen and acute management of staphylococcal toxic shock syndrome?

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Question 377

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?

A. Interleukin 3
B. Platelet-derived growth factor
C. Sargramostim
D. Thrombopoietin

https://openevidence.com/ask/7e5a39f3-9ce6-4e03-a9bd-4eb37922bad5

The answer is **C. Sargramostim** (GM-CSF, granulocyte-macrophage colony-stimulating factor). The acute reaction described — **dyspnea, severe myalgia, vomiting, tachycardia, and hypotension occurring 30 minutes after the first dose** — is the classic "**first-dose reaction**" of GM-CSF, a well-characterized syndrome that occurs after the initial but not subsequent doses of sargramostim.[1][2]

Why sargramostim was chosen for this patient

This patient has **severe pancytopenia** on effective HAART, most critically **neutropenia** (WBC 700/mm³, ANC ~280/mm³) and **thrombocytopenia** (platelets 20,000/mm³). GM-CSF (sargramostim) is a multilineage hematopoietic growth factor used in HIV/AIDS patients to treat

neutropenia and permit continued use of myelosuppressive therapies (including HAART and co-trimoxazole).[3][4][5] This fits the clinical scenario of starting a "blood improving" medication to avoid modifying effective antiretroviral therapy.

The first-dose reaction of GM-CSF

Lieschke et al. characterized this syndrome in detail: it occurred in 24 of 78 cycles of GM-CSF therapy, exclusively after the first dose, and was **not observed after any of more than 600 subsequent consecutive doses**.[1] The reaction was characterized by:

- **Flushing** (67%), **tachycardia** (67%), **hypotension** (58%)
- **Musculoskeletal pain** (54%), **dyspnea** (50%)
- **Nausea and vomiting** (46%)

Risk factors included doses ≥3 μg/kg and IV (rather than subcutaneous) administration.[1] The FDA label for sargramostim (Leukine) similarly lists **infusion-related reactions including dyspnea, hypoxia, flushing, hypotension, syncope, and tachycardia**.[6]

Why not the other options

- **A. Interleukin 3**: A multilineage growth factor but not FDA-approved or commercially available for clinical use; does not have this characteristic first-dose reaction profile.
- **B. Platelet-derived growth factor (PDGF)**: Involved in wound healing and connective tissue growth, not used to treat hematopoietic cytopenias.
- **D. Thrombopoietin**: While the patient has thrombocytopenia, thrombopoietin and its receptor agonists are not associated with this distinctive acute first-dose reaction syndrome. The adverse-reaction pattern — not which cell line is targeted — is the key distinguishing feature.

Would you like to explore how G-CSF compares to GM-CSF for managing HIV-associated neutropenia?

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Question 378

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?

A. Check serum TSH level
B. Check serum electrolytes
C. Perform CT scan of the head
D. Perform chest x-ray

https://openevidence.com/ask/006adddd-f196-49df-9078-796c64095660

The correct answer is **B. Check serum electrolytes**.

This patient presents with **classic delirium**: acute onset over 2 days, fluctuating course (worse in evenings), impaired attention (serial sevens errors), disorganized speech, and psychomotor agitation.[1] The most appropriate first step is checking serum electrolytes given the high pretest probability of an **electrolyte-driven etiology**.

Several features strongly point toward electrolyte derangement:

- **Hydrochlorothiazide use in an elderly woman** — thiazide diuretics are a well-established cause of hyponatremia, particularly in older women. A 2026 cohort study of over 159,000 individuals found that among women ≥80 years on thiazides, the number needed to harm for profound hyponatremia (<125 mEq/L) was only **53**.[2][3][4]
- **Poor oral intake for 6 days** — dehydration and reduced solute intake compound thiazide-associated electrolyte disturbances, particularly hyponatremia.[3]

- **History of breast cancer** — while remote (12 years), this raises the possibility of hypercalcemia from occult bone metastases, another cause of confusion.[5]

An NEJM review of delirium in hospitalized older adults identifies measurement of **electrolytes, BUN, and creatinine** as routinely required in the workup.[6] A JAMA review similarly emphasizes that all patients with delirium need **rapid, targeted evaluation for electrolyte or metabolic derangements**.[1]

Why not the other options:

- **A (Serum TSH)** — Thyroid dysfunction can contribute to mental status changes, but this is a targeted test for specific clinical scenarios rather than the initial step in acute delirium evaluation.[7]
- **C (CT head)** — Neuroimaging is indicated when there is head trauma, deteriorating mental status, or **new focal neurologic findings**. This patient has no focal deficits, and the supple neck argues against meningeal irritation.[1]
- **D (Chest x-ray)** — Infection is a common precipitant of delirium, and chest radiography is often helpful. However, given the absence of fever, respiratory symptoms, and the strong clinical suspicion for an electrolyte cause, electrolytes are higher yield as the immediate next step.[8]

Would you like to explore the management of thiazide-induced hyponatremia in elderly patients?

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Question 379

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?

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

https://openevidence.com/ask/8ae620f2-0d16-4d6a-be12-df15974dab07

The answer is **A: Alpha-Ketoglutarate + NAD+ + CoA ⇌ Succinyl-CoA + CO2 + NADH**.

This patient presents with classic **Wernicke-Korsakoff syndrome** — confusion, retrograde amnesia with confabulation, and horizontal nystagmus in a chronic alcoholic — caused by **thiamine (vitamin B1) deficiency**.[1][2] The pretibial pitting edema and perioral erythema further support thiamine deficiency, reflecting wet beriberi and dermatologic manifestations, respectively. CT is typically normal in the acute phase of Wernicke encephalopathy.[3]

Why option A is correct

Thiamine is phosphorylated intracellularly to **thiamine pyrophosphate (TPP)**, which serves as an essential cofactor for the **alpha-ketoglutarate dehydrogenase complex** in the TCA cycle — the reaction shown in option A.[4][5][6] This is also the earliest enzyme to show decreased activity in thiamine deficiency (within ~4 days).[5] TPP additionally serves as a cofactor for **pyruvate dehydrogenase** and **transketolase** (pentose phosphate pathway).[6][7]

Why the other options are incorrect

- **B (Succinate → Fumarate):** Catalyzed by succinate dehydrogenase (Complex II), which requires **FAD** (derived from riboflavin/B2), not TPP.
- **C (Isocitrate → Alpha-Ketoglutarate):** Catalyzed by isocitrate dehydrogenase, which requires **NAD+** but does not use TPP as a cofactor.

- **D (Succinyl-CoA → Succinate):** Catalyzed by succinyl-CoA synthetase, a substrate-level phosphorylation step that does not require TPP.

Would you like to explore the recommended thiamine dosing regimen for treatment of Wernicke encephalopathy?

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Question 380

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?

A. Beta-2 antagonist
B. Histone deacetylase inhibitor
C. Muscarinic antagonist
D. Anticoagulant

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The answer is **C. Muscarinic antagonist**.

This child presents with classic **allergic asthma** — wheezing, dyspnea, eosinophilia, and positive allergen skin tests. Among the listed options, **muscarinic antagonists** (anticholinergic agents) such as **ipratropium bromide** are established bronchodilators in asthma management. Ipratropium is a short-acting muscarinic acetylcholine receptor antagonist that relieves cholinergic bronchomotor tone and decreases mucosal edema and secretions.[1][2] Long-acting muscarinic antagonists (e.g., tiotropium) are also used as add-on controllers in persistent asthma.

Multiple Cochrane reviews and GINA 2026 guidelines support the use of inhaled anticholinergics (ipratropium) combined with short-acting beta-2 agonists for moderate-to-severe acute asthma exacerbations in children, with an approximately **27% reduction in hospitalizations** compared to beta-2 agonists alone.[3][4] A 2025 meta-analysis of 24 RCTs (n = 3,238) confirmed that nebulized ipratropium bromide significantly lowered hospitalization rates (RR 0.76, 95% CI 0.64–0.90) with no serious adverse events.[5]

Why the other options are incorrect:

- **A. Beta-2 antagonist** — Beta-2 *agonists* (e.g., albuterol) are first-line bronchodilators in asthma. Beta-2 *antagonists* (beta-blockers) would cause bronchoconstriction and are contraindicated.
- **B. Histone deacetylase inhibitor** — These are antineoplastic agents (e.g., vorinostat), not used in asthma management.
- **D. Anticoagulant** — No role in the treatment of asthma.

Would you like to explore the role of long-acting muscarinic antagonists (e.g., tiotropium) as step-up controller therapy in pediatric asthma?

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Question 381

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?

A. Pituitary tumor
B. Absence of second X chromosome
C. Androgen receptor mutation
D. Failure of paramesonephric duct development

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The answer is **D. Failure of paramesonephric duct development**.

This presentation is classic for **Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome**, caused by embryologic underdevelopment of the paramesonephric (Müllerian) duct, resulting in **agenesis of the uterus and upper vagina** in an otherwise phenotypically normal 46,XX female.[1][2] MRKH syndrome is the second most common cause of primary amenorrhea, accounting for approximately 10–15% of cases.[3]

The critical features that point to MRKH over other diagnoses:

- **Normal female-range testosterone** — excludes complete androgen insensitivity syndrome (CAIS), which presents with **male-range testosterone**[4][5]
- **Normal pubic hair** — CAIS patients have **absent or sparse pubic hair** due to nonfunctional androgen receptors, whereas MRKH patients (46,XX with functional ovaries) have normal androgen-mediated hair growth[2][5]
- **Absent uterus with normal external genitalia and breast development** — the ovaries are embryologically separate from the Müllerian ducts and function normally in MRKH, producing estrogen for breast development and androgens for pubic hair[1][2]

Why the other options are incorrect:

- **A. Pituitary tumor** — Would cause hormonal dysfunction (hypogonadotropic hypogonadism) leading to absent breast development and possibly absent pubic hair; would not cause a congenitally absent uterus.
- **B. Absence of second X chromosome (Turner syndrome, 45,X)** — These patients have streak gonads and absent breast development without exogenous estrogen, but they do have a uterus (derived from Müllerian ducts, which develop by default without Müllerian inhibiting substance).
- **C. Androgen receptor mutation (CAIS)** — Shares the absent uterus finding, but testosterone would be in the **male range** and pubic hair would be **absent or sparse**. This patient's normal female testosterone and normal pubic hair distribution effectively rule out CAIS.[2][4]

Would you like to explore the current management and fertility options for MRKH syndrome?

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Question 382

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?

A. Elevated serum CA-125 level
B. Elevated serum beta-hCG level
C. Prolonged prothrombin time
D. Cervical dysplasia on Pap smear

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The answer is **A. Elevated serum CA-125 level**.

This presentation is classic for **advanced epithelial ovarian cancer**: a 61-year-old **postmenopausal, nulliparous** woman with **increasing abdominal girth, weight loss, ascites** (shifting dullness), and a **right adnexal mass**. Risk factors present include nulliparity and early menarche (age 10).[1][2] Approximately 80% of patients with epithelial ovarian cancer have advanced-stage disease at diagnosis, and the symptoms described — abdominal bloating, increased abdominal size, weight loss, and ascites with a palpable pelvic mass — are characteristic of advanced-stage disease.[1]

CA-125 is elevated in approximately 80% of women with epithelial ovarian cancer overall, and in **75%–92% of advanced-stage disease**.[1][3][4] It is the most extensively studied serum tumor marker for ovarian malignancy and is particularly useful in postmenopausal women, where it has a sensitivity of 69%–87% and specificity of 81%–93% for distinguishing benign from malignant adnexal masses.[3] ACOG recommends that all **postmenopausal women with a worrisome adnexal mass and CA-125 ≥35 U/mL be referred to a gynecologic oncologist**.[3][4]

Why the other options are incorrect:

- **B. Elevated beta-hCG** — Beta-hCG elevation occurs with germ cell tumors (dysgerminoma, choriocarcinoma) or pregnancy-related conditions. Germ cell tumors predominantly affect younger women (teens to early 20s) and are exceedingly rare in a 61-year-old postmenopausal patient. Epithelial ovarian cancer, which accounts for ~90% of ovarian malignancies, does not elevate beta-hCG.[1][4]
- **C. Prolonged prothrombin time** — This would suggest hepatic synthetic dysfunction (e.g., cirrhosis). Although cirrhosis can cause ascites, the combination of an adnexal mass, weight loss, and fatigue in a postmenopausal nulliparous woman points strongly to malignant ascites rather than hepatic disease.
- **D. Cervical dysplasia on Pap smear** — Her prior ASCUS with **negative HPV testing** 3 years ago carries a very low risk of underlying or progressive cervical dysplasia. HPV-negative ASCUS is considered low-risk and warrants repeat co-testing at 3 years per standard guidelines, not immediate concern for dysplasia.

Would you like to explore the recommended initial workup and staging evaluation for suspected ovarian malignancy in this patient?

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Question 383

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?

A. Renal biopsy
B. Ultrasound
C. Abdominal-pelvic CT scan
D. Blood analysis

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The answer is **B. Ultrasound**.

Renal and bladder ultrasound is the recommended first-line imaging modality for evaluating suspected urinary tract obstruction.[1][2][3] It is non-invasive, can be performed at the bedside, requires no intravenous contrast, and provides rapid assessment of **hydronephrosis** — the hallmark sonographic finding of obstructive uropathy.[2][3]

The Society of Critical Care Medicine guidelines suggest that ultrasonography may be used to exclude mechanical causes of acute renal failure in the ICU, as it can readily detect the presence or absence of hydronephrosis.[3] A Lancet review on AKI diagnostics similarly states that imaging

studies are usually performed to rule out urinary tract obstruction, and that point-of-care ultrasound has been shown to accurately detect hydronephrosis.[1]

Why not the other options:

- **A. Renal biopsy** — An invasive procedure used to evaluate parenchymal renal disease (e.g., glomerulonephritis, interstitial nephritis), not urinary tract obstruction. It has no role in assessing mechanical obstruction.
- **C. Abdominal-pelvic CT scan** — While CT provides superior anatomic detail and is better at identifying the etiology of obstruction (e.g., malignancy, retroperitoneal fibrosis), it is generally considered a **second-line study** after ultrasound. CT may be pursued if ultrasound is nondiagnostic, particularly in cases where obstruction may occur without hydronephrosis (e.g., malignant encasement). However, as an initial evaluation, ultrasound remains the standard first step.[1][4][5]
- **D. Blood analysis** — BUN and creatinine can confirm renal dysfunction, but blood tests cannot localize or characterize an obstruction anatomically. They are part of the overall workup but do not evaluate the urinary tract itself.

Notably, ultrasound does have limitations: it may be falsely negative in early or nondilated obstruction, which can occur with malignancy or retroperitoneal fibrosis.[1][5] In this patient — with recent pelvic surgery, radiation, and aggressive prostate cancer — if ultrasound is unrevealing, CT or retrograde pyelography should be pursued promptly to exclude causes such as ureteral injury, abscess, or malignant obstruction.[5][6]

Would you like to explore management options for infected obstructive uropathy in this patient, such as percutaneous nephrostomy versus retrograde stenting?

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Question 384

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?

A. Alprazolam
B. Primidone
C. Propranolol
D. Trihexyphenidyl

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The answer is **C. Propranolol**.

This presentation is consistent with **essential tremor (ET)**: a bilateral, high-frequency action tremor elicited on finger-to-nose testing, with a gradual course over years and an otherwise unremarkable neurological examination.[1][2] The tremor improving over the course of the day as the patient consumes alcohol is a classic feature of ET, as alcohol typically decreases tremor in these patients.[1] Despite the family history of Parkinson disease, this patient lacks the cardinal features of PD — **resting tremor, bradykinesia, rigidity, and asymmetric onset** — making ET far more likely.[2][3]

Propranolol and primidone are both first-line pharmacotherapy for ET (AAN Level A, established as effective), with propranolol being the **only FDA-approved** treatment.[1][4] Across randomized trials, propranolol reduced tremor amplitudes by approximately **55%** at doses of **120–240 mg/day**.[5] In this patient, propranolol is preferred over primidone for several reasons:

- **Concurrent hypertension** (BP 159/84) — propranolol provides an additional antihypertensive benefit.

- **Daily alcohol use** (2–3 beers/day) — primidone is metabolized to **phenobarbital**, which carries risk of additive CNS depression with alcohol.[5]
- Primidone also has a higher rate of early adverse effects (dizziness, fatigue, malaise in 23–32% vs. 8% with propranolol).[5]

The other options are not appropriate:

- **Alprazolam** — classified as only Level B (probably effective) by AAN guidelines and is not first-line; benzodiazepine use is particularly concerning in a patient with regular alcohol intake.[4]
- **Trihexyphenidyl** — an anticholinergic used for **Parkinson disease tremor**, not essential tremor.

> "Propranolol and primidone are the two compounds with the highest level of evidence to treat essential tremor by reducing the severity of upper-limb symptoms. The nonselective beta-blocker propranolol has been shown to be an effective treatment in randomized, controlled trials at doses ranging from 120 to 240 mg per day."
>
> —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.
>
> Used under license from The New England Journal of Medicine.

Would you like to explore second-line treatment options for essential tremor refractory to first-line agents?

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Question 385

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?

A. Amphotericin B
B. Ivermectin
C. Praziquantel
D. Pyrantel pamoate

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The answer is **D. Pyrantel pamoate**.

This presentation — intense **perianal pruritus**, severe excoriations, and a **positive scotch tape test** — is classic for **Enterobius vermicularis (pinworm)** infection. The scotch tape (cellophane tape) test detects characteristic flattened, asymmetric ova deposited by female worms in the perianal region, ideally collected in the early morning.[1][2]

Standard treatment for pinworm includes **albendazole, mebendazole, or pyrantel pamoate**, all with cure rates exceeding 90%.[1] Treatment is given as a single dose with a repeat dose at 2 weeks to address reinfection from eggs in the environment.[1][3]

Given this patient's **documented allergy to albendazole**, **pyrantel pamoate** is the appropriate alternative among the listed choices. It is dosed at **11 mg/kg orally once** (max 1 g), repeated in 2 weeks, and is available over the counter.[1]

Why the other options are incorrect:

- **A. Amphotericin B** — An antifungal agent (polyene class) used for invasive fungal infections; it has no antihelminthic activity.

- **B. Ivermectin** — Effective against several nematodes (e.g., Strongyloides, Ascaris) but is **not a standard treatment for pinworm** infection.[4]
- **C. Praziquantel** — Active against cestodes (tapeworms) and trematodes (flukes); it has no clinically relevant activity against nematodes like Enterobius.

Mebendazole (another benzimidazole) would also be an acceptable alternative in practice, though potential cross-reactivity with albendazole could be a concern and it was not listed as a choice.[5]

Would you like to explore household treatment and hygiene strategies to prevent pinworm reinfection?

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Question 386

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?

A. Inferior vena cava
B. Internal iliac vein
C. Renal artery
D. Portal vein

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The correct answer is **A. Inferior vena cava**.

The **IVC runs in direct contact with the anterior vertebral column** from its formation (confluence of the common iliac veins, typically at L4–L5) upward through the abdomen. At L3, the IVC is consistently present along the right anterolateral aspect of the vertebral body.[1][2] A cadaveric and CT-based study specifically noted that the IVC was **the most frequently involved vessel in close proximity to the vertebral body from T12 to L3**.[2]

The other choices are incorrect based on anatomical landmarks:

- **C. Renal artery** — The renal arteries arise from the aorta at approximately **L1–L2**, well above L3.[3][4]
- **D. Portal vein** — The portal vein forms behind the neck of the pancreas at approximately **L1–L2**, also above L3.
- **B. Internal iliac vein** — The internal iliac veins are **pelvic vessels**, located well below L3. The common iliac veins themselves typically join to form the IVC at L4–L5, and the internal iliacs branch off even more distally in the pelvis.[5][6][7]

Notably, the **abdominal aorta** is also present at L3 (bifurcation most commonly occurs at L4 in ~67–83% of individuals), but it is not among the answer choices.[3][8] The IVC is the only listed structure anatomically located at L3.

Would you like to explore the management of penetrating IVC injuries, including surgical approach and repair techniques?

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Question 387

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?

A. Low-dose prednisolone
B. High-dose prednisolone
C. Paroxetine
D. Allopurinol

https://openevidence.com/ask/68fdcd93-80bb-469e-9b4d-9503b097a6d2

C. Paroxetine.

The presentation is classic **fibromyalgia**: a 38-year-old woman with >3 months of chronic widespread pain, sleep disturbance, functional impairment, tenderness at classic ACR 1990 tender-point sites (occiput, elbows, medial knee fat pads), and unremarkable laboratory workup. [1][2][3] Of the four choices, paroxetine is the only agent with any supporting evidence, and it additionally addresses her comorbid generalized anxiety disorder.

Why paroxetine

- A Cochrane review found **very low-quality evidence that citalopram, fluoxetine, and paroxetine produce a small benefit over placebo** in the proportion of patients achieving ≥30% pain reduction and 25% global improvement, as well as in pain intensity and depression. The same review cautions that evidence for improvement in sleep, fatigue, and tenderness is uncertain, and that a class effect should not be assumed.[4]

- Practice guidelines nonetheless include SSRIs among options for fibromyalgia, and EULAR/EAAR specifically lists fluoxetine among recommended antidepressants. A network meta-analysis found SSRIs improved quality of life and pain, though not fatigue.[5][6][7]
- Her untreated GAD is an independent reason favoring an antidepressant; SSRIs are first-line for GAD, and coexisting mood/anxiety symptoms in chronic pain make antidepressant therapy particularly attractive.[8]

Why the others are wrong

- **Low- or high-dose prednisolone (A, B):** no inflammatory or autoimmune disease is present — labs are unremarkable and fibromyalgia is a centralized (non-inflammatory) pain disorder. Corticosteroids offer no benefit and carry substantial harm with chronic use.[2]
- **Allopurinol (D):** urate-lowering therapy for gout. There is no monoarticular inflammatory arthritis, tophi, or hyperuricemia; the tender-point distribution is not articular.

Practical caveats beyond the exam answer

Paroxetine would not be the preferred agent in real practice. The FDA-approved drugs for fibromyalgia are **duloxetine, milnacipran, and pregabalin**, which have moderate-to-good evidence that roughly 1 in 10 patients with moderate-to-severe pain achieves ≥50% pain reduction over 4–12 weeks.[9] Duloxetine 120 mg had the largest effect on pain and depressive symptoms in a network meta-analysis, while **amitriptyline** ranked best for sleep, fatigue, and quality of life and had the best acceptability.[10] Given comorbid anxiety and prominent sleep disturbance, **duloxetine** or **low-dose amitriptyline/cyclobenzaprine at bedtime** would be more evidence-based choices.[1][11] Combination of a bedtime gabapentinoid with a daytime SNRI outperformed either alone in a randomized trial.[1]

Before restarting paroxetine, confirm the prior response, reason for discontinuation, and tolerability; also assess pregnancy status, since paroxetine is generally avoided in pregnancy when alternatives exist. Counsel on discontinuation syndrome (short half-life), sexual dysfunction, weight gain, and CYP2D6 inhibition. Allow an adequate trial of **6–12 weeks** before judging effectiveness.[7]

Failure of self-directed yoga does not equate to failure of exercise therapy — **graded aerobic and strength exercise plus patient education remain the foundation** of fibromyalgia management and carry the only strong EULAR recommendation.[11]

Would you like to explore duloxetine dosing and titration for fibromyalgia with comorbid anxiety?

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Question 388

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?

A. Baroreceptor-mediated vasodilation
B. Increased acetylcholine at the sinoatrial node
C. Increased atrial natriuretic peptide release
D. Increased norepinephrine at the sinoatrial node

https://openevidence.com/ask/27cceb58-1aba-4db3-86c7-36cf814c5cb8

The correct answer is **D. Increased norepinephrine at the sinoatrial node**.

This patient with actively bleeding lacerations is in the **compensatory phase of early hemorrhage**. Despite active blood loss, his vital signs remain relatively preserved (BP 110/74, HR 82), with **anxiety as the earliest clinical manifestation** of sympathetic activation — consistent with Class I hemorrhage (<15% blood volume loss).[1]

Mechanism at play: Decreased blood volume reduces venous return and cardiac output, lowering pulse pressure sensed by **baroreceptors in the aortic arch and carotid sinus**. Reduced baroreceptor stretch decreases their afferent firing rate, which triggers **increased sympathetic outflow** and **decreased parasympathetic (vagal) tone**.[2][3] Sympathetic postganglionic fibers release **norepinephrine at the SA node**, increasing heart rate and contractility, while also causing peripheral vasoconstriction to maintain blood pressure.[3][4]

Why the other choices are incorrect:

- **A. Baroreceptor-mediated vasodilation** — Baroreceptor unloading during hemorrhage produces **vasoconstriction**, not vasodilation. Vasodilation occurs only during decompensated hemorrhage (>30% blood volume loss) when sympathetic outflow paradoxically decreases.[2][5]

- **B. Increased acetylcholine at the SA node** — Hemorrhage causes **withdrawal of vagal (parasympathetic) tone**, meaning less acetylcholine at the SA node, not more.[6]
- **C. Increased atrial natriuretic peptide (ANP) release** — ANP is released in response to **atrial stretch from volume overload**. Hemorrhage reduces venous return and atrial filling, so ANP secretion would decrease, not increase.

Would you like to explore the classification and staged management of hemorrhagic shock (Class I–IV)?

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Question 389

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?

A. Chemotherapy, surgical resection and radiation
B. Chemotherapy and radiation
C. Surgical resection
D. Hormone replacement therapy

https://openevidence.com/ask/09c5aa4a-4631-42d0-9d47-722ecc9b7ab2

The answer is **C. Surgical resection**.

This presentation is consistent with a **craniopharyngioma** — a benign (WHO Grade I) embryonic tumor of the sellar/suprasellar region. The key diagnostic features include **bitemporal hemianopsia** and **papilledema** (suprasellar mass compressing the optic chiasm and causing raised intracranial pressure), **central hypothyroidism** (low TSH 0.1 mIU/L with low free T4 6 pmol/L), **short stature with weight gain** (growth hormone deficiency), **polyuria**, **hypoglycemia**

(cortisol/GH deficiency), and **orthostatic hypotension** (adrenal insufficiency).[1][2] Nonpitting edema and decreased reflexes reflect the hypothyroid state.[3]

Why surgical resection is the necessary treatment:

Surgical resection is the primary definitive treatment for craniopharyngioma.[2][4][5] The goals are to establish diagnosis, relieve mass effect on the optic chiasm and other structures, and achieve maximal safe tumor removal.[6] In pediatric patients, the adamantinomatous subtype predominates, and the approach ranges from gross total resection (when safely achievable without hypothalamic injury) to subtotal resection followed by adjuvant radiotherapy when hypothalamic involvement precludes safe complete removal.[3][7][8]

Why the other options are incorrect:

- **A and B (chemotherapy-containing regimens):** Chemotherapy is **not** a standard component of craniopharyngioma treatment. Craniopharyngiomas are benign tumors that do not respond to conventional chemotherapy. Targeted therapies (e.g., BRAF inhibitors) have a limited role only in the papillary subtype with BRAF V600E mutations, which occurs almost exclusively in adults.[5][7][9]
- **D (hormone replacement therapy):** While hormone replacement is essential for managing the panhypopituitarism and will be required lifelong postoperatively, it does not address the mass effect causing papilledema, visual field loss, and progressive neurological deterioration. The tumor itself requires removal.[10]

Notably, while surgical resection is the definitive treatment, this patient's **acute endocrine derangements** (hypoglycemia, severe hyponatremia, orthostatic hypotension) require urgent stabilization — including stress-dose glucocorticoids and glucose correction — before surgery can proceed safely. Glucocorticoid replacement must precede thyroid hormone replacement to avoid precipitating adrenal crisis.[3]

Would you like to explore the long-term complications and management after craniopharyngioma surgery in pediatric patients?

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Question 390

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?

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.

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The answer is **D: A Western blot will show increased HIF-1α compared to a normoxic control**.

The central mechanism described in this question is **post-translational regulation** of HIF-1α. In normal cells under normoxic conditions, VHL targets HIF-1α for proteasomal degradation via prolyl hydroxylation and ubiquitination. In RCC with VHL loss-of-function, HIF-1α protein escapes degradation and **constitutively accumulates** even under normoxia.[1][2] Because Western blot detects **protein**, it is the correct technique to identify this accumulation.

Key points distinguishing each answer choice:

- **Western blot (protein detection) — correct.** VHL-deficient RCC cells constitutively express HIF-1α protein under normoxic conditions. Immunoblotting studies have demonstrated increased HIF-1α protein in 75% of clear cell RCCs, and re-introduction of functional VHL restores protein instability under normoxia. Compared to a normoxic control cell (where functional VHL degrades HIF-1α), the RCC cell will show markedly **elevated HIF-1α protein**. [1][2]

- **Northern blot (mRNA detection) — choices A and B are incorrect.** The regulation of HIF-1α in this scenario is at the protein level, not the transcriptional level. HIF-1α mRNA levels were **not significantly different** between tumors and adjacent normal kidney tissue. The question stem specifically describes a post-translational mechanism (inhibition of hydroxylation preventing proteasomal degradation), making mRNA-based detection uninformative.[2]
- **Southern blot (DNA detection) — choice C is incorrect.** Southern blot detects genomic DNA. The HIF-1α gene itself is not amplified or structurally altered in this scenario; the dysregulation occurs entirely at the protein stability level.

Would you like to explore how HIF-2α inhibitors like belzutifan therapeutically target this VHL-HIF pathway in renal cell carcinoma?

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Question 391

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?

A. Elevated transaminases
B. Leukocytosis
C. Hyponatremia
D. Proteinuria

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The answer is **D. Proteinuria**.

This presentation — a primigravida at 36 weeks with **new-onset tonic-clonic seizure, hypertension (160/90 mmHg), headache, edema, hyperreflexia, and ankle clonus** — is classic for **eclampsia**, defined as the occurrence of seizures in the setting of preeclampsia.[1]

Proteinuria is the most common laboratory finding in preeclampsia/eclampsia. Renal involvement is most commonly manifested as proteinuria because of the pathognomonic lesion of **glomerular endotheliosis** and associated loss of podocyte integrity.[2] Proteinuria (≥300 mg/24h or protein/creatinine ratio ≥0.3) is a core diagnostic criterion alongside hypertension.[3][4]

Why the other options are less likely:

- **A. Elevated transaminases** — Liver involvement occurs in only **20–30% of preeclampsia** cases and is described as an infrequent expression of the disease. Transaminase elevation is more characteristic of HELLP syndrome, which complicates only 10–20% of severe preeclampsia cases.[5][6][7]

- **B. Leukocytosis** — Not a hallmark laboratory finding. While relative neutrophilia can occur as part of the hematologic changes of preeclampsia, it is not a defining or common laboratory abnormality.[2]

- **C. Hyponatremia** — Not a characteristic feature of preeclampsia or eclampsia.

Would you like to explore the acute management of eclampsia, including magnesium sulfate dosing and delivery timing?

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Question 392

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?

A. Total caloric intake
B. Relative protein intake
C. Relative carbohydrate intake
D. Relative fat intake

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The answer is **B. Relative protein intake**.

This presentation — a **listless child from a food-insecure region with a protuberant abdomen, ascites (positive fluid wave), and lower extremity edema** — is classic for **kwashiorkor**, the form of severe acute malnutrition caused by **relative protein deficiency with still-substantial caloric (energy) intake**.[1][2]

Distinguishing kwashiorkor from marasmus:

- **Kwashiorkor** results from diets adequate in calories but deficient in protein (e.g., cassava- or maize-based weaning diets). It is characterized by **edema, fatty liver, hypoalbuminemia, abdominal distension, and behavioral changes** such as listlessness and irritability. The term itself derives from a Ghanaian word meaning "the disease the older child develops when the new child is born," reflecting loss of breast milk protein upon weaning.[1][3]
- **Marasmus** results from **total caloric and protein deficiency**, presenting with severe wasting, loss of subcutaneous fat, and muscle atrophy — but **without edema**.[2][4]

The edema in kwashiorkor is driven primarily by **hypoalbuminemia** (reduced hepatic albumin synthesis due to amino acid scarcity), though inflammatory mediators and electrolyte

disturbances (particularly potassium depletion) also contribute.[1][5][6] A low ratio of protein to energy disrupts the usual hypometabolic adaptation to undernutrition, leading to continued tissue turnover with defective protein synthesis.[7]

Option A (total caloric intake) would describe marasmus. Options C and D (relative carbohydrate or fat intake) are not recognized as primary drivers of this clinical syndrome.

Would you like to explore the recommended refeeding protocol and prevention of refeeding syndrome in children with severe acute malnutrition?

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Question 393

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?

A. Factor VII
B. Factor VIII
C. Factor IX
D. Factor XII

https://openevidence.com/ask/98ef5ef3-ac66-4327-b05b-5cfa96fafca2

The answer is **D. Factor XII**.

The combination of an **isolated prolonged PTT** with **decreased bradykinin formation** and **no clinical bleeding diathesis** is pathognomonic for **Factor XII (Hageman factor) deficiency**.

Why Factor XII fits every clue:

- **Prolonged PTT with normal PT and normal bleeding time:** Factor XII is part of the intrinsic (contact activation) pathway. Its deficiency prolongs the PTT without affecting the PT (extrinsic pathway) or platelet-dependent primary hemostasis (bleeding time).[1][2]
- **Decreased bradykinin formation:** Factor XII activates prekallikrein to kallikrein, which cleaves high molecular weight kininogen (HMWK) to release **bradykinin**. Without Factor XII, this kallikrein-kinin pathway is impaired, directly explaining the decreased bradykinin. [3][4][5]

- **No spontaneous bleeding despite prolonged PTT:** Factor XII deficiency is unique among coagulation factor deficiencies in that it **does not cause clinical bleeding**. The knee swelling here is traumatic (fall from jungle gym), not a spontaneous hemarthrosis. The history of "abnormal coagulation labs before appendectomy" reflects the classic scenario of Factor XII deficiency being incidentally discovered on preoperative screening.[1][6]

Why the other options are incorrect:

- **A. Factor VII** — Part of the extrinsic pathway; deficiency prolongs PT, not PTT, and has no role in bradykinin generation.
- **B. Factor VIII (Hemophilia A)** — Prolongs PTT, but causes significant clinical bleeding (spontaneous hemarthroses) and has no effect on bradykinin formation.
- **C. Factor IX (Hemophilia B)** — Same reasoning as Factor VIII; prolongs PTT with clinical bleeding, no bradykinin involvement.

The distinguishing feature in this question is the **decreased bradykinin formation**, which exclusively localizes the defect to the contact activation system — specifically Factor XII, which sits at the apex of both the intrinsic coagulation cascade and the kallikrein-kinin (bradykinin-generating) pathway.[3][4]

Would you like to explore the perioperative management and clinical significance of Factor XII deficiency?

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Question 394

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?

A. Carpopedal spasm
B. Photodermatitis
C. Night blindness
D. Intracranial hypertension

https://openevidence.com/ask/57656599-3743-4bc6-aee8-775049994b13

The answer is **C. Night blindness**.

The cystoscopic finding of **pearl-like plaques** (leukoplakia) with biopsy showing **stratified squamous epithelium with hyperkeratosis** represents **keratinizing squamous metaplasia** of the bladder. When caused by a vitamin deficiency, this is the hallmark of **vitamin A deficiency** — vitamin A (retinoic acid) is essential for maintaining normal epithelial differentiation, and its absence leads to squamous metaplasia with keratinization of transitional and columnar epithelia, including the urothelium.[1][2][3][4]

This patient's **Crohn disease** predisposes to malabsorption of fat-soluble vitamins (A, D, E, K), particularly with ileal involvement.

Night blindness (nyctalopia) is the earliest clinical manifestation of vitamin A deficiency, resulting from impaired rhodopsin regeneration in rod photoreceptors.[2][5] Progressive deficiency leads to xerophthalmia, Bitot spots, corneal xerosis, keratomalacia, and ultimately permanent blindness.[5]

The other options correspond to different conditions:

- **A. Carpopedal spasm** — hypocalcemia (e.g., vitamin D deficiency or hypoparathyroidism), not vitamin A deficiency
- **B. Photodermatitis** — niacin (vitamin B3) deficiency (pellagra)

- **D. Intracranial hypertension** — associated with hypervitaminosis A (vitamin A excess), not deficiency

Would you like to explore screening and supplementation strategies for fat-soluble vitamin deficiencies in Crohn disease?

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Question 395

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?

A. Goblet cells
B. Bronchial epithelial cells
C. Type II pneumocytes
D. Vascular smooth myocytes

https://openevidence.com/ask/78d14591-229f-4d3b-88d9-dad3351d16e7

The answer is **C. Type II pneumocytes**.

Antenatal betamethasone accelerates fetal lung maturation primarily by stimulating **type II pneumocytes** to increase **surfactant production**. Surfactant, composed largely of phospholipids and surfactant proteins (SP-A, SP-B, SP-C, SP-D), reduces alveolar surface tension and prevents atelectasis at birth. Antenatal corticosteroid therapy improves fetal lung mechanics and gas exchange through accelerated morphologic development of type I and type II pneumocytes, with enhanced production of surfactant-binding proteins and fetal lung antioxidant enzymes.[1]

The mechanism involves corticosteroids crossing the placenta (as they resist degradation by placental 11β-HSD2) and acting on fetal pneumocytes to trigger RNA synthesis coding for proteins involved in **phospholipid biosynthesis** and glycogen breakdown.[2][3] Microphysiological platform studies have directly demonstrated that corticosteroid exposure improves surfactant production from immature pneumocytes.[4]

Beyond surfactant, betamethasone also increases lung compliance, decreases vascular permeability, matures lung parenchymal architecture, and enhances clearance of fetal lung fluid.[2] Clinically, this translates to significant reductions in respiratory distress syndrome (RR 0.71), neonatal death (RR 0.78), and perinatal death (RR 0.85).[5]

The other options are incorrect:

- **Goblet cells** produce mucus in the airways and are not the target of antenatal corticosteroids for lung maturity.
- **Bronchial epithelial cells** line the airways but are not the primary mediators of surfactant production.
- **Vascular smooth myocytes** are not involved in surfactant synthesis or the principal mechanism of corticosteroid-induced lung maturation.

Would you like to explore the optimal dosing regimen and timing of antenatal betamethasone administration?

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Question 396

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?

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.”

https://openevidence.com/ask/1c00d2b8-9f18-4cb6-85c4-4730646ca5e9

The best response is **C. "I can not help you due to the ethical principle of nonmaleficence."**

Nonmaleficence — the obligation not to intentionally inflict harm ("primum non nocere") — is the principle most directly violated by this proposal. The plan involves **deliberately infecting healthy individuals with chlamydia**, which constitutes direct, intentional infliction of disease. As outlined in JAMA, "the principle of nonmaleficence states that one ought not to inflict harm on a person," and this justifies the need to minimize risks in research.[1] The AHA/ACC consensus similarly defines nonmaleficence as "the duty to do no harm in every interaction with patients".[2]

Why not the other choices:

- **Autonomy (A):** While autonomy is also violated (prisoners are a vulnerable population with limited capacity to provide truly voluntary consent), the core ethical problem here is not about consent — it is about the act of intentionally causing disease.
- **Justice (B):** Justice concerns the fair selection of research participants and equitable distribution of research burdens. Targeting prisoners does raise justice concerns, but again, the most fundamental issue is the deliberate infliction of harm.
- **Beneficence (D):** Beneficence refers to the obligation to act in the best interest of the patient. While the study fails this standard too, nonmaleficence more precisely captures the prohibition against actively causing harm, as opposed to the failure to do good.

Notably, challenge studies involving deliberate infection have historically drawn scrutiny precisely because they "directly flout the Hippocratic principle of primum non nocere".[3] When ethically conducted, such studies are limited to treatable or self-limiting diseases with robust informed consent and safety measures — none of which are met in this scenario.[4]

Would you like to explore the ethical requirements for conducting controlled human infection studies, particularly in vulnerable populations?

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Question 397

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?

A. IL-28
B. TGF-β
C. IFN-α
D. IL-4

https://openevidence.com/ask/bcfad376-50a3-4815-9e69-9f512464e017

The answer is **D. IL-4**.

This clinical presentation — refractory asthma, **peripheral eosinophilia**, **elevated serum IgE**, bronchial wall thickening with perihilar opacities, and **septate hyphae branching at 45 degrees** on sputum culture — is classic for **allergic bronchopulmonary aspergillosis (ABPA)**.

ABPA is driven by an exaggerated **Th2 immune response** to *Aspergillus fumigatus* antigens. The hallmark cytokines of this response are **IL-4, IL-5, and IL-13**.[1][2] Among the answer choices, **IL-4** is the Th2 cytokine central to ABPA pathogenesis:

- **IL-4 drives IgE class switching** in B lymphocytes, accounting for the markedly elevated total and Aspergillus-specific IgE seen in ABPA.[3]
- It **promotes Th2 differentiation** while suppressing Th1 (IFN-γ) responses, perpetuating the allergic inflammatory cycle.[3][4]
- It **enhances eosinophil recruitment** by upregulating VCAM-1 on endothelial cells.[3]
- ABPA patients demonstrate **increased sensitivity to IL-4 stimulation** compared with non-ABPA asthmatics, with skewing toward Th2 responses specifically to Aspergillus allergens.[4][5]

BAL fluid analysis in ABPA patients shows significantly elevated IL-4 and IL-5, with low IFN-γ — a pattern consistent with Th2-dominant inflammation.[6]

Why not the other options:

- **IL-28 (IFN-λ)** — an antiviral interferon, not involved in allergic fungal disease.
- **TGF-β** — associated with fibrosis and regulatory T-cell function, not the primary driver of ABPA.
- **IFN-α** — a type I interferon involved in antiviral immunity; IFN-γ (Th1) is actually *decreased* in ABPA.[7]

Would you like to explore the diagnostic criteria and treatment approach for ABPA?

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Question 398

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?

A. Renal agenesis
B. Pulmonary hypoplasia
C. Duodenal atresia
D. Posterior urethral valve

https://openevidence.com/ask/1846f06f-628c-4e2e-a750-48b5a902b093

The answer is **C. Duodenal atresia**.

The ultrasound findings describe **polyhydramnios** — excess amniotic fluid (2.5 L; AFI 34) — which results from conditions that either **impair fetal swallowing/GI absorption** of amniotic fluid or **increase fetal urine production**.[1] Amniotic fluid volume is maintained by a balance between fetal swallowing (which removes fluid) and fetal urination (which adds fluid). **Duodenal atresia** causes GI obstruction that prevents the fetus from effectively swallowing and absorbing amniotic fluid, leading to its accumulation.[1][2] Polyhydramnios is reported in **30–81% of duodenal atresia cases**.[2][3]

The other options are incorrect:

- **A. Renal agenesis** — Absence of kidneys eliminates fetal urine production, the major contributor to amniotic fluid in the second and third trimesters. This causes **oligohydramnios** (decreased fluid), not polyhydramnios, and is the hallmark of Potter sequence.
- **B. Pulmonary hypoplasia** — Underdeveloped lungs are typically a **consequence** of oligohydramnios (insufficient fluid impairs lung expansion), not a cause of polyhydramnios.
- **D. Posterior urethral valves** — This obstructs fetal urinary outflow, reducing urine entering the amniotic space and causing **oligohydramnios**.

The SMFM classifies fetal etiologies of polyhydramnios into two major categories: **impaired swallowing** (GI obstruction including duodenal atresia, neuromuscular disorders, craniofacial anomalies) and **excess urine production** (renal/urinary anomalies such as UPJ obstruction, Bartter syndrome).[1]

Would you like to explore the characteristic prenatal ultrasound findings and associated anomalies seen with duodenal atresia?

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Question 399

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?

A. Alpha-2 adrenergic receptor
B. Beta-1 adrenergic receptor
C. Beta-2 adrenergic receptor
D. D2 receptor

https://openevidence.com/ask/7d9dad6d-45ad-4ddd-a45f-3b59708f2f4e

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The answer is **B. Beta-1 adrenergic receptor**.

This patient is presenting with an **acute anterolateral STEMI** (ST elevations in I, aVL, V3–V6) complicated by **cardiogenic shock** — evidenced by acute hemodynamic collapse with hypotension (88/50 mmHg), tachycardia (130/min), loss of consciousness, and signs of poor perfusion (pale, cold, clammy skin). The fundamental problem is **pump failure** with severely reduced cardiac output.

Why Beta-1 stimulation is correct

The hemodynamic derangement in cardiogenic shock is primarily due to depressed myocardial contractility. **Dobutamine**, the prototypical inotrope used in this setting, exerts its primary activity through **stimulation of beta-1 adrenergic receptors** on the heart, increasing contractility (inotropy) and thereby augmenting cardiac output.[1][2] The FDA label for dobutamine states that its "primary activity results from stimulation of the β receptors of the heart while producing comparatively mild chronotropic, hypertensive, arrhythmogenic, and vasodilative effects".[1]

Dobutamine raises blood pressure solely by increasing cardiac output rather than peripheral vasoconstriction.[3] It is the most frequently used inodilator in cardiogenic shock.[4]

Why the other options are incorrect

- **A. Alpha-2 adrenergic receptor** — Alpha-2 agonists (e.g., clonidine) are centrally-acting sympatholytics that reduce sympathetic outflow, lowering heart rate and blood pressure — exactly the opposite of what is needed.
- **C. Beta-2 adrenergic receptor** — Beta-2 stimulation causes bronchodilation and peripheral vasodilation, which would further reduce systemic vascular resistance and worsen hypotension without directly augmenting cardiac contractility.
- **D. D2 receptor** — Dopamine-2 receptor stimulation (as with low-dose dopamine) causes renal and splanchnic vasodilation but does not meaningfully improve cardiac contractility or hemodynamics in shock.

While **norepinephrine** is recommended as the first-line vasopressor in cardiogenic shock with refractory hypotension, norepinephrine acts on both alpha-1 and beta-1 receptors and is not described as "primarily" stimulating one over the other.[5][6] Among the answer choices, **beta-1 receptor stimulation** best addresses the core hemodynamic defect — impaired contractility — that defines cardiogenic shock.

Would you like to explore the role of mechanical circulatory support in AMI-related cardiogenic shock?

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Question 400

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?

A. Dimercaprol
B. Deferoxamine
C. Protamine
D. Succimer

https://openevidence.com/ask/62975e1d-0f6b-4c5f-be79-9a6697b09af4

The answer is **B. Deferoxamine**.

This scenario describes **acute iron poisoning** in a child. The key clues are the mother's supplements for **chronic microcytic anemia** (iron deficiency anemia treated with oral iron), combined with the child's presentation of **abdominal pain, vomiting, and melena** (dark/black stool from GI mucosal injury) — classic features of the first (gastrointestinal) stage of iron toxicity.

Deferoxamine mesylate is an iron-chelating agent FDA-indicated as an adjunct to standard measures for the treatment of **acute iron intoxication**.[1] It chelates iron by forming a stable complex (ferrioxamine), which is renally excreted, producing a characteristic **"vin rosé" (reddish-orange) urine**.[1] Safety and efficacy in pediatric patients ≥3 years old are established for this indication.[1]

Why the other options are incorrect:

- **A. Dimercaprol** — A chelator used for **lead, arsenic, mercury, and gold** poisoning; not indicated for iron toxicity.
- **C. Protamine** — The reversal agent for **heparin** overdose; irrelevant to iron poisoning.
- **D. Succimer (DMSA)** — An oral chelator used primarily for **lead poisoning** in children; it does not chelate iron effectively.

Would you like to explore the clinical stages and management of acute iron poisoning in more detail?

References

1. Deferoxamine Mesylate. Food and Drug Administration. Updated date: 2026-04-06

Question 401

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?

A. Antitoxin
B. Neostigmine
C. Plasmapheresis
D. Riluzole

https://openevidence.com/ask/88cc1464-cf34-4517-85d5-929fb9f66ea1

The answer is **A. Antitoxin**.

This presentation is classic for **foodborne botulism**: a farmer who cans his own foods presenting with **descending paralysis** — beginning with blurry vision, dysarthria, and dysphagia, progressing to facial weakness and respiratory failure requiring intubation — along with preceding GI symptoms (diarrhea) and diminished reflexes.[1][2][3]

Botulinum antitoxin is the specific treatment. It prevents further toxin binding at presynaptic nerve terminals, halting disease progression. A systematic review found 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).[4] Heptavalent botulinum antitoxin (HBAT) is the only available treatment for noninfant botulism in the United States and is available through state health departments and the CDC on a 24/7 basis.[5] Early administration is associated with shorter ICU and hospital stays.[5][6]

The other options are incorrect:

- **Neostigmine** (an acetylcholinesterase inhibitor) treats myasthenia gravis, a postsynaptic neuromuscular junction disorder — botulism is a **presynaptic** disorder.[2][7]
- **Plasmapheresis** is used for Guillain-Barré syndrome or myasthenia gravis crisis; it has no established role in botulism.[8]
- **Riluzole** is used in amyotrophic lateral sclerosis (ALS) to slow disease progression and is not relevant here.

Would you like to explore how to differentiate botulism from other causes of acute neuromuscular weakness such as GBS and myasthenia gravis?

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Question 402

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?

A. Vaginal rhabdomyosarcoma
B. Cystocele
C. Rectocele
D. Uterine leiomyomata

https://openevidence.com/ask/881b3882-7701-4e3e-8f30-8c36bc2b8041

The answer is **B. Cystocele**.

The presentation — **difficulty initiating urination, pelvic fullness, and a mass protruding from the anterior vaginal wall** that worsens with coughing — is classic for a **cystocele** (anterior vaginal wall prolapse). A cystocele occurs when weakened pelvic floor support allows the bladder to herniate into the anterior vaginal wall.[1][2] The prolapse becomes more prominent with maneuvers that increase intra-abdominal pressure, such as coughing or Valsalva.[2][3] Voiding difficulty, including hesitancy and incomplete emptying, results from urethral kinking or bladder outlet obstruction caused by the prolapsed bladder.[4]

Key features that distinguish cystocele from the other options:

- **Rectocele (C):** Involves the **posterior** vaginal wall, not the anterior wall, and typically causes defecatory symptoms (incomplete evacuation, need for splinting) rather than voiding difficulty.[1][5]
- **Vaginal rhabdomyosarcoma (A):** A rare malignancy occurring predominantly in **young children** (sarcoma botryoides), presenting as a grape-like mass. It would be exceedingly rare in a 79-year-old.
- **Uterine leiomyomata (D):** Fibroids are benign uterine smooth-muscle tumors that would not present as a prolapsing anterior vaginal wall mass provoked by coughing.

The anterior vaginal wall origin and the associated urinary symptoms are the most important clinical clues pointing to cystocele in this scenario.[2][4]

Would you like to explore the management options for symptomatic cystocele, including pessary versus surgical approaches?

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Question 403

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?

A. Crohn's disease
B. Acute infective colitis
C. Pseudomembranous colitis
D. Irritable bowel syndrome

https://openevidence.com/ask/617741de-40bf-4dbc-91a0-bbb361d4b8a8

The answer is **A. Crohn's disease**.

The defining clue in this presentation is the **patchy erythema and ulceration distributed across non-contiguous colonic segments** (cecum, ascending colon, descending colon, sigmoid colon) — the classic **skip-lesion** pattern. Crohn's disease features patchy inflammation with skip lesions and areas of macroscopically normal mucosa in between, distinguishing it from ulcerative colitis (which is continuous) and from most infectious colitides.[1][2] The ACG guideline identifies these segmental, discontinuous mucosal changes as among the most useful endoscopic features of Crohn's disease.[3][4]

The **histological findings** of colonic crypts with both lymphocytic and neutrophilic infiltrates (cryptitis with mixed inflammation) are consistent with Crohn's disease. Hallmark histological features include a **focal, patchy inflammatory infiltrate** and lymphoid aggregates; epithelioid granulomas, while pathognomonic, are seen in fewer than 20% of mucosal biopsies.[5] A mixed acute and chronic infiltrate pattern favors IBD over acute self-limited colitis, which typically shows preserved crypt architecture with predominantly acute lamina propria inflammation.[6][7]

Why the other options are less likely:

- **B. Acute infective colitis** — While infectious colitis can occasionally appear patchy, acute self-limited colitis typically resolves within **2–3 weeks**. The 1-month duration with intermittent, relapsing bloody diarrhea favors a chronic inflammatory process. Additionally, classic histologic features of chronicity (mixed lymphocytic and neutrophilic infiltrate) point toward IBD.[6][8]
- **C. Pseudomembranous colitis** — Strongly associated with **antibiotic use**; this patient is on no medications. Endoscopy would characteristically show pseudomembranes, not patchy ulceration with skip lesions.[2]
- **D. Irritable bowel syndrome** — A functional disorder that does **not** produce bloody stools, mucosal ulceration, or inflammatory infiltrates on biopsy.

The nursing home employment raises the question of infectious exposure, but the **skip-lesion pattern on colonoscopy**, the **1-month intermittent course**, and the **mixed inflammatory infiltrate on biopsy** collectively favor Crohn's disease over an infectious etiology.

Would you like to explore initial treatment strategies for newly diagnosed Crohn's disease?

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Question 404

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?

A. Cardiac tamponade
B. Cervical spinal cord transection
C. Pulmonary embolism
D. Undiagnosed pneumonia

https://openevidence.com/ask/4a8b6048-b3b6-4b63-b52e-fc963b6fbb09

The answer is **A. Cardiac tamponade**.

The combination of **profoundly low ScvO2 (39%)**, **cold extremities**, and **refractory hypotension despite adequate volume resuscitation with no active surgical bleeding** in a patient with penetrating thoracoabdominal trauma points to an **obstructive low-cardiac-output state** — specifically cardiac tamponade from hemopericardium.

ScvO2 as the key discriminator

The ScvO2 reflects the balance between systemic oxygen delivery and consumption. A value of **39% (normal ~65–75%)** indicates critically reduced oxygen delivery with compensatory increased tissue oxygen extraction, characteristic of **low-flow states** such as cardiogenic or obstructive shock.[1] In contrast, **distributive shock** (e.g., neurogenic shock from spinal cord injury, sepsis) typically produces a **normal or elevated** ScvO2 because cardiac output is maintained or increased while peripheral extraction is impaired.[1]

Cold extremities confirm low cardiac output

Cold extremities reflect **compensatory peripheral vasoconstriction** driven by sympathetic activation in response to low cardiac output — the expected response in obstructive shock from tamponade.[2] In **neurogenic shock** (option B), loss of sympathetic vascular tone causes **vasodilation and warm extremities**, which is the opposite of what is observed here.

Why not the other options?

- **B. Cervical spinal cord transection** — would produce distributive shock with **warm extremities** (from loss of sympathetic vasomotor tone) and a **normal or high ScvO2**. While the bradycardia (HR 80) could fit neurogenic shock, the cold extremities and severely low ScvO2 are inconsistent with this diagnosis.[1]
- **C. Pulmonary embolism** — although PE is an obstructive cause of shock that could lower ScvO2, it is an unlikely diagnosis in the immediate setting of penetrating trauma without risk factors for thromboembolism.
- **D. Undiagnosed pneumonia** — would cause septic/distributive shock with warm extremities and a normal or high ScvO2; this does not match the clinical picture.

Clinical correlation

Cardiac tamponade is a recognized complication of penetrating chest or upper abdominal wounds.[2][3] In acute traumatic hemopericardium, even a small volume of blood accumulating rapidly in the pericardial space can cause hemodynamic collapse because the pericardium has no time to stretch.[4] The diagnosis should be confirmed emergently with **bedside echocardiography (eFAST)**, and definitive management requires **operative pericardial decompression and repair** — needle pericardiocentesis may temporize but often fails with clotted hemopericardium.[3][5]

Was this question from a board review resource, and would a discussion of the hemodynamic profiles (cardiac output, SVR, filling pressures) across the four shock categories be helpful for review purposes?

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Question 405

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?

A. Imipramine
B. Lithium
C. Donepezil
D. Sulpiride

https://openevidence.com/ask/0ecf14e9-63e2-48b3-b59a-81332acbf308

The answer is **C. Donepezil**.

This patient presents with a clinical picture consistent with **Alzheimer's disease dementia**: insidious onset of progressive memory impairment (inability to retain new information), visuospatial dysfunction (getting lost en route to a familiar location), preserved basic activities of daily living, no focal neurological deficits, a positive family history, and a **MoCA score of 18/30** — well below the ≤25 threshold indicative of cognitive impairment.[1] The absence of major cardiovascular events, head trauma, or other chronic conditions makes vascular or secondary causes of dementia unlikely, and the gradual, progressive course fits the DSM-5 criteria for probable Alzheimer's disease.[2][3]

Donepezil, an **acetylcholinesterase inhibitor**, is the standard first-line pharmacotherapy for mild to moderate Alzheimer's disease. It promotes cholinergic neurotransmission by inhibiting

brain acetylcholinesterase, yielding modest but consistent improvements in cognition, activities of daily living, and global clinical impression.[4][5] The FDA label recommends starting at **5 mg once daily**, with titration to 10 mg after 4–6 weeks for mild to moderate disease.[6] Meta-analyses show approximately a **2.7-point improvement on the ADAS-Cog** and about a **1-point improvement on the MMSE** at 24 weeks compared with placebo.[7]

Why the other options are incorrect:

- **A. Imipramine** — A tricyclic antidepressant with significant anticholinergic properties, which would worsen cognitive function in a patient with Alzheimer's disease. There is no indication of depression in this vignette.
- **B. Lithium** — A mood stabilizer used for bipolar disorder. Not indicated here; there are no features of mania or mood cycling.
- **D. Sulpiride** — An antipsychotic (dopamine D2 antagonist). Antipsychotics carry a **boxed warning** for increased mortality in elderly patients with dementia-related psychosis and are not appropriate here in the absence of psychotic symptoms or behavioral disturbances.

Would you like to explore when to add memantine to donepezil and the evidence for combination therapy in Alzheimer's disease?

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Question 406

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?

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

https://openevidence.com/ask/88def6cf-10e7-4c8f-b363-54efcb24f027

The answer is **B: WBC/mm³ 53,000; % PMN > 75%; Viscosity low**.

This presentation — acute atraumatic monoarticular joint pain, erythema, warmth, swelling, fever (39.1°C), tachycardia, and elevated CRP and procalcitonin — is classic for **septic arthritis**, a musculoskeletal emergency requiring urgent arthrocentesis and empiric antibiotics.

Synovial fluid in septic arthritis characteristically demonstrates:

- **WBC > 50,000 cells/mm³** (often exceeding 100,000/mm³), with neutrophil predominance[1][2]
- **>75% PMNs** — a PMN percentage ≥90% yields a likelihood ratio of 3.4 for septic arthritis[3]
- **Low viscosity** — the IDSA guidelines note that arthrocentesis of a septic joint "usually reveals purulent, low-viscosity synovial fluid with an elevated neutrophil count"[1]

Why the other options are incorrect:

- **A (WBC 1,600; >25% PMN; normal viscosity)** — consistent with a mildly inflammatory process (e.g., early osteoarthritis or mild reactive arthritis), not an acute bacterial infection.

- **C (WBC 160; <20% PMN; high viscosity)** — consistent with **normal synovial fluid**, which has low cellularity, minimal PMNs, and high viscosity from intact hyaluronic acid.
- **D (WBC 2,400; <20% PMN; low viscosity)** — a low PMN percentage and modest WBC count are inconsistent with bacterial infection; this pattern might be seen in a non-inflammatory or early inflammatory process.

The PIDS/IDSA 2023 guidelines further distinguish septic arthritis from transient synovitis, noting that in acute bacterial arthritis the WBC count is "usually greater than 50,000/μL and often exceeds 100,000/μL, with a neutrophil predominance," whereas transient synovitis typically shows WBC counts of 5,000–15,000/μL with mononuclear predominance.[2]

Would you like to explore the empiric antibiotic regimen recommended for septic arthritis in this age group?

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Question 407

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?

A. Carcinoid tumor
B. Sarcoidosis
C. Squamous cell carcinoma of the lung
D. Adenocarcinoma of the lung

https://openevidence.com/ask/a15fcbed-568d-48b3-83b8-17084200b689

The answer is **D. Adenocarcinoma of the lung**.

Adenocarcinoma is the most common lung cancer in non-smokers, accounting for **60%–80%** of cases in this population.[1] This patient's non-smoking status is the most important distinguishing feature. Among NSCLC subtypes, **squamous cell carcinoma has the strongest association with cigarette smoking**, making it far less likely in a lifelong non-smoker.[2]

Several features support adenocarcinoma over the other choices:

- **Peripheral nodule with irregular borders:** Adenocarcinomas classically present as **peripheral lung nodules** with spiculated or irregular margins, consistent with this imaging finding. Squamous cell carcinoma, by contrast, tends to present as a **central, near-hilar mass** associated with endobronchial growth and is more commonly linked to lobar collapse or obstructive pneumonia.[2][3][4][5]
- **No hilar or mediastinal lymphadenopathy:** This argues strongly against **sarcoidosis** (option B), which classically manifests with **bilateral hilar lymphadenopathy**, particularly in African-American women. A solitary irregular pulmonary nodule with constitutional symptoms and no adenopathy is not a typical sarcoidosis presentation.

- **Against carcinoid tumor (option A):** Carcinoid tumors are typically **central, well-circumscribed endobronchial lesions**, not peripheral nodules with irregular borders. Their imaging appearance and clinical behavior differ markedly from what is described here.[6]
- **Constitutional symptoms:** The 8-month course of cough, significant weight loss (9 kg), fatigue, and hemoptysis is consistent with a primary lung malignancy.

In summary, the combination of a **non-smoking woman** with a **peripheral, irregular pulmonary nodule** and constitutional symptoms points most strongly to adenocarcinoma, the predominant histologic subtype of lung cancer in non-smokers.[1][7][8]

Would you like to explore the recommended molecular and biomarker testing for lung adenocarcinoma in non-smokers?

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Question 408

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?

A. Chorionic gonadotropin therapy
B. Exploratory laparoscopy
C. Orchiectomy
D. Orchiopexy

https://openevidence.com/ask/7751b279-b2b5-4300-a112-6ff5926a2582

The answer is **D. Orchiopexy**.

This 11-month-old presents with a classic case of **unilateral cryptorchidism** — a palpable undescended testis located in the inguinal canal, with a poorly rugated hemiscrotum reflecting the absence of the testis on that side. The normal urethral meatus and otherwise normal exam make an isolated undescended testis the diagnosis.

Why orchiopexy is correct:

The **AUA guideline** recommends that in the absence of spontaneous descent by 6 months (corrected for gestational age), **surgery should be performed within the next year** (i.e., by 12–18 months of age).[1][2] For prepubertal boys with **palpable** cryptorchid testes, scrotal or inguinal **orchiopexy** is the standard procedure.[1][2] At 11 months, this child falls squarely within the recommended surgical window. Early orchiopexy preserves fertility potential and reduces the long-term risk of testicular malignancy.[1][3]

Why the other options are incorrect:

- **A. Chorionic gonadotropin therapy** — The AUA guideline explicitly states that **hormonal therapy should not be used** to induce testicular descent, given low response rates, lack of long-term efficacy, and potential harm to germ cells through increased apoptosis.[2][3]

- **B. Exploratory laparoscopy** — Reserved for **nonpalpable** testes. This testis is palpable in the inguinal canal, so open orchiopexy is appropriate without laparoscopic exploration.[1][2]
- **C. Orchiectomy** — Removal of the testis is considered only in specific circumstances, such as a **postpubertal** patient with cryptorchidism, a dysmorphic/hypoplastic testis, or very short vessels — none of which apply to this infant with a palpable, presumably viable testis. [1][2]

Would you like to explore the long-term cancer risk and fertility outcomes after orchiopexy for cryptorchidism?

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Question 409

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?

A. Urinalysis
B. Cervical swab
C. Blood culture
D. CT scan of the abdomen

https://openevidence.com/ask/bac24807-048a-4964-8405-fcd20884fe1c

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The answer is **A. Urinalysis**.

This presentation — **right costovertebral angle (CVA) tenderness**, low-grade fever, nausea, leukocytosis, and elevated CRP in a young woman — is highly suggestive of **acute pyelonephritis**. The most appropriate initial diagnostic step is a **urinalysis** (with urine culture), which serves as the foundational test to confirm this clinical suspicion.

Per a 2018 NEJM review, in a patient with flank pain or tenderness plus a urinalysis showing **pyuria, bacteriuria, or both**, pyelonephritis is an appropriate presumptive diagnosis.[1] Urine culture is described as the **cardinal confirmatory test**, typically yielding ≥10,000 CFU/mL of a uropathogen.[1]

Why not the other options:

- **Cervical swab (B):** While this patient has risk factors for sexually transmitted infections, her presentation localizes to the upper urinary tract (CVA tenderness, no lower abdominal/pelvic tenderness), making pyelonephritis far more likely than pelvic inflammatory disease. Urinalysis remains the priority first step.
- **Blood culture (C):** Blood cultures are not routinely recommended in uncomplicated pyelonephritis; they rarely alter management and are reserved for patients with sepsis, immunocompromise, or diagnostic ambiguity.[1][2]
- **CT abdomen (D):** Imaging at initial presentation is reserved for patients with **sepsis/septic shock, suspected urolithiasis, urine pH ≥7.0, or significant GFR decline** — none of which apply here.[1][3]

Would you like to explore the recommended empiric antibiotic regimen for outpatient management of uncomplicated pyelonephritis?

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Question 410

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?

A. Pulmonary embolism
B. Cellulitis
C. Breast cancer
D. Hypercholesterolemia

https://openevidence.com/ask/68703454-6633-4fe8-a037-84e284faec32

The answer is **A. Pulmonary embolism**.

Raloxifene, a selective estrogen receptor modulator (SERM), carries a **boxed warning for increased risk of venous thromboembolism**, including both deep vein thrombosis and **pulmonary embolism**.[1] High-quality evidence from the ACP guideline demonstrates 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.[2] The RUTH trial and MORE trial confirmed approximately a **2-fold increased risk of VTE** with raloxifene use, with the highest risk occurring during the initial months of treatment.[1][3]

The other options are incorrect:

- **B (Cellulitis)** — Not a recognized adverse effect of raloxifene.
- **C (Breast cancer)** — Raloxifene acts as an **estrogen antagonist in breast tissue** and actually **reduces** the risk of invasive breast cancer (RR 0.44; 95% CI, 0.24–0.80), which is one of its FDA-approved indications. This is particularly relevant for this patient given her family history.[4]
- **D (Hypercholesterolemia)** — Raloxifene does not increase cholesterol; it has a favorable effect on the lipid profile.

Notably, other important adverse effects of raloxifene include hot flashes, leg cramps, peripheral edema, and an increased risk of death due to stroke in women with coronary heart disease or major coronary risk factors.[1][5]

Would you like to explore the optimal osteoporosis treatment choice for this patient given her breast cancer family history?

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Question 411

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?

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

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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 — a phenomenon known as **supplier-induced demand**.[1] Multiple Cochrane reviews confirm that FFS-compensated physicians may provide more unnecessary services compared to salaried or capitation-paid physicians.[2] As summarized by Saini et al., under FFS "many specialties deliver higher volumes of services, distorted referral rates, and lower prevention activity than with fixed payment schemes" and "physicians react to fee reductions by increasing their activity".[3] Critically, this increased utilization is **volume-driven, not quality-driven** — FFS offers no inherent incentive to consider overall healthcare costs or quality outcomes.[4]

Why the other options are incorrect:

- **A. Capitation poses the least financial risk to physicians** — This is the opposite. Capitation pays a **fixed amount per enrolled patient per unit time** regardless of services needed. If patients require more care than anticipated, the physician absorbs the cost difference, placing **greater** financial risk on the physician. FFS, by contrast, reimburses for each service rendered, placing the utilization risk primarily on the payer.[1][2][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 is defined as "fixed

payments per patient per unit time", whereas FFS reimburses physicians for each item of service provided.[1][4]

- **D. Fee-for-service poses the most amount of financial risk to physicians** — FFS actually poses the **least** utilization-related financial risk to physicians because they are paid per service delivered. Capitation places the most financial risk on physicians for unanticipated utilization, as the medical group bears the cost of care exceeding the fixed per-patient payment.[5]

Would you like to explore how pay-for-performance models compare as an alternative compensation strategy?

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Question 412

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?

A. Aspirin and heparin
B. Aspirin and warfarin
C. No treatment indicated
D. Rivaroxaban

https://openevidence.com/ask/10f415e2-248b-4fe2-a7e1-e1deb3e39104

The answer is **A. Aspirin and heparin**.

This patient's presentation — **SLE, recurrent pregnancy loss (4 miscarriages), and a history of DVTs and PE** — is classic for **antiphospholipid syndrome (APS)** meeting both obstetric and thrombotic criteria. Guidelines uniformly recommend **low-dose aspirin combined with heparin** (usually LMWH) during pregnancy in this setting.[1][2][3]

The 2020 ACR guidelines **strongly recommend low-dose aspirin with therapeutic-dose heparin** for pregnant women with thrombotic APS, given this patient's prior DVTs and PE.[1] A meta-analysis of five trials (1,295 women) demonstrated that heparin plus aspirin improved live birth rates compared with aspirin alone (RR 1.27; 95% CI 1.09–1.49).[4][5] ACOG similarly recommends prophylactic heparin and low-dose aspirin for women with APS and recurrent fetal loss, with anticoagulation continued for at least 6 weeks postpartum.[6]

Why the other options are incorrect:

- **B. Aspirin and warfarin** — Warfarin is **teratogenic**, particularly during the first trimester (highest risk during weeks 6–12), causing warfarin embryopathy. Patients on warfarin must transition to heparin immediately upon pregnancy confirmation.[7]

- **C. No treatment** — Withholding treatment in a patient with both thrombotic and obstetric APS would be inappropriate; untreated APS carries a ~25% pregnancy loss rate even with therapy, and substantially higher without it.[1][6]
- **D. Rivaroxaban** — Direct oral anticoagulants are **contraindicated in pregnancy** due to lack of safety data and potential teratogenicity. EULAR additionally recommends against rivaroxaban in patients with triple-positive aPL profiles.[8]

Would you like to explore postpartum anticoagulation management in antiphospholipid syndrome?

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Question 413

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?

A. 5-α reductase deficiency
B. Sex chromosome mosaicism
C. Sex chromosome monosomy
D. Androgen insensitivity

https://openevidence.com/ask/7aba3a31-9495-4717-8661-daca563d411a

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D. Androgen insensitivity — specifically complete androgen insensitivity syndrome (CAIS), a 46,XY disorder of sex development caused by loss-of-function variants in the androgen receptor (AR) gene.[1][2]

Why the presentation fits

Every element of this vignette maps onto CAIS:[1][3][4]

- **Primary amenorrhea with normal breast development** — testicular androgens are aromatized to estrogen, and unopposed estrogen action drives thelarche and a female body habitus despite complete androgen resistance.[4]
- **Absent uterus and ovaries with a blind vaginal pouch** — Sertoli-cell AMH causes müllerian regression, so the uterus, fallopian tubes, and upper vagina never form; the gonads are testes, not ovaries.[1][4]
- **Scant axillary hair** — sexual hair is androgen-dependent, so pubic/axillary hair is absent or sparse. Some pubic hair may be present and does not exclude the diagnosis.[2]
- **Firm nontender inguinal mass** — an undescended testis in the inguinal canal, the other classic presentation of CAIS (inguinal "hernia" or labial swelling in a phenotypic girl).[3][4]
- **Normal-to-tall stature** — consistent with a Y chromosome.

Expected labs: **testosterone in the normal male range or higher, elevated LH, normal or slightly elevated FSH, elevated estradiol, and a 46,XY karyotype**.[2][5] The American Society for Reproductive Medicine notes that serum testosterone is the simplest way to distinguish CAIS from müllerian agenesis, with karyotype confirming the diagnosis.[6]

Why the other options are wrong

- **A. 5-α reductase deficiency** — impaired conversion of testosterone to DHT. External genitalia are typically ambiguous at birth (pseudovaginal perineoscrotal hypospadias, clitoromegaly), and wolffian structures are present because they respond to testosterone. Critically, these patients **virilize markedly at puberty** via SRD5A1 expressed in skin — deepening voice, phallic growth, muscle mass, pubic hair — which is absent here.[5][7][8]
- **B. Sex chromosome mosaicism** (e.g., 45,X/46,XY) — mixed gonadal dysgenesis usually produces ambiguous genitalia, asymmetric gonads, a streak gonad, and **müllerian structures are typically present** because dysgenetic gonads produce insufficient AMH. Normal thelarche with complete müllerian absence argues against it.
- **C. Sex chromosome monosomy** (45,X, Turner syndrome) — presents with **short stature, absent/incomplete breast development from gonadal dysgenesis, and a present uterus** with streak ovaries and markedly elevated FSH/LH. This patient's height of 168 cm and normal breast development exclude it.[9]

Management implications

Gonadectomy is recommended because of the risk of germ cell tumors (reported 14%–22%, though malignancy rarely occurs before age 20), with the ASRM advising removal through a patient-centered process **after breast development and attainment of adult stature**, followed by estrogen replacement.[6] This patient's palpable inguinal gonad is an additional reason to plan surgical management. Care should include vaginal length assessment (dilator therapy is first-line if the pouch is short), bone density monitoring, and psychological support with careful disclosure of the karyotype.[1]

Would you like to explore the optimal timing of gonadectomy versus gonadal surveillance in CAIS?

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Question 414

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?

A. IgM monoclonal gammopathy of undetermined significance (MGUS)
B. Multiple myeloma
C. Waldenstrom's macroglobulinemia
D. Non-Hodgkin's lymphoma

https://openevidence.com/ask/86a1e20e-2276-4e11-a835-f8636141169f

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The answer is **C. Waldenström's macroglobulinemia (WM)**.[1][2]

This presentation is classic for WM: a **monoclonal IgM gammopathy** (6.3 g/dL, well above the threshold at which hyperviscosity becomes likely) combined with symptoms of **hyperviscosity syndrome** — blurred vision, headache, and cognitive changes — along with anemia, fatigue, weight loss, and elevated ESR.[2][3]

Why the other options are incorrect:

- **A. IgM MGUS** — MGUS is by definition an **asymptomatic** precursor condition with an M protein **<3 g/dL** and <10% bone marrow lymphoplasmacytic infiltration. This patient's IgM of 6.3 g/dL and symptomatic hyperviscosity exclude MGUS.[4]
- **B. Multiple myeloma** — MM is overwhelmingly caused by **non-IgM** monoclonal proteins (IgG, IgA); IgM myeloma is exceedingly rare. The clinical features here (hyperviscosity, absence of lytic bone lesions or hypercalcemia) are far more consistent with WM.[1][5]
- **D. Non-Hodgkin lymphoma** — While WM is classified under the lymphoplasmacytic lymphoma subtype of B-cell NHL, a **monoclonal IgM spike** of this magnitude with hyperviscosity syndrome specifically defines WM rather than a generic NHL.[1][6]

Key diagnostic features of WM include IgM monoclonal gammopathy of any concentration plus bone marrow infiltration by lymphoplasmacytic cells (CD19+, CD20+, sIgM+), with the **MYD88 L265P mutation** present in >95% of cases.[1][2] **Hyperviscosity syndrome** — seen in 10–15% of WM patients — manifests as headache, blurred vision, confusion, and mucosal bleeding, and is rare when IgM is below 4,000 mg/dL.[2][3] This patient's IgM of 6,300 mg/dL places him well within the range for symptomatic hyperviscosity.

Would you like to explore the initial management of symptomatic hyperviscosity in WM?

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Question 415

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?

A. VII
B. VIIa
C. X
D. XII

https://openevidence.com/ask/d0ba3c9b-3c2d-4478-83c7-29471367a669

The answer is **C. Factor X**.

This patient with sickle cell disease is presenting with a **splenic sequestration crisis** (severe LUQ pain, splenomegaly). The DVT prophylaxis administered as part of the hospital admission protocol is **heparin** (unfractionated heparin or LMWH), which explains the **elevated PTT with a normal PT**.

Heparin's mechanism of action centers on binding to antithrombin III (AT), inducing a conformational change that markedly enhances AT's ability to inhibit activated coagulation factors — most importantly **Factor Xa** and **Factor IIa (thrombin)**.[1][2] Critically, the FDA label states that "small amounts of heparin inhibit Factor Xa, and larger amounts inhibit thrombin (Factor IIa)".[1] At **prophylactic doses**, the predominant effect is **anti-Xa activity**, making Factor X (via its activated form Xa) the factor most directly affected.[3][4]

Why not the other choices:

- **A/B (VII/VIIa):** Factor VII is part of the extrinsic pathway and is a target of **warfarin** (vitamin K antagonism), not heparin. Heparin does not significantly affect Factor VII, which is why the **PT remains normal** in this patient.

- **D (XII):** While the heparin-AT complex can inactivate Factor XIIa, this is a minor effect and not the primary mechanism of heparin's anticoagulant activity.[5][6]

The normal PT confirms the extrinsic pathway is unaffected, while the elevated PTT reflects heparin's inhibition of factors in the intrinsic and common pathways — predominantly **Factor Xa** at prophylactic doses.[1][3]

Would you like to explore the management of acute splenic sequestration crisis in adult sickle cell patients?

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Question 416

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?

A. gp120
B. gp160
C. p24
D. Reverse transcriptase

https://openevidence.com/ask/f65ba614-ac3d-4766-9890-cb5bb7ab49d5

The answer is **A. gp120**.

Maraviroc is a CCR5 co-receptor antagonist that selectively binds the human chemokine receptor CCR5 on the host cell membrane, **preventing the interaction of HIV-1 gp120 with CCR5** necessary for viral entry into CD4+ cells.[1] By occupying CCR5, maraviroc allosterically blocks gp120 from recognizing and binding the co-receptor, thereby inhibiting fusion and entry of **CCR5-tropic (R5) HIV-1**.[2]

This is why a **tropism assay** is required before initiating maraviroc: the drug is effective only against R5-tropic virus. Patients harboring CXCR4-tropic (X4) or dual/mixed-tropic virus will not benefit, as gp120 on those strains uses CXCR4 instead of CCR5 for cell entry.[1][3]

The other choices are incorrect:

- **gp160** is the uncleaved precursor envelope polyprotein that is processed into gp120 and gp41; it is not the direct target of maraviroc's mechanism.[4]
- **p24** is the HIV capsid protein used as a marker of viral replication (e.g., p24 antigen testing) and is unrelated to viral entry.

- **Reverse transcriptase** is the viral enzyme targeted by NRTIs and NNRTIs, a completely different drug class.

Would you like to explore the types of tropism assays available and how they are used to guide maraviroc therapy?

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Question 417

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?

A. Ibuprofen
B. Lumbar puncture
C. MRI
D. Tissue plasminogen activator

https://openevidence.com/ask/e4fa9302-b88d-402e-bc45-7ed8486ff520

The answer is **B, lumbar puncture**. This presentation is classic for **idiopathic intracranial hypertension (IIH)**, previously known as pseudotumor cerebri, which occurs most commonly in **young women with obesity** and is characterized by headache (often worse when lying down), **transient visual obscurations**, blurred vision, and **pulse-synchronous tinnitus**.[1][2] The association with PCOS has also been noted in the literature.[3]

Why lumbar puncture is the best next step

Once neuroimaging (here, head CT) has excluded a mass lesion, **lumbar puncture is performed to measure the CSF opening pressure and analyze CSF composition**.[1][2] An opening pressure **≥25 cm H_2O** (measured in the lateral decubitus position) with normal CSF constituents is diagnostic for IIH.[2][4][5] LP is also therapeutic — removal of 30–40 mL of CSF can acutely lower intracranial pressure and protect the optic discs.[2]

Why not the other options

- **A (Ibuprofen):** The patient has already failed ibuprofen, and NSAIDs do not address the underlying elevated intracranial pressure.

- **C (MRI):** While MRI with MR venography is part of the ideal workup to exclude cerebral venous sinus thrombosis, the question has already established a normal CT and asks for the best next step toward confirming the most likely diagnosis. LP is the key diagnostic maneuver.[1][2][5]
- **D (tPA):** There is no evidence of acute ischemic stroke — the CT is normal, and the clinical picture does not suggest stroke.

Would you like to explore first-line treatment of idiopathic intracranial hypertension, including acetazolamide dosing?

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Question 418

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?

A. Inhibition of gonadotropin-releasing hormone release
B. Intrauterine scar tissue accumulation
C. Nondisjunction of chromosomes
D. Nutritional imbalance

https://openevidence.com/ask/915b5ac7-cab7-4a1c-8eb3-ffa4b9056c6e

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The answer is **A. Inhibition of gonadotropin-releasing hormone release**.[1][2][3]

This patient's constellation of **amenorrhea, galactorrhea, bitemporal hemianopia, and headaches** is classic for a **prolactinoma** — a prolactin-secreting pituitary adenoma compressing the optic chiasm. The mechanism by which hyperprolactinemia produces amenorrhea is **suppression of pulsatile GnRH secretion** from the hypothalamus, resulting in hypogonadotropic hypogonadism.[2][3][4]

Specifically, excess prolactin **suppresses kisspeptin neurons** in the arcuate nucleus, which are major excitatory inputs to GnRH neurons, thereby reducing GnRH pulsatility.[1][5] Increased opioid tone from elevated prolactin further contributes to GnRH suppression.[1] The resulting decrease in FSH and LH leads to anovulation and amenorrhea. Restoration of ovulatory menstrual cycles with pulsatile GnRH administration in hyperprolactinemic women confirms this hypothalamic-level defect.[4]

Why the other options are incorrect:

- **B. Intrauterine scar tissue accumulation** — This describes Asherman syndrome, which follows uterine instrumentation (e.g., D&C) and would not explain galactorrhea, visual field defects, or headaches.
- **C. Nondisjunction of chromosomes** — This would suggest Turner syndrome (45,X), which typically presents with primary amenorrhea. This patient had normal menarche at 13 and regular menses for years before developing secondary amenorrhea.
- **D. Nutritional imbalance** — Functional hypothalamic amenorrhea from caloric deficit or excessive exercise would not produce galactorrhea or bitemporal hemianopia.

Would you like to explore first-line treatment of prolactinomas and indications for surgery?

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Question 419

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?

A. Gangrenous necrosis
B. Liquefactive necrosis
C. Caseous necrosis
D. Fibrinoid necrosis

https://openevidence.com/ask/a449ba21-7bd7-4642-8c54-9176ce24b339

The answer is **B. Liquefactive necrosis**.

This patient presents with an acute stroke — right-sided hemiparesis with upper motor neuron signs (hypertonic reflexes, positive Babinski), disorientation, and major vascular risk factors (longstanding diabetes, hypertension, recent ischemic heart disease). The CT scan would show a hypodense area consistent with cerebral infarction.

Brain infarcts characteristically undergo liquefactive necrosis, distinguishing them from ischemic injury in most other organs (which undergo coagulative necrosis). Over subsequent days and weeks after infarction, the brain tissue undergoes **liquefactive necrosis and then cavitation**.[1] This occurs because brain tissue has a relatively **high lipid content and low protein content**, along with abundant hydrolytic enzymes, which promote rapid enzymatic degradation of necrotic debris rather than preservation of tissue architecture.[2]

Why the other options are incorrect:

- **A. Gangrenous necrosis** — a form of coagulative necrosis seen in ischemic limbs and other dry tissues; not characteristic of brain infarction.
- **C. Caseous necrosis** — the hallmark of granulomatous inflammation, classically seen in tuberculosis; not relevant to ischemic stroke.

- **D. Fibrinoid necrosis** — occurs in blood vessel walls in conditions such as malignant hypertension and vasculitis; it is not the pattern of parenchymal necrosis seen in cerebral infarction.

Would you like to explore how the histopathological changes in cerebral infarction evolve over time?

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Question 420

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?

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

https://openevidence.com/ask/fa7d2c1c-b55a-4301-98bc-88e46cfa76d3

B. Amniotic fluid entering the endocervical veins — this is amniotic fluid embolism (AFE).

The presentation matches the classic AFE triad: abrupt intrapartum cardiopulmonary collapse (hypotension 70/30, tachycardia, SpO_2 82%, crackles from pulmonary edema), altered mental status, and severe consumptive coagulopathy with hyperfibrinolysis — here an undetectable fibrinogen with hemorrhage and anemia.[1][2][3] Onset was during labor after rupture of membranes, the period when a breach of the maternal–fetal barrier allows amniotic fluid and fetal antigens to enter the maternal circulation via endocervical or uterine veins or the placental site.[4][5] The mechanism is not mechanical obstruction by fetal debris but an anaphylactoid/immune-mediated response to fetal antigens, with tissue factor and endothelin driving DIC and pulmonary vasoconstriction.[1][6] The Society for Maternal-Fetal Medicine research case definition requires exactly this constellation: sudden cardiorespiratory compromise, strictly defined DIC, onset during labor or within 30 minutes of placental delivery, and absence of fever.[2][3]

Vaginal bleeding with an undetectable fibrinogen and a nontender abdomen fits DIC-driven hemorrhage rather than a local bleeding source; in AFE, fibrinogen typically falls out of proportion to measured blood loss.[7][8]

Why the other options are wrong

- **A. Apical ballooning of the left ventricle (Takotsubo):** would not produce an undetectable fibrinogen or DIC-related hemorrhage. Echocardiography in AFE characteristically shows acute right ventricular failure with a D-shaped septum and pulmonary hypertension, not apical ballooning.[3]
- **C. Anesthetic agent entering the subarachnoid space (high/total spinal):** causes hypotension and respiratory compromise from sympathectomy and phrenic blockade, but occurs within minutes of dosing, produces bradycardia rather than tachycardia at 130/min, and never causes coagulopathy or hemorrhage.
- **D. Systemic bacterial infection (GBS sepsis/chorioamnionitis):** temperature is only 37.6 °C — the Clark criteria specifically require absence of fever — the abdomen is nontender, and septic DIC does not typically evolve to an undetectable fibrinogen within two hours of membrane rupture. She also received intrapartum penicillin prophylaxis.[3]

Management implications: immediate high-quality supportive care with oxygenation/intubation, hemodynamic support favoring right ventricular function, and aggressive early correction of coagulopathy with fibrinogen replacement (cryoprecipitate or fibrinogen concentrate), FFP, and platelets, guided by viscoelastic testing; tranexamic acid is used given the hyperfibrinolytic component, while routine recombinant factor VIIa is discouraged because of increased mortality.[8][9] Prompt delivery and consideration of ECMO for refractory collapse are part of the multidisciplinary response.[1][6]

Would you like to explore the evidence behind the A-OK regimen in amniotic fluid embolism?

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Question 421

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?

A. Lidocaine
B. Midazolam
C. Halothane
D. Desflurane

https://openevidence.com/ask/89ac6484-c0b2-49c1-801d-60af1417619d

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The answer is **C. Halothane**.

Halothane is the volatile inhaled anesthetic classically associated with **massive hepatic necrosis** (halothane hepatitis). Two forms of hepatotoxicity are recognized:[1][2]

- **Type I**: Self-limited transaminase elevation in 20–30% of patients; clinically benign.
- **Type II**: A rare (1 in 3,500 to 1 in 35,000), immune-mediated idiosyncratic reaction causing **massive liver cell necrosis** frequently progressing to fulminant hepatic failure. The onset **5 days postoperatively** is typical.

The mechanism involves **CYP2E1-mediated oxidative metabolism** of halothane, producing trifluoroacetyl chloride, which covalently modifies liver microsomal proteins to form neoantigens that trigger an immune-mediated destruction of hepatocytes.[3][4]

The clinical setting — **Uruguay** — is an important clue. Halothane has been removed from use in the United States and Europe due to hepatotoxicity concerns, but it **remains widely used in lower-resource countries because of its significantly lower cost** (three to five times cheaper than alternatives).[2][5]

Why not the other options?

- **Lidocaine (A)**: A local anesthetic/antiarrhythmic, not a general anesthetic agent.
- **Midazolam (B)**: A benzodiazepine sedative; not associated with massive hepatic necrosis.

- **Desflurane (D)**: A modern volatile anesthetic that **has not been reported to cause hepatic dysfunction**, with an estimated incidence of severe liver injury less than 1 in 10,000,000.[6] [7]

Would you like to explore the risk factors and management approach for halothane hepatitis in more detail?

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Question 422

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?

A. Hyperkalemia
B. Hypernatremia
C. Thrombocytopenia
D. Anemia

https://openevidence.com/ask/7a4a5843-943b-47a8-9929-f8311eb84ec2

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-recognized, synergistic risk of **hyperkalemia**:[1]

- **Captopril** decreases aldosterone production, reducing renal potassium excretion. The FDA label explicitly lists hyperkalemia as an altered laboratory finding, particularly in patients with renal impairment or those using concomitant potassium-sparing diuretics.[1]
- **Triamterene** blocks the epithelial sodium channel (ENaC) in the collecting duct, directly inhibiting potassium secretion. The triamterene label warns that potassium-sparing agents "should be used with caution in conjunction with ACE inhibitors due to an increased risk of hyperkalemia".[2]

Population-based data confirm this interaction: concomitant use of ACE inhibitors with potassium-sparing diuretics has been associated with up to a **20-fold increased risk** of hospital admission for hyperkalemia.[3] The AHA statement on ACE inhibitor therapy specifically advises that potassium-sparing diuretics "should be given only for documented hypokalemia, and then with caution" in patients on ACE inhibitors.[4] The risk is further amplified in this 72-year-old patient, as older age is independently associated with declining renal function and impaired potassium excretion.[5]

The other options are not expected consequences of this drug combination: neither captopril nor triamterene typically causes hypernatremia (B), thrombocytopenia (C), or anemia (D) as a predictable pharmacologic effect.

Would you like to explore monitoring and management strategies for hyperkalemia in patients on this drug combination?

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Question 423

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?

A. Reversal of TIPS
B. Paracentesis
C. Administer IV ceftriaxone
D. Administer lactulose

https://openevidence.com/ask/6bdecb88-08b3-4880-be9b-002a0bbe8f16

The correct answer is **D. Administer lactulose**.

This patient presents with **overt hepatic encephalopathy (HE), West Haven Grade 2**, one month after TIPS placement. The hallmark features include **confusion** (unable to recall husband's name or address), **personality changes** (irritability), **sleep-wake inversion** (insomnia with daytime sleepiness), **constipation**, and **asterixis** — all in the context of cirrhosis with portal-systemic shunting. The abnormal number connection test further supports the diagnosis. Post-TIPS HE occurs in **30–50%** of patients.[1][2][3]

Lactulose is the established first-line treatment for overt HE per ACG, AASLD, and SCCM guidelines.[1][4] It reduces intestinal ammonia absorption through gut lumen acidification, prebiotic effects favoring non-urease-producing bacteria, and catharsis. The recommended dose is **10–20 g (15–30 mL) every 1–2 hours until two soft bowel movements**, then titrated to **2–3 bowel movements daily**.[1][5] In a meta-analysis of 38 RCTs, nonabsorbable disaccharides

reduced HE (RR 0.58) and serious liver-related adverse events (RR 0.47) compared with placebo.[6] Once the acute episode resolves, **rifaximin 550 mg twice daily** should be added for secondary prophylaxis.[1][5]

Post-TIPS HE management follows the same algorithm as non-TIPS HE, with lactulose and rifaximin as first-line agents.[1][7] **TIPS reduction or occlusion** (option A) is reserved for **refractory or recurrent HE** unresponsive to medical therapy, and carries significant procedural risk.[1][7]

Why not the other options:

- **A (Reversal of TIPS):** An invasive measure reserved for medically refractory post-TIPS HE, not as the initial step before attempting pharmacotherapy.[1][7]
- **B (Paracentesis):** While diagnostic paracentesis is appropriate in hospitalized cirrhotics with ascites to exclude spontaneous bacterial peritonitis (SBP) as a precipitant, it is not the primary therapeutic intervention for HE. This patient lacks signs of SBP (afebrile, nontender abdomen). Paracentesis should be performed concurrently, but lactulose is the most appropriate next step in management.[1]
- **C (IV ceftriaxone):** Empiric antibiotics are not indicated without clinical or laboratory evidence of active infection.[1]

Would you like to explore the evidence for prophylactic rifaximin before TIPS placement to prevent post-TIPS encephalopathy?

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Question 424

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?

A. Hyperparathyroidism
B. Hypocalcemia
C. Osteosarcoma
D. Multiple myeloma

https://openevidence.com/ask/c57d00a4-dc22-46f7-9ca1-0a22021a0d8c

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The answer is **A. Hyperparathyroidism**.

This presentation is a classic case of **primary hyperparathyroidism** with its pathognomonic skeletal manifestation, **osteitis fibrosa cystica**. The constellation of findings — **brown tumors**, **thinned bones**, and **osteolysis of the distal phalanges** on hand X-ray — is characteristic of prolonged exposure to elevated parathyroid hormone (PTH) levels.[1][2] Brown tumors are focal osteolytic lesions caused by increased osteoclastic activity and fibroblastic proliferation, with hemosiderin deposition giving them their characteristic brown color; common sites include the hands, pelvis, mandible, ribs, and long bones.[2][3]

The non-skeletal features in this patient are explained by **hypercalcemia** resulting from excess PTH:

- **Progressive confusion** reflects the neurocognitive manifestations of hypercalcemia, which range from poor concentration and "brain fog" to lethargy and altered mental status, and in severe cases, stupor and coma.[4][5]

- **Chronic nausea** is a gastrointestinal manifestation of hypercalcemia, caused by slowed peristalsis from hyperpolarization of neuromuscular cell membranes.[4][6]

This triad — bone disease, gastrointestinal complaints, and neuropsychiatric symptoms — is captured in the classic mnemonic "**stones, bones, groans, and psychiatric overtones**".[7]

Why not the other choices:

- **B. Hypocalcemia** — would not cause brown tumors or bone resorption; hypocalcemia causes neuromuscular excitability (tetany, Chvostek/Trousseau signs), not confusion and nausea.
- **C. Osteosarcoma** — produces aggressive, destructive bone lesions (sunburst pattern, Codman triangle), not the well-defined, expansile lytic lesions with cortical thinning seen in brown tumors.[2]
- **D. Multiple myeloma** — can cause lytic bone lesions and hypercalcemia but produces characteristic "punched-out" lesions without the surrounding sclerotic margins of brown tumors, and would not show subperiosteal resorption of distal phalanges, which is specific to hyperparathyroidism.[8]

Would you like to explore the indications for parathyroidectomy versus medical management in primary hyperparathyroidism?

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Question 425

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?

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

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The answer is **B. Increase in circulating fetal hemoglobin**.

The clinical presentation — **thrombocytosis** (900,000/mm^3), elevated LDH and uric acid, history of thrombophlebitis, lightheadedness, headaches, and easy bruising — is consistent with a **myeloproliferative neoplasm**, most likely essential thrombocythemia. The medication used for both myeloproliferative neoplasms and sickle cell disease is **hydroxyurea**, a ribonucleotide reductase inhibitor.[1][2]

In sickle cell disease, the **primary beneficial effect of hydroxyurea is induction of fetal hemoglobin (HbF)**. HbF interferes with intracellular HbS polymerization — the fundamental pathologic event in SCD — thereby reducing red cell rigidity, hemolysis, and vaso-occlusion.[1][3] Randomized controlled trials have demonstrated that hydroxyurea significantly increases HbF levels, with a pooled mean difference of approximately 6% compared to placebo.[3] This translates to a **44% reduction in the median incidence of painful crises** per year.[4]

While hydroxyurea does have additional mechanisms (reducing leukocyte adhesion, enhancing nitric oxide bioavailability, improving RBC deformability), **HbF induction is recognized as its most powerful and direct therapeutic effect** in SCD.[2][5]

The other options are incorrect:

- **A (Inhibition of thrombocyte aggregation):** Hydroxyurea reduces platelet counts via myelosuppression but does not primarily work through platelet aggregation inhibition in SCD.
- **C (Inhibition of stem cell differentiation):** While hydroxyurea is cytostatic, inhibiting stem cell differentiation is not its beneficial mechanism in SCD.
- **D (Restoration of iron stores):** Hydroxyurea has no role in iron restoration; iron overload (not deficiency) is actually a concern in SCD due to chronic transfusions.

Would you like to explore hydroxyurea dosing and monitoring recommendations in sickle cell disease?

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Question 426

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?

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

https://openevidence.com/ask/a76167f6-5a91-409b-8ca4-d9bb6c842684

The correct answer is **D. Type IV hypersensitivity; CD4+ T cells**.

The Candida skin test is a classic example of **delayed-type hypersensitivity (DTH)**, a **Type IV** reaction. The hallmark features described — a **raised, indurated area** read at **48 hours** — are characteristic of this reaction type.[1][2] Most immunocompetent adults have prior exposure to Candida and mount a DTH response when the antigen is injected intradermally, making it one of the most commonly used antigens for assessing intact cellular immunity (reactive in ~92% of normal subjects).[2]

CD4+ Th1 cells are the principal mediators. Upon encountering Candida antigen presented via MHC class II molecules on antigen-presenting cells, previously sensitized CD4+ T cells release cytokines (IFN-γ, TNF-α) that recruit and activate macrophages, producing the induration.[3][4] This corresponds to the **Type IVa** subclassification in the revised Gell and Coombs system.[3][4] The correlation between skin induration at 48 hours and in vitro lymphocyte proliferative response (a measure of T-cell–mediated immunity) has been well demonstrated.[1]

Why the other options are incorrect:

- **A (Type I; eosinophils):** Type I reactions are IgE-mediated, occur within minutes (not 48 hours), and involve mast cell degranulation — not the delayed induration described here.
- **B (Type IV; mast cells):** While the hypersensitivity type is correct, mast cells are the effector cells of Type I reactions, not the primary mediators of DTH.

- **C (Type III; CD4+ T cells):** Type III reactions are immune complex–mediated (IgG/IgM), typically peaking at 4–8 hours (Arthus reaction), and involve complement activation and neutrophil recruitment — not CD4+ T cell–driven induration at 48 hours.

Would you like to explore how Candida DTH skin testing is used clinically to assess cellular immune function?

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Question 427

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?

A. Inflammatory polyp
B. Adenomatous polyp
C. Hamartomatous polyp
D. Colorectal cancer

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The answer is **B. Adenomatous polyp**.

A colonic polyp with **75% tubular architecture** is classified as a **tubular adenoma**, which falls under the broader category of adenomatous polyps. Adenomatous polyps (adenomas) are neoplastic polyps subclassified by the proportion of villous versus tubular architecture:[1][2]

- **Tubular adenoma**: ≥75–80% tubular architecture (i.e., <20–25% villous)
- **Tubulovillous adenoma**: 25–75% villous component
- **Villous adenoma**: >75% villous component

With 75% tubular and therefore ~25% villous features, this polyp sits at the tubular adenoma end of the spectrum. Tubular adenomas are the **most common type of adenomatous polyp**, comprising approximately 66% of all colorectal adenomas.[3][4]

Why the other options are incorrect:

- **A. Inflammatory polyp** — These arise in the setting of chronic inflammation (e.g., IBD) and lack the dysplastic, gland-forming tubular architecture described here.[5]
- **C. Hamartomatous polyp** — These consist of a disorganized overgrowth of tissues native to the site (e.g., Peugeot-Jeghers, juvenile polyps) and do not exhibit the organized tubular glandular pattern characteristic of adenomas.[5]

- **D. Colorectal cancer** — The biopsy describes adenomatous architecture without mention of invasion through the muscularis mucosae, which is required to classify a polyp as clinically malignant. Additionally, the clinical presentation (positive FOBT, single polyp, asymptomatic) and family history are classic for an adenomatous polyp in the adenoma-carcinoma sequence.[1]

The clinical significance is that adenomatous polyps are recognized precursors of colorectal cancer, and complete excision with subsequent surveillance colonoscopy is standard management.[6][7]

Would you like to explore the recommended surveillance intervals after removal of this type of adenoma?

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Question 428

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?

A. Cryptosporidiosis
B. C. difficile colitis
C. Bacillus cereus infection
D. Norovirus infection

https://openevidence.com/ask/2f78537c-6c78-4c8c-80a4-8d767dd90342

The answer is **C. Bacillus cereus infection**. This presentation is classic for the **emetic form of B. cereus food poisoning**, characterized by ingestion of preformed heat-stable cereulide toxin in improperly stored and reheated food. The key diagnostic clues are:

- **Reheated leftover food**: B. cereus spores are heat-resistant and survive cooking; when food is left at room temperature, spores germinate and produce the heat-stable emetic toxin cereulide, which persists even after reheating. Rice and starchy dishes are the most commonly implicated vehicles — rice dishes accounted for 50% of B. cereus outbreaks in one U.S. surveillance study. This is colloquially known as "**fried rice syndrome**".[1][2][3][4]
- **Rapid onset (~1 hour)**: The emetic syndrome has an incubation period of **0.5–6 hours**, consistent with a preformed toxin intoxication rather than an infection. As described in the NEJM, B. cereus from contaminated fried rice or other food items produces toxins that may result in disease resembling S. *aureus* food poisoning.[1][2][5]
- **Afebrile with prominent GI symptoms**: The absence of fever supports a toxin-mediated process rather than an invasive infection.

Why not the other options:

- **Cryptosporidiosis** — Transmitted via contaminated water, with an incubation period of 2–10 days; presents with prolonged watery diarrhea, not acute vomiting 1 hour after a meal.

- **C. difficile colitis** — Associated with antibiotic exposure and healthcare settings, not with reheated food; incubation is days to weeks.
- **Norovirus** — Incubation period is **12–48 hours**, much longer than the 1-hour onset described here, and is typically spread person-to-person or via contaminated produce/shellfish.

Would you like to explore the management approach for B. cereus emetic food poisoning, including when more aggressive treatment may be warranted?

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Question 429

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?

A. Blastomycosis
B. Sporotrichosis
C. Histoplasmosis
D. Onychomycosis

https://openevidence.com/ask/7b721490-92ba-4f18-a26a-bbcc128dd0a8

The correct answer is **C. Histoplasmosis**.

The combination of **travel to St. Louis, Missouri** (located along the Mississippi River Valley, a highly endemic area for *Histoplasma capsulatum*), a[1][2] **cavitary pulmonary lesion**, and biopsy showing **necrotic granulomatous inflammation with oval yeast within macrophages** is pathognomonic for histoplasmosis.[3][4]

Key supporting features:

- **Epidemiology:** *H. capsulatum* is endemic to the Ohio and Mississippi River Valleys. Infection is acquired by inhalation of microconidia from the environment.[1][5]
- **Clinical presentation:** Non-productive cough and dyspnea after a presumed upper respiratory infection are consistent with subacute or chronic pulmonary histoplasmosis. Cavitary lesions on imaging can mimic tuberculosis or malignancy.[6][7]

- **Histopathology:** *Histoplasma* organisms appear as **small (2–5 µm), uniform, oval-shaped yeasts** found within macrophages, often in the most necrotic areas of granulomas. Narrow-based budding may be seen. This pattern of **intracellular yeast within macrophages** is characteristic of histoplasmosis specifically.[4][8]

Why the other options are incorrect:

- **Blastomycosis (A):** *Blastomyces* produces **large (8–15 µm), broad-based budding yeast**, not small oval intracellular yeast.
- **Sporotrichosis (B):** *Sporothrix* primarily causes **lymphocutaneous disease** (not cavitary pulmonary lesions) and appears as cigar-shaped yeast.
- **Onychomycosis (D):** This is a **fungal nail infection** with no pulmonary involvement.

Would you like to explore the treatment approach for chronic pulmonary histoplasmosis?

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Question 430

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?

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

https://openevidence.com/ask/e1f38381-85a4-41e9-abf5-1adf9756d680

The answer is **A. Pregnancy success rate with donor oocytes is similar to patients with primary ovarian failure**.

This clinical vignette describes **Turner syndrome (45,X)**: the combination of **short stature**, **broad chest with widely spaced nipples**, **low posterior hairline**, **cubitus valgus** (increased carrying angle), **shortened fourth metacarpals**, **primary amenorrhea**, and **Tanner stage 1** at age 14 is classic. Infertility in Turner syndrome results from **gonadal dysgenesis** leading to primary ovarian insufficiency — approximately 95% of patients are infertile, and only **2–8%** achieve spontaneous pregnancy.[1][2]

Why A is correct

Studies directly comparing donor oocyte IVF outcomes in Turner syndrome versus other causes of premature ovarian insufficiency (POI) demonstrate **comparable live birth rates per embryo transfer**. A 2026 retrospective cohort found live birth rates per embryo transfer of **29% in Turner syndrome vs. 27% in other POI etiologies**.[3] Similarly, Burt et al. reported that pregnancy rate per cycle was similar between TS and POI, though Turner syndrome patients had higher miscarriage rates and may require more transfer attempts.[4] A meta-analysis estimated a pooled live birth rate per patient of **40%** (95% CI 29–51%) with donor oocytes in Turner syndrome.[5] These results confirm that donor oocyte IVF in Turner syndrome achieves success comparable to other forms of primary ovarian failure.

Why the other options are incorrect

- **B – Gonadotropin administration**: Exogenous gonadotropins cannot restore fertility when the underlying problem is **streak gonads** with absent or depleted follicles. There is no ovarian tissue for gonadotropins to stimulate.[1][2]
- **C – Impaired tubal ciliary function**: Tubal ciliary dysfunction is characteristic of **primary ciliary dyskinesia** (Kartagener syndrome), not Turner syndrome. The infertility in Turner syndrome is ovarian, not tubal.
- **D – Majority conceive without assistance**: Only **3–8%** of Turner syndrome patients achieve spontaneous pregnancy; the vast majority require donor oocytes or other ART.[1][6]

Would you like to explore the cardiovascular screening and safety precautions required for pregnancy in Turner syndrome?

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Question 431

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?

A. Perichondrium
B. Proteoglycans
C. Osteoblasts
D. Mature chondrocytes

https://openevidence.com/ask/b99665a7-699d-40e5-95d6-eeb487f33b67

The answer is **A. Perichondrium**.

Cartilage heals poorly because it is **avascular, aneural, and alymphatic**, with sparse chondrocytes that have limited proliferative capacity.[1][2] Unlike bone — which has a robust blood supply and periosteum rich in osteoprogenitor cells — mature cartilage lacks an intrinsic source of progenitor cells to regenerate damaged matrix.[3][4]

The **perichondrium** is the dense connective tissue surrounding cartilage that contains **chondrogenic stem/progenitor cells** within its inner (cambium) layer.[5][6][7] These cells can proliferate and differentiate into new chondrocytes capable of producing hyaline cartilage matrix. Key evidence supporting this:

- **Cartilage repair depends on intact perichondrium.** In a mouse rib cartilage resection model, full cartilage replacement occurred within 1–2 months only when the perichondrium was preserved; without it, repair failed.[5]
- **Perichondrium harbors label-retaining progenitor cells.** These slow-cycling cells reside specifically in the perichondrium (not the chondrium itself), express stem cell markers (CD44, CD90), and possess clonogenic and chondrogenic capacity.[7][8]

- **Perichondrium transplants regenerate hyaline cartilage.** When transplanted into full-thickness articular cartilage defects, perichondrium-derived cells differentiate into SOX9+/Col2a1+ chondrocytes and form proteoglycan-rich hyaline cartilage.[9]

The other options are incorrect:

- **Proteoglycans (B)** are extracellular matrix components, not cells, and cannot serve as progenitors.
- **Osteoblasts (C)** are terminally differentiated bone-forming cells that do not give rise to chondrocytes.
- **Mature chondrocytes (D)** have very limited proliferative capacity and tend to dedifferentiate in culture — they are not effective progenitors for matrix regeneration.[1][2]

Would you like to explore current clinical strategies for articular cartilage repair?

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Question 432

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?

A. Muscle biopsy
B. Rapid plasma reagin test
C. MRI of the brain and spine
D. Lumbar puncture

https://openevidence.com/ask/6d8c81d7-931e-47af-8278-409d568c8a32

The answer is **C. MRI of the brain and spine**.[1][2][3]

This presentation is classic for **relapsing-remitting multiple sclerosis (MS)**. Key features include:

- **Relapsing neurological deficits separated in time**: current bilateral upper extremity weakness/numbness with a prior episode of right lower extremity weakness last summer that resolved over 3 weeks
- **Heat sensitivity** (worsening when outside in summer, consistent with Uhthoff phenomenon during a demyelinating relapse)
- **Upper motor neuron signs**: spasticity, 4+ deep tendon reflexes, absent abdominal reflex, impaired tandem gait
- **Posterior column dysfunction**: decreased vibration and fine touch
- **Bladder dysfunction**: urinary incontinence (not stress-related)

MRI of the brain and spine is the recommended initial diagnostic test when MS is suspected. Per the McDonald Criteria and ACR Appropriateness Criteria, MRI is the most sensitive paraclinical tool for detecting demyelinating plaques, demonstrating T2-hyperintense lesions in characteristic locations (periventricular, juxtacortical/cortical, infratentorial, spinal cord).[1][3] MRI establishes **dissemination in space and time** — and is also essential here to exclude compressive myelopathy given the acute bilateral limb deficits and new bladder dysfunction.[2][3]

Why not the other options:

- **Rapid plasma reagin test (B)**: The sexual history is a distractor. Neurosyphilis can mimic MS, but the **relapsing-remitting course with heat sensitivity and classic UMN signs** strongly favors MS. Syphilis serology may be checked later as part of the differential workup to exclude MS mimics, but it is not the most appropriate initial step.[1]
- **Lumbar puncture (D)**: CSF analysis for oligoclonal bands can support a diagnosis of MS and fulfill the criterion for dissemination in time, but **MRI should be obtained first** when available. CSF is most useful when clinical and MRI findings are insufficient for diagnosis.[2][4]
- **Muscle biopsy (A)**: This is a **central nervous system process**, not a myopathy. Myopathies cause proximal weakness without sensory deficits or UMN signs, none of which fits here.

Would you like to explore first-line disease-modifying therapy options for relapsing-remitting MS and the role of early high-efficacy treatment?

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Question 433

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?

A. Parasympathetic inhibition
B. Reversible block of H2 receptors
C. Inhibition of primary active transport
D. Inhibition of 50S ribosomal subunit

https://openevidence.com/ask/78a646e8-4463-46e7-950f-716d08d49edc

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The correct answer is **C. Inhibition of primary active transport**.

Omeprazole is a **proton pump inhibitor (PPI)** that suppresses gastric acid secretion by **irreversibly inhibiting the H^+ /K^+ ATPase enzyme** on the secretory surface of the gastric parietal cell.[1][2] The H^+ /K^+ ATPase is a **primary active transporter** — it directly hydrolyzes ATP to pump H^+ ions into the gastric lumen in exchange for K^+ ions. Omeprazole is a prodrug that becomes activated in the acidic environment of the parietal cell canaliculus, forming a sulfenamide that **covalently binds to cysteine residues** on the pump, irreversibly blocking the final step of acid production.[3][4]

Why the other options are incorrect:

- **A. Parasympathetic inhibition** — Describes anticholinergic agents (e.g., pirenzepine), which block muscarinic (M3) receptors on parietal cells. This is not how omeprazole works.
- **B. Reversible block of H2 receptors** — Describes H2 receptor antagonists (e.g., famotidine, ranitidine), which competitively block histamine at H2 receptors on parietal cells.
- **D. Inhibition of 50S ribosomal subunit** — This is the mechanism of **clarithromycin**, the macrolide antibiotic in the same triple-therapy regimen, not omeprazole.

A key distinction tested here is that the H^+ /K^+ ATPase uses ATP hydrolysis directly to transport ions against their concentration gradient, classifying it as **primary active transport** — distinguishing it from secondary active transport or channel-mediated processes.[1][3]

Would you like to explore the current recommended regimen for H. pylori eradication, including dosing and duration?

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Question 434

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?

A. Diamondback rattlesnake
B. Brown recluse spider
C. Striped bark scorpion
D. Deer tick

https://openevidence.com/ask/41611af4-7681-43db-8670-629c429c6b89

The answer is **B. Brown recluse spider** (*Loxosceles reclusa*).

This presentation is classic for **cutaneous loxoscelism**. Several features are characteristic:

- **Initially painless bite during sleep** — brown recluse spiders are nocturnal, non-aggressive, and bite when inadvertently pressed against the skin; the bite itself is often painless and may go unnoticed.[1][2]
- **Progressive wound evolution** — cutaneous loxoscelism initially manifests as mild pain and erythema, evolving over 12–24 hours into painful edema with induration and hemorrhagic blisters, with frank necrosis typically appearing after ~72 hours. The classic "**red, white, and blue" sign** — a bluish plaque with central ischemic necrosis surrounded by a rim of erythema — is the hallmark dermonecrotic pattern.[2][3]
- **Low-grade fever (38°C)** — non-specific systemic symptoms including fever, malaise, and headache occur in up to 50% of cutaneous loxoscelism cases within the first 24–48 hours.[2]

- **Geographic and environmental context** — brown recluse spiders are found predominantly in the **Southwest and southern Midwest United States**, including Texas.[1]

Why not the other options:

- **Diamondback rattlesnake** — pit viper envenomation causes immediate severe pain, rapid swelling, and ecchymosis; bites are not painless initially.[4]
- **Striped bark scorpion** (*Centruroides*) — stings cause **severe localized pain and muscle cramping**, not progressive dermonecrosis.[5]
- **Deer tick** — causes a localized reaction or, in the case of Lyme disease, **erythema migrans** (an expanding targetoid erythematous macule), not necrotic ulceration.

Would you like to explore the management approach for cutaneous loxoscelism, including wound care and indications for surgical intervention?

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Question 435

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?

A. Catatonic schizophrenia
B. Heat stroke
C. Neuroleptic malignant syndrome
D. Oversedation

https://openevidence.com/ask/1177204a-aa9f-4659-b0ce-1f254a24752a

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The answer is **C. Neuroleptic malignant syndrome (NMS)**.

This vignette presents the **classic tetrad of NMS** — hyperthermia, muscular rigidity, altered mental status, and autonomic instability — developing after administration of **haloperidol**, a high-potency first-generation antipsychotic and the drug most frequently implicated in NMS.[1] Per DSM-5 criteria, NMS requires exposure to a dopamine antagonist (typically within 72 hours), severe muscular rigidity, fever, and at least two additional features such as tachycardia, elevated blood pressure, or altered consciousness.[1][2]

This patient fulfills all criteria:

- **Dopamine antagonist exposure**: haloperidol
- **Hyperthermia**: 104°F (40°C)
- **Lead-pipe rigidity**: extremities cannot be freely manipulated — a **cardinal feature** of NMS described as uniform resistance to passive movement, distinct from spasticity or dystonia[1]

- **Altered mental status**: somnolent, non-responsive
- **Autonomic instability**: tachycardia (120/min) and hypertension (147/98 mmHg)

While the median onset is approximately 4 days after drug initiation, NMS can develop **within 24 hours** of exposure.[1][2] Known risk factors present in this case include dehydration (dry mucous membranes), agitation, and use of a first-generation parenteral antipsychotic.[3] Diphenhydramine's anticholinergic properties may further impair thermoregulation.

Why not the other options:

- **Heat stroke (B)**: Although the patient was in 110°F heat, heat stroke does **not** produce **lead-pipe extrapyramidal rigidity** — it causes CNS dysfunction (confusion, delirium, seizures) but the characteristic muscular rigidity described here is specific to NMS. The DSM-5 explicitly lists heat stroke as a differential to distinguish from NMS.[1][2][4][5]
- **Catatonic schizophrenia (A)**: While the patient likely has an underlying psychotic disorder, catatonia features **waxy flexibility, posturing, stereotypy, and negativism** rather than lead-pipe rigidity with hyperthermia and autonomic instability emerging after antipsychotic administration. Many experts consider NMS a drug-induced form of malignant catatonia.[1][6][7]
- **Oversedation (D)**: Would explain somnolence but cannot account for the hyperthermia, rigidity, or autonomic instability.

Would you like to explore the acute management of NMS, including the roles of dantrolene and bromocriptine?

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Question 436

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?

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

https://openevidence.com/ask/aa8d51ce-85c3-473b-aca9-16b018e3cef0

The correct answer is **C. Activating natural killer cells and cytotoxic T cells**.

Aldesleukin (Proleukin) is a **recombinant form of interleukin-2 (IL-2)**, a lymphocyte growth factor. Per the FDA label, its mechanism of action includes **enhancement of lymphocyte mitogenesis and cytotoxicity, induction of killer cell activity (lymphokine-activated killer [LAK] and natural killer [NK] cells), and interferon-gamma production**.[1] It stimulates the **proliferation and activation of T cells and NK cells**, thereby triggering release of cytokines such as interferon-gamma and tumor necrosis factor from activated lymphocytes.[2]

Why the other options are incorrect:

- **A (Stimulating release of acute-phase reactants):** This describes the action of IL-6, not IL-2. While IL-2 does induce downstream cytokine production (TNF, IL-1, IFN-gamma), its primary antitumor mechanism is direct immune cell activation, not acute-phase reactant release.[1]
- **B (Stimulating antigen-processing cells):** This better describes interferon-alpha, whose mechanism in melanoma is linked to immunostimulatory effects on antigen-presenting cells. Aldesleukin's primary targets are T cells and NK cells, not antigen-processing cells.[3]

- **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. Aldesleukin actually causes dose-dependent thrombocytopenia rather than bone marrow stem cell expansion.[1]

Would you like to explore the toxicity profile and monitoring requirements for high-dose aldesleukin therapy?

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Question 437

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?

A. Decreased cardiac contractility
B. Increased left ventricular end-diastolic pressure
C. Decreased stroke volume
D. Decreased pulmonary capillary wedge pressure

https://openevidence.com/ask/81f75b8d-38e1-4072-9784-dbf27c25a902

The correct answer is **D. Decreased pulmonary capillary wedge pressure**.

The medication described is **sodium nitroprusside**, a direct-acting vasodilator used in hypertensive emergencies. Its mechanism — releasing nitric oxide, activating guanylate cyclase, and increasing cGMP — results in **balanced arterial and venous vasodilation**.[1][2]

The FDA label states explicitly that 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)," while arteriolar relaxation reduces systemic vascular resistance and mean arterial pressure (afterload).[1][3]

Why the other options are incorrect:

- **A. Decreased cardiac contractility** — Nitroprusside has no direct negative inotropic effect. It acts exclusively on vascular smooth muscle, not myocardial contractility.[1]
- **B. Increased LVEDP** — The opposite occurs. Venodilation reduces venous return and therefore **decreases** LVEDP.[1][3]
- **C. Decreased stroke volume** — In the setting of severely elevated afterload (as in this hypertensive emergency), reducing SVR enhances LV ejection. The failing or afterload-

stressed ventricle is highly afterload-sensitive, so nitroprusside-mediated afterload reduction tends to **maintain or increase** stroke volume rather than decrease it.[4][5]

Would you like to explore how nitroprusside compares with other IV antihypertensives like nicardipine and clevidipine for hypertensive emergencies?

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Question 438

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?

A. Normal saline bolus and re-evaluation of hemodynamics after infusion
B. CT abdomen and pelvis
C. Morphine
D. Exploratory laparotomy

https://openevidence.com/ask/5360b2ae-5400-41bb-8c62-94645e96e2b5

The answer is **D. Exploratory laparotomy**.

This patient presents with classic findings of **hemorrhagic shock from blunt abdominal trauma** — likely a **splenic injury** given the left upper quadrant pain — with a positive FAST (hemoperitoneum), peritoneal signs (rigidity, involuntary guarding), and **hemodynamic instability refractory to fluid resuscitation** (worsening hypotension and tachycardia despite IV fluids).

Why exploratory laparotomy is indicated:

- The Eastern Association for the Surgery of Trauma (EAST) practice management guidelines state as a **Level 1 recommendation** that patients who are **hemodynamically unstable or who have diffuse peritonitis** after blunt abdominal trauma should be taken urgently for laparotomy.[1][2]
- Indications for emergent exploratory laparotomy in blunt abdominal trauma include **peritonitis, hemodynamic instability with free intra-abdominal fluid, or high-grade organ injury**.[3]

- A hemodynamically unstable trauma patient with a positive FAST does not belong in the CT scanner. CT abdomen/pelvis is the reference standard for **hemodynamically stable** patients.[4][5][6]

Why the other options are incorrect:

- **A (NS bolus and re-evaluation):** This patient has already received IV fluids with worsening hemodynamics — a classic **non-responder** pattern. Continued fluid resuscitation without surgical hemorrhage control will not correct the underlying problem and delays definitive management.[7]
- **B (CT abdomen/pelvis):** Transporting a hemodynamically unstable patient to the CT scanner risks cardiovascular collapse. The FAST has already confirmed hemoperitoneum, which is sufficient for operative decision-making in the unstable patient.[4][5]
- **C (Morphine):** While pain management is important, administering a vasodilatory opioid to a patient in hemorrhagic shock can worsen hypotension. Furthermore, analgesia alone does not address the surgical emergency.

Would you like to explore the principles of damage control surgery and resuscitation in blunt abdominal trauma?

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Question 439

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?

A. Perform tracheostomy
B. Continue using the non-rebreather mask
C. Reintubate
D. Start BiPAP

https://openevidence.com/ask/437b3ae9-3f18-4fb7-a7be-307989c1d407

The answer is **C. Reintubate**.[1][2][3]

This patient is **unresponsive with severe, refractory hypoxemia** (SpO2/SaO2 73%) that has not improved after 3 minutes on 100% FiO2 via non-rebreather mask. Immediate **reintubation** is required to secure the airway and provide definitive ventilatory support.

Why reintubation is the best next step:

- **Unresponsiveness** is the critical factor. An unresponsive patient cannot protect the airway and is at high risk for aspiration and airway obstruction.

- **Non-rebreather mask is failing** — the severe hypoxemia is refractory to 100% FiO2 after an adequate trial, and the patient remains unconscious. Continuing it (choice B) offers no benefit.
- **BiPAP is contraindicated** in patients with altered mental status who cannot protect their airway. Established contraindications to noninvasive ventilation include inability to protect the airway, altered consciousness, and uncooperative/apneic patients.[1][2][3]
- **Tracheostomy** is an inappropriate first step — endotracheal intubation should always be attempted before a surgical airway.

Notable ABG finding: The PaO2 of 73 mmHg would normally correspond to an SaO2 of approximately **94%** on the oxyhemoglobin dissociation curve, yet the measured saturation is only **73%** — a significant "**saturation gap.**" This discrepancy, along with refractory hypoxemia despite 100% FiO2, raises concern for **dyshemoglobinemia** (e.g., methemoglobinemia, possibly from a topical anesthetic such as benzocaine used during airway instrumentation).[4][5][6] However, the immediate management priority is securing the airway; diagnostic workup (co-oximetry) and definitive treatment (e.g., methylene blue for methemoglobinemia) follow once the airway is controlled.

Would you like to explore the diagnosis and management of perioperative methemoglobinemia, including when to administer methylene blue?

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Question 440

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?

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

https://openevidence.com/ask/e296ab26-cb02-4704-915f-319a822011a4

The answer is **A. Insufficient production of procollagen type 1**.

This presentation is classic for **osteogenesis imperfecta (OI) type I**, the mildest form of "brittle bone disease." The key findings pointing to this diagnosis are:

- **Blue-gray sclerae** — a hallmark of OI type I, resulting from thinned scleral collagen allowing the underlying choroidal pigment to show through[1][2]
- **Fracture from minor trauma** (incomplete tibial diaphyseal fracture after hitting a chair) — bone fragility with fractures disproportionate to the mechanism of injury is the defining feature of OI[1][3]

- **Joint hypermobility and decreased muscle tone** — well-recognized extra-skeletal manifestations of the generalized connective tissue disorder[4][5]
- **Normal growth parameters** — OI type I is characterized by normal or near-normal stature, unlike more severe forms[2][6]

Why answer A is correct

OI type I results from heterozygous mutations in **COL1A1** (or less commonly COL1A2) that cause **haploinsufficiency** — a quantitative reduction in type I procollagen production, while the molecules that are made are structurally normal.[2][7] Approximately 85–90% of all OI cases are caused by mutations in COL1A1 or COL1A2.[1][4][5] OI type I, which represents roughly half of the OI population, predominantly results from this mechanism of reduced collagen type I output.[7]

Why the other answers are incorrect

- **B. Fibrillin-1 mutation** — causes **Marfan syndrome**, characterized by tall stature, arachnodactyly, lens subluxation, and aortic root dilation — none of which are present here.
- **C. Defective collagen type 3** — causes **vascular Ehlers-Danlos syndrome (type IV)**, which presents with arterial dissection/rupture and organ perforation, not bone fragility or blue sclerae.
- **D. Dysfunctional laminins** — laminins are basement membrane proteins; their dysfunction causes disorders such as congenital muscular dystrophies or epidermolysis bullosa, not the bone fragility and blue sclerae seen here.

Would you like to explore the management approach for pediatric osteogenesis imperfecta type I, including bisphosphonate therapy and monitoring?

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Question 441

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?

A. Dobutamine
B. Norepinephrine
C. Cardiac pacing
D. Epinephrine

https://openevidence.com/ask/e0085d84-145e-4b7e-95ab-66723ab5c8c6

The correct answer is **C. Cardiac pacing**.

ECG interpretation

The ECG describes **second-degree AV block, Mobitz Type II** with 3:2 conduction. The hallmark findings are a **constant PR interval** (0.15 seconds) with intermittent nonconducted P waves (every third P wave dropped) — the absence of progressive PR prolongation before the dropped beat distinguishes this from Mobitz Type I (Wenckebach).[1] The narrow QRS (0.09 seconds) indicates the block is likely at the **level of the His bundle** itself, rather than infra-Hisian, though the prognostic and management implications are similar.[1][2]

Why cardiac pacing is indicated

This patient has **hemodynamically significant bradycardia**: HR 48/min, hypotension (89/50), altered mentation, cold extremities, and prolonged capillary refill — all consistent with inadequate cardiac output due to the conduction block. Mobitz Type II is an infranodal (or

Hisian) block, and as the 2018 ACC/AHA/HRS guideline notes, AV block within or below the His bundle **will not respond to atropine** and may sometimes improve with catecholamines.[1] Temporary pacing (transcutaneous as a bridge to transvenous) is the standard acute intervention for hemodynamically unstable Mobitz Type II.[3][4] Even **asymptomatic** Mobitz Type II is considered an indication for permanent pacing.[5][6]

Why not the other options

- **Dobutamine (A):** Primarily an inotrope with limited chronotropic effect; not a standard agent for bradycardia management.
- **Norepinephrine (B):** A vasopressor acting predominantly via alpha-1 vasoconstriction; it raises blood pressure but does not reliably increase heart rate or address the conduction abnormality.
- **Epinephrine (D):** Has chronotropic properties and is listed in ACLS guidelines as a second-line agent after atropine failure. However, it does not address the underlying infranodal conduction block, and pacing is the more definitive and appropriate intervention for Mobitz Type II causing hemodynamic instability.[3]

Would you like to explore the key differences between Mobitz Type I and Type II AV block in terms of ECG recognition and prognosis?

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Question 442

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?

A. Ulcerative colitis
B. Celiac disease
C. Irritable bowel syndrome
D. Crohn's disease

https://openevidence.com/ask/b4d5e691-033f-44e2-9770-20796f6c0629

The answer is **A. Ulcerative colitis**.

The presentation is classic for ulcerative colitis (UC), with several hallmark features pointing definitively to this diagnosis:

- **Continuous mucosal inflammation beginning at the rectum and extending proximally** (to the hepatic flexure) is the endoscopic signature of UC. As described in the 2025 ACG guideline, UC "most often presents as a continuously inflamed segment involving the distal rectum and extending proximally". This extent classifies as **extensive colitis (E3)** per the Montreal classification, since it extends proximal to the splenic flexure.[1]
- **Grossly bloody stool and urgency (tenesmus)** are the cardinal symptoms of UC.[2]
- **Conjunctival pallor** reflects anemia from chronic blood loss, which is frequent in UC.[3]
- **Erythematous, tender rectum** on physical exam is consistent with the rectal involvement that is nearly always present in UC.[4]

Why not the other options:

- **Crohn's disease (D):** Characterized by **skip lesions** (discontinuous inflammation), **transmural** involvement, **rectal sparing**, aphthous/deep ulcers, cobblestoning, and perianal fistulas — none of which are described here. The continuous mucosal pattern from the rectum proximally is the key distinguishing feature favoring UC.[4][5]
- **Celiac disease (B):** Affects the **small bowel** (duodenum/jejunum), presents with malabsorption and steatorrhea — not bloody diarrhea or colonic mucosal lesions.
- **Irritable bowel syndrome (C):** A **functional disorder** with no structural mucosal abnormalities on colonoscopy. Fecal calprotectin can reliably distinguish IBS from IBD.[6]

Would you like to explore the recommended treatment approach for extensive ulcerative colitis?

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Question 443

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?

A. Benign prostatic hyperplasia
B. Chronic, non-bacterial prostatitis
C. Chronic prostatitis by resistant Escherichia coli
D. Interstitial cystitis

https://openevidence.com/ask/5056de67-c112-474b-a348-69d283df9a15

The answer is **B. Chronic, non-bacterial prostatitis** (NIH Category IIIA — chronic prostatitis/chronic pelvic pain syndrome, inflammatory subtype).

This patient's presentation is a textbook case of **CP/CPPS (NIH Type IIIA)**. The key diagnostic features are:

- **Chronic pelvic pain ≥3 months** (2 years in this case) with irritative voiding symptoms, painful ejaculation, and hematospermia — all classic symptoms of CP/CPPS[1][2]
- **White blood cells present in expressed prostatic secretions (EPS) with negative cultures** — this distinguishes Type IIIA (inflammatory) from Type IIIB (non-inflammatory), and from chronic bacterial prostatitis (Type II), which requires positive cultures[3][4]

- **Failure of antimicrobial therapy** — consistent with a nonbacterial etiology and argues strongly against option C (resistant E. coli would still grow on culture, even if resistant to ciprofloxacin)
- **Associated somatic complaints** (recurrent abdominal pain, alternating constipation/diarrhea, fatigue with normal workup) — CP/CPPS is frequently associated with other chronic pain conditions such as **irritable bowel syndrome (IBS)** and **chronic fatigue syndrome**, as noted in the 2025 AUA guideline[5]

Why the other options are incorrect:

- **A. Benign prostatic hyperplasia** — BPH primarily causes obstructive voiding symptoms in older men and does not explain hematospermia, painful ejaculation, or WBCs in EPS.
- **C. Chronic prostatitis by resistant E. coli** — The EPS culture is **negative**. Resistant organisms still grow on culture; they simply demonstrate antimicrobial resistance on susceptibility testing. Chronic bacterial prostatitis (NIH Type II) requires a positive prostate-localizing culture.[4][6]
- **D. Interstitial cystitis** — While IC/BPS can overlap with CP/CPPS, the **localization of WBCs to the EPS** with a negative midstream urine points to a prostatic rather than bladder source. Additionally, the clinical phenotype (painful ejaculation, hematospermia, tender prostate) is more characteristic of CP/CPPS.[5]

CP/CPPS accounts for **>90% of chronic prostatitis cases**, and it is a diagnosis of exclusion made when pelvic pain persists in the absence of demonstrable bacterial infection.[5][6][7]

Has this patient been assessed with the NIH-Chronic Prostatitis Symptom Index (NIH-CPSI), and have treatments beyond antibiotics — such as alpha-blockers, pelvic floor physical therapy, or a UPOINT-based multimodal approach — been considered?

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Question 444

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

A. Administer hepatitis B vaccine
B. Administer hepatitis B immunoglobulin (HBIG)
C. Administer hepatitis B vaccine and HBIG
D. Check hepatitis B serology

https://openevidence.com/ask/7821e836-15c2-48e2-bcb1-f592af023b2b

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C. Administer hepatitis B vaccine and HBIG.

The mother is HBsAg-positive, HBeAg-positive with HBV DNA >1 million IU/mL — the highest-risk profile for perinatal transmission. ACOG gives a strong recommendation that neonates of HBsAg-positive mothers (or mothers with unknown status at delivery) receive **both HBIG and hepatitis B vaccine within 12 hours of birth**, and SMFM recommends the same regardless of

maternal viral load or whether the mother received antenatal antiviral therapy.[1][2] Cesarean delivery does not alter this and is not itself protective.[1]

Practical administration

- Monovalent HepB vaccine 0.5 mL IM and HBIG 0.5 mL IM in **separate limbs**, within 12 hours of birth, regardless of birth weight. At 2 hours of life, give both now — observational data in high-viremia mothers suggest earlier administration (median 0.17 h) is associated with very low transmission, though the guideline-actionable window remains ≤12 hours.[3][4]
- Birth weight is ≥2000 g, so complete the standard series: doses at birth, 1–2 months, and a final dose at 6 months (minimum age 24 weeks). A 4-dose total is acceptable if combination vaccine is used for later doses.[3][5]
- **Post-vaccination serologic testing** with HBsAg and anti-HBs at **age 9–12 months** — never before 9 months, since passively acquired HBIG antibody and maternal HBsAg confound earlier results.[3][5]
- Breastfeeding is encouraged and does not increase transmission risk once immunoprophylaxis is given.[1][6]

Why not the other options

- **A (vaccine alone):** insufficient in a known HBsAg-positive, HBeAg-positive mother; combined passive–active immunization is the standard, with overall efficacy ~95%.[7]
- **B (HBIG alone):** provides only transient passive immunity — in the original trials ~25% of infants became infected through household contact by 1 year.[2]
- **D (check serology first):** neonatal serology at birth is uninterpretable and would delay prophylaxis; testing is deferred to 9–12 months.[3][5]

Residual risk and maternal issues

Even with correct immunoprophylaxis, roughly 1% of exposed neonates overall become infected, and failures cluster in infants of HBeAg-positive mothers with HBV DNA >2×10^6 IU/mL — precisely this scenario.[1][4] With DNA >200,000 IU/mL, the mother should have received tenofovir disoproxil fumarate from gestational week 28 (initiated immediately if care began later); if she did not, transmission risk is higher despite prophylaxis.[1][8] She also needs postpartum ALT and HBV DNA monitoring every 1–3 months for up to 6 months for withdrawal or postpartum flares.[6][8]

One note on the panel as printed: total anti-HBc is listed as positive and anti-HBc as negative, which is internally inconsistent. The interpretable pattern — HBsAg+, HBeAg+, IgM anti-HBc

negative, anti-HBs negative, high HBV DNA, normal ALT — is chronic HBeAg-positive infection in the immune-tolerant phase, and neonatal management is unchanged.

Would you like to explore how to manage immunoprophylaxis failure if the infant tests HBsAg-positive at 9–12 months?

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Question 445

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?

A. Midodrine
B. Rivastigmine
C. Mirtazapine
D. Tolterodine

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The correct answer is **D. Tolterodine**.

This patient presents with classic **urge urinary incontinence** (overactive bladder) secondary to neurogenic detrusor overactivity from multiple sclerosis. The key findings — sudden urge with inability to reach the bathroom, absence of stress incontinence, normal post-void residual volume, and normal digital rectal examination — point to uninhibited detrusor contractions without outlet obstruction or urinary retention.

Antimuscarinic agents are the first-line pharmacotherapy for neurogenic detrusor overactivity in MS.[1][2] The AUA/SUFU guideline recommends antimuscarinics, beta-3 adrenergic receptor agonists, or a combination of both to improve bladder storage parameters in neurogenic lower urinary tract dysfunction.[1] **Tolterodine** is a competitive muscarinic receptor antagonist FDA-approved for overactive bladder with symptoms of urge incontinence, urgency, and frequency.[3][4] It reduces uninhibited bladder contractions and increases bladder capacity, with clinical trials demonstrating significant reduction in weekly incontinence episodes compared to placebo.[3][5]

The other choices are incorrect:

- **Midodrine** — an alpha-1 adrenergic agonist used for orthostatic hypotension; no role in urge incontinence.

- **Rivastigmine** — a cholinesterase inhibitor used for dementia; would increase cholinergic stimulation and potentially **worsen** detrusor overactivity.
- **Mirtazapine** — an antidepressant (noradrenergic/specific serotonergic); not indicated for urinary incontinence.

One important caveat in MS patients: anticholinergic medications carry a risk of **cognitive side effects**, particularly in older patients or those with pre-existing cognitive impairment, and post-void residual volume should be monitored given the potential to impair bladder emptying.[6][7]

Would you like to explore how beta-3 agonists like mirabegron compare with antimuscarinics for bladder overactivity in MS?

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Question 446

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?

A. No treatment necessary
B. 100% oxygen
C. Propranolol
D. Sumatriptan

https://openevidence.com/ask/972e3664-e3b2-4671-8809-e3aad2918169

D. Sumatriptan. The presentation is a typical migraine attack — severe pulsating headache lasting 12 hours with nausea, photophobia, and inability to function — that has failed an NSAID. The American College of Physicians 2025 guideline gives a **strong recommendation (moderate-certainty evidence) to add a triptan to an NSAID** for moderate-to-severe acute episodic migraine in nonpregnant adults who do not respond adequately to the NSAID alone.[1] Triptans and NSAIDs remain the primary acute options in patients without vascular contraindications, and the sumatriptan–naproxen combination has the largest net benefit of any regimen studied.[1][2]

Why the other options are wrong

- **A. No treatment** — she is incapacitated; untreated attacks should be aborted, and early treatment improves efficacy.[1][3]
- **B. 100% oxygen** — high-flow oxygen is the acute treatment for **cluster headache**, not migraine; her phenotype (12-hour duration, nausea, photophobia, no autonomic features) is not cluster.
- **C. Propranolol** — a **preventive** agent with no role in aborting an acute attack.

Practical points for this patient

- **The stopped sertraline is a distractor.** She is off it entirely, and even with concurrent SSRI use the risk is negligible — 0 to 4 cases of serotonin syndrome per 10,000 person-years of triptan/SSRI–SNRI coprescription, and the American Headache Society position paper concluded that available evidence does not support restricting triptan use with SSRIs/SNRIs, while advising vigilance. The sumatriptan label retains a serotonin syndrome warning.[4][5][6]
- **Prominent nausea favors a non-oral route:** subcutaneous sumatriptan **6 mg** (max 12 mg/24 h, doses ≥1 h apart) or intranasal, plus an antiemetic — ACP explicitly advises a nonoral triptan with an antiemetic when nausea or vomiting is severe.[1][6]
- **Verify triptan contraindications** before dosing: prior MI, ischemic stroke/TIA, uncontrolled hypertension, coronary or peripheral vascular disease, hemiplegic or brainstem-aura migraine, and ergot or another triptan within 24 hours.[2]
- **In the actual ED setting**, the 2025 AHS parenteral guideline rates **IV prochlorperazine 10–12.5 mg (± diphenhydramine) as level A "must offer,"** with metoclopramide 10 mg IV, ketorolac IV, and SC sumatriptan at level B; hydromorphone is level A "must not offer". Adjunctive IV dexamethasone reduces 72-hour recurrence. Sumatriptan is still the best answer among the four choices offered.[7][8][9]
- **Screen for secondary headache** (SNNOOP10) before attributing this to migraine — thunderclap onset, fever/meningismus, focal deficit, papilledema, pregnancy/postpartum status, or a pattern distinctly different from her prior headaches would mandate imaging ± lumbar puncture rather than abortive therapy. Note that a noncontrast CT loses sensitivity for subarachnoid hemorrhage beyond ~6–12 hours from onset.[10]

Would you like to explore what to do when a patient has an inadequate response to triptans?

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Question 447

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?

A. 30 breaths per minute
B. 32 breaths per minute
C. 10 breaths per minute
D. 27.7 breaths per minute

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The answer is **B. 32 breaths per minute**.

The **mode** is defined as **the most frequently occurring value** in a data set.[1][2] Among the seven respiratory rates listed:

- 22 → 1 time
- 23 → 2 times
- 30 → 1 time
- **32 → 3 times**

32 breaths per minute appears three times, more than any other value, making it the mode.

The other answer choices represent different statistical measures:

- **30 breaths per minute (A)** — the median (middle value when ordered).

- **10 breaths per minute (C)** — the range (32 − 22 = 10).
- **27.7 breaths per minute (D)** — the mean (sum of all values ÷ 7 ≈ 27.7).

As noted in the literature, the mean, median, and mode are the three primary measures of central tendency.[1][3] Each describes the center of a distribution differently, and the mode is particularly useful when identifying the most common observation in a sample.

Would you like to explore when the mode is preferred over the mean or median for describing clinical data distributions?

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Question 448

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?

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

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The correct answer is **C: Wrap finger in moist gauze, put in a plastic bag, and place on ice**.[1][2]

The standard protocol for preservation of an amputated digit involves three steps: **(1)** wrapping the part in **moist gauze** to prevent desiccation, **(2)** sealing it in a **plastic bag** to create a barrier, and **(3)** placing the bag **on ice** to achieve cold storage without direct tissue contact.[1][2] This method extends the allowable ischemia time from approximately **12 hours (warm)** to **24 hours (cold)** for digits.[1][3]

The other options are incorrect for the following reasons:

- **A (Submerge in ice water)** and **D (Moist gauze submerged in ice water):** Direct submersion causes tissue waterlogging and maceration, damaging cells needed for successful anastomosis.
- **B (Moist gauze alone):** Omits cooling entirely, leaving the digit in warm ischemia where viability declines significantly — early replantation (0–6 hours) had approximately **40% greater odds of survival** compared to the 6–12 hour warm ischemia window.[3]

Despite the importance of proper preservation, adherence remains poor — one study found only **34% of amputated parts** arrived properly preserved, and proper preservation was significantly associated with higher rates of attempted replantation (58% vs. 23%, p = 0.001).[4]

Would you like to explore the indications and contraindications for digit replantation?

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Question 449

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?

A. Uterine fibroids
B. Congenital defect of the Mullerian ducts
C. Purging behavior
D. Anovulation

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D. Anovulation.

A luteal-phase-inappropriate progesterone of 0.8 ng/mL in a girl who has not bled for 3 months documents absent ovulation, and the remaining labs exclude the other endocrine causes: prolactin, TSH, FSH, LH, and testosterone are all normal, and the pregnancy test is negative. Her cycles have been irregular (15–45 days) since menarche at 14, which is the expected pattern of hypothalamic–pituitary–ovarian axis immaturity — as many as 85% of cycles are anovulatory in the first year after menarche and up to 59% in the third year.[1] The American College of Obstetricians and Gynecologists states that **anovulation is the most common etiology of**

abnormal uterine bleeding in adolescence, most often from HPO axis immaturity in the first 12–18 months after menarche, with **obesity an increasingly important contributor**.[2][3]

Her BMI of 27 kg/m², maternal PCOS, and paternal diabetes add a second anovulatory mechanism: increased BMI is the major risk factor for persistent anovulation in adolescents, and obesity-related hyperandrogenemia can mimic or evolve into PCOS.[1][4] Formal PCOS diagnosis is not yet appropriate — testosterone is normal (2.2 nmol/L, N <3.5) and current criteria require oligo/anovulation persisting ≥2 years past menarche in this age group.[1]

Why the other options are wrong

- **Uterine fibroids** — essentially never occur at this age, and when symptomatic they cause heavy or intermenstrual bleeding, not amenorrhea. Structural causes are a small minority of adolescent abnormal uterine bleeding, which is dominated by the nonstructural (COEIN) categories.[5]
- **Congenital Müllerian defect** — excluded by the history of prior menses (obstructive anomalies present as primary amenorrhea or cyclic pain) and by a normal vagina and cervix on pelvic exam. Anatomic secondary amenorrhea implies prior uterine instrumentation or infection, neither of which is present.[6]
- **Purging behavior** — she is weight-conscious, but there is no low weight (BMI 27), bradycardia is borderline at 60/min without other findings, and functional hypothalamic amenorrhea from disordered eating typically shows low or low-normal LH with LH below FSH and low estradiol; here LH and FSH are both mid-normal. Energy-deficit amenorrhea remains worth screening for on history given the eating-attitude clues, but it does not fit this biochemical picture.[6][7]

Two clinical points worth flagging

Risperidone is a recognized medication cause of amenorrhea through hyperprolactinemia, but her prolactin of 16 ng/mL is normal, so drug-induced hyperprolactinemia is not operative here.[8] Also, a negative urine hCG at 3 months of amenorrhea with recent onset of intercourse is reliable, but repeat testing or serum hCG is reasonable if amenorrhea persists — pregnancy must be re-excluded before attributing any adolescent amenorrhea to anovulation.[2]

Would you like to explore when PCOS can be formally diagnosed in an adolescent with persistent oligomenorrhea?

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Question 450

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?

A. Adenosine deaminase
B. Caspase 1
C. Protein phosphatase
D. Tyrosine kinase

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The answer is **B. Caspase 1**.

Following ASC speck formation, the CARD domain of ASC recruits **procaspase-1 via CARD-CARD homotypic interactions**. Proximity-induced self-cleavage then converts procaspase-1 into active **caspase-1**.[1][2] This is the immediate next step after ASC oligomerization into specks.

Active caspase-1 subsequently cleaves pro-IL-1β and pro-IL-18 into their mature forms and also cleaves gasdermin D (GSDMD), which forms pores in the plasma membrane to mediate cytokine release and **pyroptosis**.[3][4]

The other options are not part of the NLRP3 inflammasome signaling cascade:

- **Adenosine deaminase** — involved in purine metabolism (deficiency causes SCID), not inflammasome signaling.
- **Protein phosphatase** — not a downstream effector of ASC speck formation.
- **Tyrosine kinase** — while spleen tyrosine kinase (SYK) can phosphorylate ASC upstream to facilitate speck formation, it is not recruited or activated as the next step after speck assembly.[5]

Would you like to explore the clinical syndromes caused by NLRP3 gain-of-function mutations and their management?

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Question 451

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?

A. Rough endoplasmic reticulum
B. Smooth endoplasmic reticulum
C. Cytosol
D. Nucleus

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The answer is **A. Rough endoplasmic reticulum**.

Secretory proteins are synthesized on ribosomes bound to the membrane of the rough endoplasmic reticulum (RER).[1] The "rough" designation itself refers to the studded appearance of ribosomes on the ER surface. Through the **signal recognition particle (SRP) pathway**, mRNAs encoding signal-sequence-bearing proteins are directed to the ER membrane during translation: SRP recognizes the emerging signal peptide, halts translation, and recruits the ribosome-mRNA complex to the ER translocon (Sec61 complex), where translation resumes and the nascent polypeptide is translocated into the ER lumen.[2][3]

Once in the ER lumen, secretory proteins undergo **folding, post-translational modification, and quality control** before being packaged into COPII-coated vesicles for transport through the Golgi and ultimately secretion.[1][4]

The other options are incorrect:

- **Smooth ER** lacks ribosomes and is involved in lipid synthesis, steroid hormone production, and detoxification — not protein translation.
- **Cytosolic (free) ribosomes** translate mRNAs encoding intracellular proteins (cytoplasmic, nuclear, mitochondrial) that are not destined for the secretory pathway.[5]
- **The nucleus** is the site of ribosomal RNA transcription and ribosomal subunit assembly, but protein translation does not occur there.

Protein-secreting cells — such as pancreatic acinar cells, plasma cells, and goblet cells — are characteristically rich in rough ER, reflecting their high demand for secretory protein synthesis. [6]

Would you like to explore how the signal recognition particle pathway directs nascent proteins to the ER?

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Question 452

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?

A. Neisseria gonorrhoeae and Chlamydia trachomatis screening
B. Beta-hCG urine test
C. Repeat Pap smear
D. No further testing is necessary

https://openevidence.com/ask/d5694b24-6a72-491f-b3e8-dc6e309d5291

The best recommendation is **A. Neisseria gonorrhoeae and Chlamydia trachomatis screening**.

The USPSTF recommends **screening for chlamydia and gonorrhea in all sexually active women aged 24 years or younger** (Grade B recommendation).[1] This patient is 24 and sexually active, meeting screening criteria regardless of symptoms or number of partners. The CDC and ACOG similarly recommend annual screening in this population.[1]

Why the other options are incorrect:

- **C. Repeat Pap smear** — The USPSTF recommends **cervical cytology every 3 years** for women aged 21–29. Her last normal Pap was at age 22, so the next is not due until age 25.[2]
- **B. Beta-hCG urine test** — There is no clinical indication for pregnancy testing. She has regular menses, her last menstrual period was 2 weeks ago, and she is using oral contraceptives with no reported missed pills or symptoms of pregnancy.
- **D. No further testing is necessary** — Incorrect because age-based STI screening is indicated per national guidelines.

The family history (mother with breast cancer at 40, father with colon cancer at 75) and upcoming travel are not directly relevant to the answer choices but would warrant separate discussion at the visit — particularly the maternal breast cancer history, which may prompt a hereditary cancer risk assessment.

Would you like to explore genetic counseling and BRCA testing recommendations given the maternal breast cancer history?

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Question 453

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?

A. Alendronate
B. Calcitonin
C. Estrogen
D. Tamoxifen

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The answer is **A. Alendronate**.

Bisphosphonates (alendronate, risedronate, zoledronic acid) are first-line pharmacotherapy for postmenopausal osteoporosis in patients at increased fracture risk.[1][2][3] This patient has a **hip T-score of −3.2** (well below the −2.5 threshold for osteoporosis) and a **prior fragility fracture** (Colles' fracture), making pharmacotherapy clearly indicated.[1][4]

Why alendronate over the other options:

- **Alendronate** has broad-spectrum antifracture efficacy, reducing vertebral, nonvertebral, and hip fractures, with strong evidence supporting its use as initial therapy. It is also the most cost-effective initial therapy as a generic oral agent. All major guidelines (ACOG, ACP, AACE/ACE, Endocrine Society) recommend bisphosphonates as first-line.[1][2][3][4][5][6]
- **Calcitonin** has low efficacy and is generally reserved for patients who cannot tolerate other osteoporosis therapies. The ACP guideline did not even consider calcitonin as it is no longer widely used.[1][2]

- **Estrogen** (hormone therapy) is **not recommended** for osteoporosis treatment due to increased risks of cerebrovascular events and venous thromboembolism that outweigh its skeletal benefits. ACOG similarly reserves it for patients who cannot tolerate other therapies.[1][7]

- **Tamoxifen** is a SERM used for breast cancer treatment/prevention, not for osteoporosis. The SERM approved for osteoporosis is **raloxifene**, which only reduces vertebral fractures (not hip or nonvertebral) and is associated with VTE risk.[7]

It is worth noting that with a T-score of −3.2 and prior fracture, this patient could be classified as **very high fracture risk**, for which some recent guidelines recommend considering an osteoanabolic agent (e.g., teriparatide, abaloparatide, romosozumab) as initial therapy.[1][8] However, among the choices provided, alendronate is the standard and correct answer.

Would you like to explore the indications for anabolic-first therapy in very high-risk osteoporosis?

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Question 454

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?

A. Decreased glomerular filtration rate (GFR)
B. Decreased extracellular fluid (ECF) volume
C. Increased renal blood flow
D. Increased renal tubular sodium reabsorption

https://openevidence.com/ask/6c7d0925-7f44-430f-910b-66461f2956f5

D. Increased renal tubular sodium reabsorption.

The presentation — orthopnea, paroxysmal nocturnal dyspnea, exertional dyspnea, bibasilar crackles, and 2+ pitting edema in a man with 20 years of heavy daily alcohol use — is congestive heart failure, with alcohol-induced dilated cardiomyopathy the leading etiology (typically men 30–55 years old drinking heavily for >5–10 years; roughly 7–8+ standard drinks/day is the classic threshold, though thresholds are debated).[1][2][3] The hallmark renal derangement in decompensated HF is **avid tubular sodium retention driven by neurohormonal activation**.[4]

Mechanism. Reduced cardiac output and effective arterial blood volume trigger baroreceptor-mediated activation of the sympathetic nervous system, RAAS, and non-osmotic arginine vasopressin release.[5][6] Angiotensin II and renal α-adrenergic stimulation act directly on proximal tubular epithelium; efferent arteriolar constriction alters peritubular Starling forces (lower hydrostatic, higher oncotic pressure) to further enhance proximal reabsorption; aldosterone increases collecting-duct sodium reabsorption, and the normal **aldosterone escape phenomenon fails in HF**, so sodium retention continues and produces edema and pulmonary congestion.[7][8] Reduced distal sodium delivery compounds this.[8]

Why the other options are wrong:

- **A. Decreased GFR** — GFR is often initially preserved despite falling renal blood flow through a compensatory rise in filtration fraction from efferent constriction; it declines only when preglomerular vasoconstriction from extreme RAAS activation and venous congestion overwhelm that compensation. GFR reduction can certainly coexist in decompensated HF, but it is not the defining or universal association here.[5][9]
- **B. Decreased ECF volume** — ECF volume is **expanded** (edema, crackles). What is reduced is the effective circulating volume, which is the stimulus for retention.[4]
- **C. Increased renal blood flow** — RBF is **decreased** by renal sympathetic nerve activity, norepinephrine spillover, angiotensin II, and vasopressin.[10][11]

Clinical note. The recorded 135/115 mm Hg (pulse pressure 20 mm Hg) should be re-verified; if accurate, marked diastolic hypertension raises hypertensive heart disease as a contributor, while a genuinely narrow pulse pressure suggests low stroke volume. In a shelter-resident heavy drinker, also consider thiamine deficiency (wet beriberi, high-output failure) and hepatic disease — both of which likewise cause arterial underfilling with increased tubular sodium reabsorption, so the answer holds. Workup: pulse oximetry, ECG, chest radiograph, natriuretic peptides, CMP/LFTs, and transthoracic echocardiography; abstinence is the single most important intervention if alcohol-induced cardiomyopathy is confirmed, since LVEF recovery in abstainers carries an excellent prognosis.[12]

Would you like to explore the likelihood and timeline of LVEF recovery after abstinence in alcohol-induced cardiomyopathy?

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Question 455

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?

A. Kwashiorkor
B. Marasmus
C. Beriberi
D. Rickets

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The answer is **A. Kwashiorkor**.

This presentation — **pitting edema, hepatomegaly, ascites, irritability/drowsiness, and missing teeth** in a malnourished refugee child — is classic for **kwashiorkor**, the edematous form of severe protein-energy malnutrition.[1][2][3]

Key features pointing to kwashiorkor:

- **Peripheral and periorbital edema** — the hallmark that distinguishes kwashiorkor from marasmus. Edema results from hypoalbuminemia (due to deficient protein intake impairing hepatic albumin synthesis) and likely inflammatory/oxidative mechanisms.[4][5][6]
- **Hepatomegaly** — caused by fatty infiltration of the liver due to impaired lipoprotein (VLDL) synthesis and defective hepatic lipid clearance from protein deficiency.[2]
- **Abdominal distension/ascites** — from a combination of hepatomegaly, weakened abdominal musculature, and hypoalbuminemia.[1][7]
- **Irritability and apathy/drowsiness** — characteristic mental status changes of kwashiorkor.[3][8]
- **Missing teeth** — a consequence of chronic malnutrition affecting dental development.

Why not the other choices:

- **Marasmus (B)** — a nonedematous form of severe malnutrition marked by extreme wasting and loss of subcutaneous fat, without the edema or hepatomegaly seen here.[2][7]
- **Beriberi (C)** — thiamine (vitamin B1) deficiency causing either "wet" beriberi (high-output cardiac failure) or "dry" beriberi (peripheral neuropathy). It does not present with hepatomegaly and generalized pitting edema in this pattern.
- **Rickets (D)** — vitamin D deficiency causing bony abnormalities (bowing of legs, rachitic rosary, craniotabes), not edema or hepatomegaly.

Would you like to explore the refeeding protocol for severe kwashiorkor and precautions against refeeding syndrome?

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Question 456

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?

A. Autosomal dominant
B. Autosomal recessive
C. Noninherited somatic mutation
D. X-linked dominant

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The answer is **D. X-linked dominant**.

This presentation — a **2-year-old male with significant speech delay, hyperactivity, and an elongated face** — is classic for **Fragile X syndrome (FXS)**, the most common inherited cause of intellectual disability.[1][2] FXS is caused by a **CGG trinucleotide repeat expansion** (>200 repeats, termed a full mutation) in the 5' untranslated region of the **FMR1 gene** on the X chromosome, which leads to gene silencing and absent FMRP production.[1]

Key clinical features supporting this diagnosis:

- **Speech and language delay by age 2** is the typical presenting concern; the syndrome is usually diagnosed around age 3 when delayed speech milestones become apparent.[1][3]
- **Hyperactivity and ADHD symptoms** are prominent behavioral features, with progressively increasing hyperactivity emerging during childhood.[3]
- **Long, narrow face and large ears** are characteristic craniofacial findings, though these become more prominent with age.[2][4]

- **Preserved motor milestones** relative to language is typical, though mild motor delays (e.g., hypotonia, coordination difficulties) can also occur.[3]

Inheritance pattern: FXS follows **X-linked dominant** inheritance.[2][5] One copy of the full mutation allele is sufficient to cause the condition. Males (hemizygous) are almost always severely affected, while approximately one-third of females with a full mutation have intellectual disability, with variable expression due to X-inactivation.[1] The expansion from premutation to full mutation occurs almost exclusively through **maternal transmission**.[5][6]

Would you like to explore the recommended diagnostic workup and genetic testing for suspected Fragile X syndrome?

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Question 457

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?

A. Delusional disorder
B. Mood disorder with psychotic features
C. Schizoid personality disorder
D. Schizophrenia

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The answer is **D. Schizophrenia**.

This presentation fulfills **DSM-5 diagnostic criteria for schizophrenia**:[1][2]

- **Criterion A (≥2 symptoms, at least one from items 1–3):**
- **Delusions** — bizarre delusions of aliens watching him and "stealing his thoughts" (thought withdrawal)
- **Disorganized speech** — "impossible to follow the patient's sequence of thoughts"
- **Negative symptoms** — flat affect and social withdrawal
- **Criterion B (functional decline)** — marked deterioration from premorbid functioning, with progressive social isolation over 7 months
- **Criterion C (duration ≥6 months)** — symptoms present for 7 months
- **Criterion D** — no concurrent major depressive or manic episodes described

- **Criterion E** — marijuana use ceased 1 year ago, making substance-induced psychosis unlikely

The onset in a **23-year-old male** is classic, with peak incidence at ages 15–25.[3]

Why not the other options:

- **Delusional disorder** is characterized by **nonbizarre, encapsulated delusions** with preservation of personality and functioning, and **without** disorganized speech, flat affect, or other prominent schizophrenia-like features. This patient has bizarre delusions, formal thought disorder, and negative symptoms — all inconsistent with delusional disorder.[4][5]
- **Mood disorder with psychotic features** requires a **prominent mood episode** (major depression or mania) during which psychotic symptoms occur. No significant mood episode is described here; the anxiety and flat affect are better explained by schizophrenia.[1]
- **Schizoid personality disorder** involves chronic social detachment and restricted affect but **no psychotic symptoms** such as delusions or disorganized thinking. This patient has active psychosis, ruling out a personality disorder as the primary diagnosis.[2]

Would you like to explore first-line treatment options for first-episode schizophrenia?

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Question 458

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?

A. Ifosfamide
B. Mesna
C. Methotrexate
D. Nitrofurantoin

https://openevidence.com/ask/5bbf83e4-a407-4a61-ab2a-f41ac2e8e408

The correct answer is **B. Mesna**.

This patient with **SLE** **and lupus nephritis** (progressive edema, proteinuria, hypertension) was started on **cyclophosphamide**, a standard induction immunosuppressant for active class III/IV lupus nephritis.[1] Two days later, she developed **hemorrhagic cystitis** — hematuria with cystoscopic findings of diffuse mucosal oozing and neovascularization, which are hallmarks of cyclophosphamide-induced bladder toxicity.[2]

Cyclophosphamide is metabolized to **acrolein**, a highly reactive aldehyde that is excreted renally and accumulates in the bladder, causing urothelial **necrosis, desquamation, ulceration, neovascularization, and hemorrhage**.[2] **Mesna (2-mercaptoethane sulfonate sodium)** is a uroprotective agent that **binds and neutralizes acrolein** in the urinary bladder, preventing this toxicity.[3][4] KDIGO guidelines note that mesna can be prescribed when the dosage of cyclophosphamide is considered high.[5]

Why the other options are incorrect:

- **A. Ifosfamide** — Another oxazaphosphorine alkylating agent that itself causes hemorrhagic cystitis via acrolein production; it would not prevent and could worsen the condition.[4]
- **C. Methotrexate** — An antimetabolite with no role in preventing cyclophosphamide-induced bladder toxicity.
- **D. Nitrofurantoin** — An antibiotic used for urinary tract infections; the cystoscopy and urinalysis findings here are consistent with chemical cystitis, not infection (negative leukocyte esterase and nitrites).

Would you like to explore dosing strategies for mesna with cyclophosphamide in lupus nephritis?

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Question 459

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?

A. Schizoid personality disorder
B. Avoidant personality disorder
C. Antisocial personality disorder
D. Agoraphobia

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The answer is **B. Avoidant personality disorder**.[1][2]

This patient demonstrates the hallmark triad of avoidant personality disorder: **social inhibition** (rarely leaving the house, avoiding parties and gatherings), **feelings of inadequacy** (timid, shy, soft-spoken with poor eye contact), and a pervasive pattern of interpersonal avoidance beginning in early adulthood (working from home for 20 years with few friends).[1] The DSM-5 defines avoidant personality disorder as a "pervasive pattern of social inhibition, feelings of inadequacy, and hypersensitivity to negative evaluation".[2][3]

The critical distinguishing feature is her **strong desire to be in a relationship**. People with avoidant personality disorder crave acceptance and companionship but fear judgment and rejection, leading them to minimize social contact.[1][4] The DSM-5 notes that these individuals "desire affection and acceptance and may fantasize about idealized relationships with others".[1]

Why not the other options:

- **Schizoid personality disorder (A):** Characterized by **limited desire for social intimacy** and detachment from social relationships with a restricted range of emotional expression. This patient's expressed longing for a relationship directly contradicts the core feature of schizoid personality disorder.[1][2]
- **Agoraphobia (D):** Avoidance in agoraphobia is motivated by fear that escape may be difficult or help unavailable if incapacitating or embarrassing symptoms (e.g., panic) occur. This patient's avoidance is driven by social inhibition and shyness, not situational fear of panic or entrapment. The DSM-5 notes that avoidant personality disorder and agoraphobia can be distinguished by the **motivation** for avoidance.[1]
- **Antisocial personality disorder (C):** Defined by disregard for and violation of the rights of others — entirely inconsistent with this patient's timid, anxious presentation.[2]

Would you like to explore evidence-based treatment options for avoidant personality disorder?

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Question 460

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?

A. Hypocellularity with fatty infiltration
B. ↓ hemosiderin stores
C. Ringed sideroblasts
D. Myeloblasts with immature precursors

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The answer is **B. ↓ hemosiderin stores**.

This patient presents with classic **iron deficiency anemia (IDA)** secondary to chronic gastrointestinal blood loss from poorly controlled peptic ulcer disease. The laboratory profile is characteristic:

- **Microcytic, hypochromic anemia**: low MCV (71), low MCH (21.3), low MCHC (28.4)

- **Elevated TIBC** (620 μg/dL) with **low transferrin saturation** (9%) — the hallmark iron studies pattern of IDA
- **Elevated RDW** (17.8%) reflecting anisocytosis
- **Low reticulocyte count** (0.2%) indicating hypoproliferative marrow response
- **Reactive thrombocytosis** (420,000/mm³), commonly seen in iron deficiency[1]

On bone marrow biopsy, the definitive finding in iron deficiency is **absent or markedly decreased hemosiderin (iron) stores** on Prussian blue (Perl's) staining. This remains the gold standard for diagnosing iron deficiency — the ferric ions in hemosiderin react with potassium ferrocyanide to produce a blue compound, and in IDA this staining is markedly reduced or absent.[2] Bone marrow reticulum cells are characteristically depleted of iron.[1]

Why the other options are incorrect:

- **A. Hypocellularity with fatty infiltration** — characteristic of **aplastic anemia**, which presents with pancytopenia, not isolated microcytic anemia.
- **C. Ringed sideroblasts** — pathognomonic for **sideroblastic anemia**, which involves defective heme synthesis with iron accumulation in mitochondria around the erythroblast nucleus; iron studies would show elevated ferritin and transferrin saturation, opposite to this patient's pattern.
- **D. Myeloblasts with immature precursors** — suggests **acute leukemia or myelodysplastic syndrome**, which would typically present with abnormal peripheral blood counts (blasts, cytopenias) rather than an isolated microcytic anemia with classic iron deficiency iron studies.

Would you like to explore the recommended evaluation and management approach for iron deficiency anemia from peptic ulcer disease?

References

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Question 461

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?

A. Antibiotics
B. Magnesium sulfate
C. Methotrexate
D. Dilation and curettage

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The answer is **D. Dilation and curettage (surgical uterine evacuation)**.

This presentation is consistent with an **inevitable abortion** — open cervical os, absent fetal cardiac activity, a low-lying gestational sac with progressive downward migration, and profuse hemorrhage causing hemodynamic instability (BP 90/60, HR 125). The ACOG Practice Bulletin on Early Pregnancy Loss states that **women who present with hemorrhage, hemodynamic instability, or signs of infection should be treated urgently with surgical uterine evacuation**.[1]

Why D&C is the priority over the other options:

- **Antibiotics (A):** The low-grade fever and cervical motion/adnexal tenderness raise concern for possible infection (septic abortion). However, even in septic abortion, **the most critical treatment remains prompt removal of infected tissue**. Antibiotics are an essential adjunct and should be started concurrently (ideally IV broad-spectrum coverage before or during

evacuation), but evacuation itself is the definitive intervention for source control. As a standalone answer, antibiotics alone would be insufficient.[2][3][4]

- **Magnesium sulfate (B):** Indicated for eclampsia prophylaxis or fetal neuroprotection in preterm labor — neither applies here.
- **Methotrexate (C):** Used to treat ectopic pregnancy. An intrauterine gestational sac has been confirmed on ultrasound, ruling out ectopic pregnancy.

At 13 weeks, surgical evacuation is best performed via **suction curettage (vacuum aspiration)**, which has replaced sharp curettage as the standard approach and carries a success rate approaching 99%.[1][5] Concurrent management should include volume resuscitation, type and crossmatch, and Rh(D) immune globulin administration if the patient is Rh-negative.[1]

Would you like to explore recommended antibiotic regimens for septic abortion and their timing relative to surgical evacuation?

References

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Question 462

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?

A. Autoantibody production
B. Intravenous drug use
C. Sexually transmitted infection
D. HLA-B 27 positivity

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The answer is **C. Sexually transmitted infection**.

This presentation is classic for **disseminated gonococcal infection (DGI)**: a young, sexually active woman with asymmetric polyarthralgia (right knee, left wrist), a **pustular acral skin lesion** on the sole of the foot, low-grade fever, and **purulent synovial fluid** (45,000 WBC/mm^3 with 90% neutrophils and intracellular organisms — consistent with gram-negative diplococci of *Neisseria gonorrhoeae*).[1][2]

DGI arises from bacteremic spread of *N. gonorrhoeae* from a primary mucosal site. The prerequisite — and therefore the strongest risk factor — is the underlying **sexually transmitted gonococcal infection** itself. The CDC STI Treatment Guidelines identify risk factors for dissemination as female sex, menstruation, pregnancy, and terminal complement deficiency, but all of these presuppose the primary STI.[1] The patient's history of a new sexual partner (camping trip 3 weeks prior) fits this epidemiology, and notably, urogenital infections are **often asymptomatic** in patients who develop DGI.[1][2]

Why the other choices are incorrect:

- **A. Autoantibody production** — Associated with autoimmune arthritis (e.g., rheumatoid arthritis, lupus). The purulent effusion with intracellular organisms and pustular skin lesion points to infection, not autoimmunity.
- **B. Intravenous drug use** — A risk factor for *Staphylococcus aureus* septic arthritis and endocarditis, not DGI.
- **D. HLA-B27 positivity** — Associated with reactive arthritis (formerly Reiter syndrome), which can follow STIs (particularly *Chlamydia*) but presents with sterile, inflammatory arthritis — not purulent fluid with intracellular organisms. Reactive arthritis is a post-infectious immune-mediated process, not a direct joint infection.

Would you like to explore the recommended antibiotic treatment for disseminated gonococcal infection?

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Question 463

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?

A. Myocardial perfusion scan under pharmacological stress
B. Upper endoscopy
C. Coronary angiography
D. Echocardiography at rest

https://openevidence.com/ask/a2004037-e174-4fd5-a618-780440e81c93

The answer is **A. Myocardial perfusion scan under pharmacological stress**.

This patient presents with **classic stable angina** — exertional retrosternal chest pain relieved by rest — in the setting of multiple CAD risk factors (age 58, hypertension, type 2 diabetes). The normal resting ECG, cardiac markers, and chest X-ray rule out acute coronary syndrome but do not exclude underlying obstructive CAD. The appropriate next step is **stress testing** to evaluate for inducible myocardial ischemia.

The critical detail is her **below-knee amputation** with current reliance on crutches (awaiting a new prosthesis), which renders her **unable to perform adequate exercise** for a standard exercise stress test. As stated in JAMA, "when exercise stress testing cannot be performed due to physical limitations...pharmacological stress testing can be performed with either vasodilators (such as adenosine derivatives) or dobutamine".[1] The ADA similarly recommends that "individuals who require stress testing and are unable to exercise should undergo pharmacologic stress echocardiography or nuclear imaging".[2] The 2021 AHA/ACC Chest Pain guidelines reinforce

that **exercise is preferred when feasible**, but pharmacologic stress with imaging is appropriate when physical limitations preclude exercise.[3]

Why not the other options:

- **B. Upper endoscopy** — The symptom pattern (exertional onset, relief with rest, associated dyspnea/palpitations) is characteristic of angina, not esophageal pathology. GI evaluation is not indicated here.
- **C. Coronary angiography** — An invasive procedure reserved for cases where noninvasive testing suggests high-risk disease, or when noninvasive results are inconclusive. It is not appropriate as the initial diagnostic step in stable angina.[1][4]
- **D. Echocardiography at rest** — Resting echocardiography assesses structural and valvular function but **does not detect inducible ischemia**. Given a normal cardiac exam and the need to provoke ischemia, a resting study would have low diagnostic yield for CAD.

Would you like to explore the recommended medical management of stable angina, including antianginal and secondary prevention strategies?

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Question 464

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?

A. Pink colonies
B. Blue-green pigment
C. Yellow sulfur granules
D. Red pigment

https://openevidence.com/ask/53ba68e7-4989-466c-b7e7-fff0f5f66553

The answer is **B. Blue-green pigment**.

This vignette describes classic **hot tub folliculitis** caused by **Pseudomonas aeruginosa**. The key features pointing to this diagnosis include:

- **Clinical presentation**: Pruritic papules and pustules on the trunk, back, and buttocks with follicular inflammation, onset after recreational water exposure (honeymoon in Cancún)[1][2]
- **Microbiologic profile**: Motile, gram-negative rods that are **non-lactose fermenting** and **oxidase positive** — the defining laboratory characteristics of *P. aeruginosa*[3][4]

Pyocyanin, the hallmark pigment of *P. aeruginosa*, is a water-soluble phenazine compound responsible for the organism's characteristic **blue-green color** on culture media. It is produced by **90–95%** of *P. aeruginosa* isolates and serves as both a virulence factor and a quorum-sensing molecule.[5][6] Production of pyocyanin on selective media (e.g., Tech agar) is sufficiently specific that it can be used as a **unique identification test** for the organism.[3][7]

Why not the other options:

- **A. Pink colonies** — Associated with lactose-fermenting organisms (e.g., *E. coli*, *Klebsiella*) on MacConkey agar; *P. aeruginosa* is a non-lactose fermenter.
- **C. Yellow sulfur granules** — Characteristic of *Actinomyces israelii*, a gram-positive, filamentous anaerobe.
- **D. Red pigment** — Associated with *Serratia marcescens* (prodigiosin). While *P. aeruginosa* can produce a minor red pigment (aeruginosin/pyorubrin), it is not the commonly tested or clinically recognized culture finding.[8]

Would you like to explore the management and treatment of Pseudomonas hot tub folliculitis?

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Question 465

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?

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.

https://openevidence.com/ask/28401b4f-588d-43a2-9a21-2af7cd43ac35

The correct answer is **A. It can lead to hydrops fetalis secondary to fetal anemia.**

Parvovirus B19 has a **tropism for erythroid progenitor cells** in the fetus, leading to inhibition of erythropoiesis and subsequent **aplastic anemia**.[1][2] This severe fetal anemia can result in **nonimmune hydrops fetalis (NIHF)**, and parvovirus B19 is the most commonly reported infectious cause of NIHF.[1][2] Per ACOG, an estimated 8–10% (potentially up to 18–27%) of NIHF cases are associated with parvovirus B19 infection.[3] The risk of severe anemia or hydrops is approximately **6–7% when primary infection occurs before 20 weeks' gestation**, which is directly relevant to this patient at 12 weeks.[4]

Why the other options are incorrect:

- **B. Aplastic crisis in the neonate** — The aplastic crisis from parvovirus B19 occurs **in utero**, not as a neonatal condition. Aplastic crises are a recognized complication in patients with pre-existing chronic hemolytic anemias (e.g., sickle cell disease), not a typical neonatal sequela of congenital parvovirus infection.
- **C. Fetal loss in more than 40% of primary infections** — This significantly overstates the risk. The overall fetal loss rate following maternal parvovirus B19 infection is **5–10%**, with ACOG citing **8–17% before 20 weeks** and **2–6% after 20 weeks** of gestation. A meta-analysis confirmed an overall fetal loss incidence of approximately **7.6%**.[3][5][6]

- **D. Slapped-cheek rash in the neonate** — The classic "slapped-cheek" rash is a feature of **erythema infectiosum (fifth disease) in children**, not a congenital manifestation. Adults with parvovirus B19 typically present with arthralgias and a lace-like (reticular) rash, as seen in this patient. Parvovirus B19 is not associated with congenital anomalies or characteristic neonatal rash.[7]

This clinical presentation — **lace-like rash, arthritis, and fever in a young woman** — is itself classic for adult parvovirus B19 infection.[8] Serial ultrasound monitoring with MCA Doppler velocimetry for 8–12 weeks after infection is the recommended surveillance approach.[3]

Would you like to explore the recommended fetal monitoring protocol and intrauterine transfusion indications for parvovirus B19 in pregnancy?

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Question 466

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?

A. Coronary artery vasospasm
B. Coronary artery vasodilation
C. Atherosclerotic plaque rupture
D. Pericardial inflammation

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The answer is **A. Coronary artery vasospasm**.

This presentation is classic for **Prinzmetal (variant) angina**, characterized by **transient ST-segment elevation occurring at rest** that **completely resolves** along with symptoms — the hallmark feature distinguishing it from acute plaque rupture. The ACC/AHA guidelines state that the key to diagnosis is "documentation of ST-segment elevation in a patient during transient chest discomfort (which usually occurs at rest) and that resolves when the chest discomfort abates".[1]

Why vasospasm fits this case:

- **Rest angina** (sitting in a chair, not exertional) with **anterior ST elevation** that spontaneously resolves within minutes is the defining presentation of coronary vasospasm. [2][3]
- **Smoking** is the most prominent coronary risk factor for vasospasm. **Alcohol consumption** is also an established trigger — studies have shown alcohol to be a strong independent risk factor for coronary artery spasm, with alcohol-induced vascular endothelial dysfunction

(elevated endothelin-1, decreased prostaglandin F1-alpha) as a proposed mechanism. **Emotional stress** can further precipitate episodes.[4][5][6][7][8]

Why the other options are incorrect:

- **Atherosclerotic plaque rupture (C):** Acute plaque rupture causes a fixed thrombotic occlusion leading to persistent ST elevation (STEMI) that does not spontaneously resolve with complete ECG normalization within 15 minutes. This patient's rapid and full resolution is inconsistent with plaque rupture.
- **Coronary artery vasodilation (B):** Vasodilation increases coronary blood flow and would not cause ischemia or ST elevation.
- **Pericardial inflammation (D):** Pericarditis produces diffuse, concave-upward ST elevation (not limited to one vascular territory) and does not resolve within minutes.

Would you like to explore the treatment approach for vasospastic angina?

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Question 467

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?

A. Malingering
B. Primary adrenal insufficiency
C. Conversion disorder
D. Factitious disorder imposed on another

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The correct answer is **D. Factitious disorder imposed on another** (FDIA, formerly Munchausen syndrome by proxy).

The defining clue is the **dissociation between markedly elevated insulin (108 mIU/L) and suppressed C-peptide (0.3 ng/mL)**. Insulin and C-peptide are co-secreted in equimolar amounts from pancreatic beta cells. In any form of **endogenous hyperinsulinism** (e.g., insulinoma, congenital hyperinsulinism), both insulin and C-peptide would be elevated.[1][2][3] A high insulin with low C-peptide is the hallmark of **exogenous insulin administration**, because exogenous insulin suppresses endogenous beta-cell secretion and therefore C-peptide.[4][5]

Several contextual features support FDIA:

- The **mother has type 2 diabetes**, providing potential access to insulin at home.
- The child is **5 years old**, too young to intentionally self-administer insulin, effectively excluding malingering (A) or factitious disorder imposed on self.
- The **hypokalemia (K 2.4 mEq/L)** is consistent with exogenous insulin, which drives potassium intracellularly.

- **Recurrent episodes** occurring in the hospital overnight are characteristic of FDIA, where the caregiver induces illness even under observation.[4][6]

Per the DSM-5, FDIA is diagnosed when there is falsification or induction of signs/symptoms in another person, associated with identified deception, and not motivated by obvious external rewards. The diagnosis is assigned to the **perpetrator**, not the victim.[7]

Why not the other options?

- **Primary adrenal insufficiency (B)** can cause hypoglycemia via impaired gluconeogenesis, but insulin levels would be appropriately suppressed — not markedly elevated.
- **Conversion disorder (C)** produces neurological symptoms without corresponding organic pathology. Here, there are objective, measurable laboratory derangements (true hypoglycemia, hyperinsulinemia, hypokalemia), which are incompatible with a functional neurological disorder.
- **Malingering (A)** requires the patient to intentionally produce symptoms for external gain. A 5-year-old cannot plausibly self-administer insulin, and malingering implies conscious intent by the patient, not the caregiver.

Would you like to review the recommended workup steps when exogenous insulin administration is suspected in a pediatric patient, including sulfonylurea screening and child-protective reporting requirements?

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Question 468

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?

A. Installing a vaginal pessary
B. Bladder catheterization
C. Cystostomy
D. Prescribing prostaglandin E2

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B. Bladder catheterization. This is acute-on-chronic urinary retention with overflow incontinence, and the immediate step is prompt, complete bladder decompression via urethral catheter after confirming urethral patency.[1][2] A multidisciplinary panel considered catheterization appropriate for PVR ≥300 mL in patients with suprapubic discomfort, small-volume voids, or acute incontinence — all present here.[2]

Why the picture fits overflow incontinence from a hypocontractile bladder

- **Continuous leakage day and night, unrelated to exertion**, with hesitancy, incomplete emptying, and 2 days of anuria plus a palpable, ultrasonographically overdistended bladder without structural abnormality.

- **Diabetic cystopathy** from 8 years of poorly controlled T2DM: impaired bladder sensation, increased capacity, reduced detrusor contractility, and increased PVR leading to overflow incontinence and an atonic bladder. The corroborating signs of distal polyneuropathy — diminished Achilles reflexes, reduced vibration and fine touch — support established neuropathy.[3][4][5][6]
- **Amitriptyline** adds antimuscarinic bladder outlet/detrusor effects; the label specifically lists urinary retention and dilatation of the urinary tract among anticholinergic reactions and warns against use in patients with a history of urinary retention. Tricyclics are associated with a high risk of urinary retention.[7][8]
- The **posterior vaginal wall bulge (rectocele)** is an incidental finding here; it does not obstruct the urethra and does not explain retention.

Why the other options are wrong

- **Vaginal pessary** treats pelvic organ prolapse and stress incontinence; it does nothing for a hypocontractile, overdistended bladder and delays decompression.[9]
- **Cystostomy/suprapubic catheter** is reserved for failed or contraindicated urethral catheterization or anticipated long-term drainage; it requires a urologist or interventional radiologist and carries a 0%–2.7% risk of bowel injury.[2][10]
- **Prostaglandin E2** is a cervical ripening/uterotonic agent with no role in urinary retention.

After decompression

- Record drained volume; **monitor for post-obstructive diuresis**, hypotension, and electrolyte shifts.
- **Urinalysis and culture** (retention predisposes to cystitis and ascending infection), **creatinine** to assess for obstructive nephropathy, and glucose/HbA1c.[3]
- **Discontinue or substitute amitriptyline** for a non-anticholinergic antidepressant.[7][8]
- If PVR remains elevated after a voiding trial, **clean intermittent catheterization is first-line for neurogenic/atonic bladder**, with urodynamics and urology referral; patients with a neurologic cause should be co-managed with neurology and urology.[1][3][9][10]
- Reassess for a **spinal cause** (cauda equina/conus) if there is back pain, saddle anesthesia, new lower-extremity weakness, or bowel dysfunction, since lumbosacral lesions produce an acontractile bladder.[5]

Would you like to explore the protocol for a voiding trial and transition to clean intermittent catheterization in diabetic cystopathy?

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Question 469

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?

A. Flexion, abduction, and external rotation of the thigh
B. Straight leg raise
C. Internal rotation of the extended hip
D. Radiography

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B. Straight leg raise.

The history — sudden onset with heavy lifting, buttock pain radiating down the leg, described as electrical — is classic for **lumbosacral radiculopathy from an acute disc herniation**. The straight leg raise (Lasègue test) is the bedside maneuver that supports this diagnosis: with the patient supine, passive elevation of the extended leg tensions the sciatic nerve and lumbosacral roots, and the test is positive when the patient's radicular leg pain is reproduced between 30° and 70° of elevation.[1][2]

Test characteristics

- Pooled **sensitivity 0.92 (95% CI, 0.87–0.95)** with **specificity 0.28 (95% CI, 0.18–0.40)** for lumbar disc herniation — a good rule-out test.[1][3]
- The **crossed straight leg raise** (contralateral leg elevation reproducing the affected-side pain) is the more specific confirmatory maneuver: pooled sensitivity 0.28, **specificity 0.90 (95% CI, 0.85–0.94)**.[1][2]
- Sensitivity is increased by adding ankle dorsiflexion at end-range (Bragard maneuver).[2][4]

- The SLR and crossed SLR are among the diagnostic maneuvers consistently recommended across international guidelines for lumbosacral radicular pain, along with mapping pain distribution and gait assessment.[5]

Complete the exam with L4–S1 neurologic testing (quadriceps strength/patellar reflex, great toe and foot dorsiflexion, plantar flexion/Achilles reflex, dermatomal sensation), since >95% of herniations occur at L4–L5 or L5–S1.[1][6]

Why the other options are wrong

- **A. FABER (Patrick test)** — flexion, abduction, external rotation stresses the **sacroiliac joint and hip**, not the lumbar nerve roots.
- **C. Internal rotation of the extended hip** — a maneuver for **hip joint pathology (osteoarthritis, femoroacetabular impingement)**; hip disease causes groin/anterior thigh pain, not electrical pain radiating below the knee.
- **D. Radiography** — plain films are **not indicated** in acute low back pain with or without radiculopathy in the absence of red flags, and are explicitly discouraged by the American College of Radiology and other guidelines given no demonstrated clinical benefit and a high rate of age-related degenerative findings in asymptomatic people. Imaging would be warranted only for red flags (significant trauma or minor trauma with osteoporosis/chronic steroids, cauda equina features, history of cancer or unexplained weight loss, fever/immunosuppression/IVDU, or severe or progressive neurologic deficit), and MRI — not radiography — is the preferred modality for non-trauma red flags.[1][7][8][9]

Would you like to explore the evidence-based initial management of acute lumbar radiculopathy?

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Question 470

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?

A. Sorbitol dehydrogenase
B. Galactocerebrosidase
C. Arylsulfatase A
D. Sphingomyelinase

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The answer is **A. Sorbitol dehydrogenase**.

This patient presents with findings consistent with **diabetic retinopathy** — progressive blurry vision with microaneurysms on fundoscopy in the setting of long-standing (20-year) diabetes. The question asks which enzyme's tissue-specific expression pattern accounts for the preferential damage to certain tissues in diabetes.

The polyol pathway and sorbitol dehydrogenase

In hyperglycemia, excess glucose that cannot be processed through glycolysis enters the **polyol pathway**, where **aldose reductase** converts glucose to sorbitol using NADPH as a cofactor.[1][2] Sorbitol should then be oxidized to fructose by **sorbitol dehydrogenase (SDH)** using NAD+.[3][4] The critical concept is that **tissues susceptible to diabetic complications — the retina, lens, Schwann cells, and kidneys — have relatively low sorbitol dehydrogenase activity** compared to aldose reductase activity. SDH has a high affinity but **low capacity** for sorbitol, meaning that under hyperglycemic conditions, sorbitol production overwhelms its metabolism.[2]

Because sorbitol **cannot easily cross cell membranes**, it accumulates intracellularly, causing **osmotic stress, cellular swelling, and tissue damage**.[1][3][5] Additionally, polyol pathway flux depletes NADPH (needed for glutathione regeneration), contributing to oxidative stress, and the

increased NADH/NAD+ ratio from SDH activity promotes formation of advanced glycation end-products (AGEs) and protein kinase C activation.[6][7]

The other answer choices — **galactocerebrosidase** (Krabbe disease), **arylsulfatase A** (metachromatic leukodystrophy), and **sphingomyelinase** (Niemann-Pick disease) — are lysosomal enzymes whose deficiencies cause inherited storage diseases unrelated to diabetic complications.

Would you like to explore the clinical staging of diabetic retinopathy and screening recommendations?

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Question 471

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?

A. Chronic granulomatous disease
B. Atopic dermatitis
C. Wiskott-Aldrich syndrome
D. Chediak-Higashi syndrome

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The answer is **A. Chronic granulomatous disease (CGD)**.

This presentation — a **male infant with onset at 2 months**, **recurrent pus-secreting skin lesions refractory to treatment**, **recurrent respiratory infections**, **bilateral lymphadenopathy**, **recurrent fevers**, and **growth failure** — is classic for CGD.[1][2] CGD is a primary immunodeficiency of phagocytes caused by defective NADPH oxidase, resulting in impaired generation of reactive oxygen species and inability to kill catalase-positive organisms (e.g., *S. aureus*, *Aspergillus*, *Serratia*, *Burkholderia*).[1][3] The X-linked form accounts for ~70% of cases and is generally more severe.[1] The median age of diagnosis is 2.5–3 years, with the vast majority diagnosed before age 5.[2]

Characteristic findings include **deep-seated abscesses** (skin, lymph nodes, lung, liver, bone), **granuloma formation**, **lymphadenopathy** (~50–60% of patients), and **growth failure**.[1][4] Skin infections — including abscesses and cellulitis — occur in approximately 40% of patients.[1][4]

Why not the other options:

- **Atopic dermatitis (B):** Presents with pruritic, eczematous lesions rather than pus-secreting abscesses. While secondary bacterial infection can occur, the combination of refractory purulent skin lesions with systemic infections from early infancy, diffuse lymphadenopathy, and growth failure points away from atopic dermatitis. The brother's asthma history is a distractor.
- **Wiskott-Aldrich syndrome (C):** Characterized by the triad of **thrombocytopenia** (with bleeding/bruising), eczema, and recurrent infections with encapsulated organisms. No thrombocytopenia or bleeding is described here.[1]
- **Chediak-Higashi syndrome (D):** Features **partial oculocutaneous albinism** and giant granules in leukocytes alongside recurrent pyogenic infections. No albinism is mentioned.

Would you like to explore the diagnostic workup and prophylactic management of CGD?

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Question 472

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?

A. Acquired immunodeficiency syndrome (AIDS)
B. Common variable immunodeficiency
C. Chediak-Higashi syndrome
D. Leukocyte adhesion deficiency–1

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C. Chediak-Higashi syndrome. The triad of recurrent pyogenic bacterial infections beginning in infancy, partial oculocutaneous albinism with silvery hair, and giant peroxidase-positive granules/inclusions in neutrophils — confirmed by biallelic **LYST** mutation — is diagnostic.[1][2]

Why the findings fit

- **LYST** encodes the lysosomal trafficking regulator. Loss of function disrupts lysosome fission and the size/structure of lysosome-related organelles, producing the pathognomonic **giant azurophilic granules in all granule-containing cells**.[2][3][4]
- The same defect in **melanosomes** traps melanin, causing partial oculocutaneous albinism with **silvery-metallic hair** and light skin.[1][4]
- Neutrophil dysfunction is multifactorial: mild neutropenia from intramedullary destruction, impaired chemotaxis and diapedesis, and delayed/defective fusion of giant granules with phagosomes, with deficient elastase and cathepsin G — hence recurrent **S. aureus** and streptococcal skin and respiratory infections.[5][6][7]

Why the other options are wrong

- **AIDS** — perinatal HIV causes opportunistic rather than predominantly pyogenic infection, and does not cause albinism or giant granules; no LYST involvement.

- **Common variable immunodeficiency** — hypogammaglobulinemia with sinopulmonary infection, typically presenting in the second-to-fourth decade, with normal pigmentation and normal granule morphology.
- **LAD-1** — ITGB2 (CD18) mutation causing delayed umbilical cord separation, omphalitis, marked leukocytosis without pus, and no albinism or giant inclusions.

Clinically relevant next steps

Confirmation rests on the peripheral smear, which AAAAI recommends as the first diagnostic test.[2] Beyond infection risk, anticipate **platelet dense-body deficiency with a mild bleeding diathesis**, and — critically — **hemophagocytic lymphohistiocytosis (the "accelerated phase")**, which develops in nearly all untreated classic CHS patients and is usually fatal without treatment.[1][2][8] **Allogeneic HSCT** corrects the immunologic and hematologic disease and should be pursued early, but does not prevent the progressive neurodegeneration that occurs regardless of genotype.[3][8][9]

Would you like to explore the optimal timing and conditioning approach for HSCT in classic Chediak-Higashi syndrome?

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Question 473

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?

A. Leuprolide
B. Finasteride
C. Flutamide
D. Anastrozole

https://openevidence.com/ask/e4a9403e-7021-4f30-a81e-c6614beca6d0

C. Flutamide. Drug X is described as a direct androgen receptor blocker that does not lower testosterone (the patient retains a clinical picture of gynecomastia and hot flashes from receptor blockade with unopposed estrogenic activity) and is renally excreted — this is the profile of a **first-generation nonsteroidal antiandrogen**, of which flutamide is the prototype.[1][2][3]

Why flutamide fits

- **Mechanism match:** Flutamide is a pure nonsteroidal antiandrogen that competitively blocks binding of testosterone and DHT to the intracellular androgen receptor, inhibiting nuclear binding of androgen in target tissues, with no androgen agonist activity. Bicalutamide, nilutamide, and the second-generation agents (enzalutamide, apalutamide, darolutamide) share this class mechanism.[1][3][4][5][6]
- **Renal excretion:** Flutamide and its metabolites are excreted mainly in the urine, with only ~4.2% of a dose recovered in feces over 72 hours. Notably, no dose adjustment is required in chronic renal insufficiency; the active 2-hydroxyflutamide half-life is only slightly prolonged at CrCl <29 mL/min, and neither parent nor metabolite is well dialyzed.[4][7]
- **Side-effect match:** Because receptor blockade leaves testosterone (and aromatization to estradiol) intact, **gynecomastia and breast pain are the hallmark toxicities** of

antiandrogen monotherapy — gynecomastia RR 8.43 (95% CI 3.19–22.28) versus castration, and reported in 30–79% of flutamide-treated men. Plasma testosterone and estradiol rise on flutamide. Hot flashes/sweating occur but are far less frequent than with castration.[4][8][9][10]

Why the others are wrong

- **Leuprolide** is a GnRH/LHRH agonist that suppresses gonadotropins and testosterone production; it does not block the receptor, and gynecomastia is uncommon (13–16%).[9][11][12]
- **Finasteride** is a 5α-reductase inhibitor blocking conversion of testosterone to DHT — it spares testosterone but does not antagonize the receptor.[13]
- **Anastrozole** is an aromatase inhibitor; it lowers estrogen and would not cause gynecomastia by this mechanism, and it has no role as prostate cancer androgen blockade.

Clinically relevant caveat: Flutamide carries a **boxed warning for hepatic injury**, including fatal fulminant hepatitis; serum transaminases must be monitored at baseline, monthly for the first 4 months, and periodically thereafter, and the drug stopped for ALT >2× ULN or jaundice.[14][15] It also potentiates warfarin (prolonged prothrombin time).[4] Nonsteroidal antiandrogen monotherapy is inferior to castration for overall survival in metastatic disease (HR 1.24, 95% CI 1.05–1.48), so these agents are used with medical/surgical castration rather than alone.[8] Flutamide is now largely supplanted by bicalutamide and second-generation agents, and in current NCCN guidance first-generation antiandrogens appear mainly as secondary hormone therapy options in CRPC and for flare prophylaxis when starting an LHRH agonist.[12]

Would you like to explore how to prevent and manage antiandrogen-induced gynecomastia and mastodynia?

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Question 474

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?

A. Complete blood count (CBC)
B. Erythrocyte sedimentation rate (ESR)
C. MRI of the knee
D. No further work-up needed

https://openevidence.com/ask/ad69aa13-be82-4b56-830e-ca53f6365a03

The answer is **D — no further work-up needed**. This patient presents with a classic clinical picture of **bilateral knee osteoarthritis (OA)**, which can be confidently diagnosed on history and physical examination alone without additional laboratory tests or imaging.[1][2][3]

Why this is OA:

This patient fulfills essentially every clinical diagnostic feature of knee OA:

- **Age >45** with **insidious-onset**, activity-related knee pain that worsens with use and improves with rest
- **Brief morning stiffness** (<30 minutes; here 5–10 minutes)
- **Crepitus**, **bony enlargement**, **restricted range of motion**, **bony tenderness** — all cardinal signs of knee OA on exam[1][4]
- **Cool joints** with no palpable warmth — argues strongly against inflammatory arthritis

Per the 2022 NICE guidelines and multiple professional society recommendations, **OA can be diagnosed clinically without imaging** in patients aged ≥45 presenting with activity-related joint pain and morning stiffness lasting <30 minutes.[1][5] The ACR clinical classification criteria similarly allow diagnosis based on knee pain plus a combination of findings including crepitus, bony enlargement, bony tenderness, no palpable warmth, and brief morning stiffness.[3][6]

Why the other options are incorrect:

- **A (CBC) and B (ESR):** There are **no blood or urine tests that diagnose osteoarthritis**. Laboratory tests are indicated only when the presentation is atypical or an alternative diagnosis (e.g., inflammatory arthritis, infection) is strongly suspected. This patient's brief morning stiffness, cool joints, and lack of warmth or erythema argue against an inflammatory process that would warrant CBC or ESR.[1][2]
- **C (MRI):** MRI is **not indicated for a typical OA presentation**. MRI findings of degenerative changes are common even in asymptomatic individuals and may be misleading. MRI is reserved for rare circumstances such as persistent mechanical symptoms with objective locking, suggesting a displaced meniscal tear.[2][5]

Would you like to explore evidence-based first-line management strategies for knee osteoarthritis?

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Question 475

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?

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

https://openevidence.com/ask/db3d54b2-975f-4fe2-8733-140d7d63d38c

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B — determining the patient's life expectancy without treatment.

Under the Medicare Hospice Benefit (Part A), the gating requirement is prognosis: the attending physician and the hospice medical director must certify a life expectancy of **6 months or less if the disease follows its usual course**.[1][2][3] A biopsy diagnosis of gastric adenocarcinoma alone does not establish that. Without staging or prognostic assessment, this patient could have early-stage disease with expected untreated survival well beyond 6 months, whereas untreated metastatic gastric cancer carries a median survival of roughly **3–4 months with best supportive care alone**.[4][5] Prognostication in this setting draws on performance status, weight loss/cachexia, symptom burden, laboratory markers (albumin, hemoglobin, LDH), and extent of disease.[6]

Why the other options are wrong

- **A. Trial of life-extending treatment** — Not a prerequisite for hospice, and imposing one on a decisional patient who has refused disease-directed therapy violates autonomy. The benefit is designed precisely for patients who decline or stop treatment aimed at altering the disease course.[1]
- **C. Establishing the presence of metastasis** — Metastatic disease is not a formal eligibility criterion; **prognosis is**. Documented metastases are one common route to a ≤6-month

estimate, but a patient with unresectable locally advanced disease, poor performance status, and progressive cachexia may qualify without them. He may also decline staging imaging, in which case prognosis must be estimated clinically.

- **D. No further steps required** — He satisfies the goals-of-care side of the equation, but hospice election is a separate formal step taken after a hospice is selected, and certification of the ≤6-month prognosis remains mandatory.[2][3]

Practical implications

- **If prognosis is ≤6 months**, hospice enrollment addresses his cost concern directly: the Medicare hospice benefit covers medications, durable medical equipment, nursing, aide, social work, chaplaincy, respite, and bereavement services related to the terminal illness. Election involves waiving standard Medicare payment for services related to the terminal condition that fall outside the hospice plan of care; unrelated care remains covered, and hospice may provide disease-directed interventions when included for palliation.[1][2][3][7]
- **If prognosis exceeds 6 months**, refer to specialized (non-hospice) palliative care now for symptom management, nutritional support, and advance care planning, with hospice referral when the prognosis shortens. Cost sharing applies to these services, so a social work referral to review coverage is worthwhile given his stated financial priority.[8]
- Certification periods are two 90-day periods followed by unlimited 60-day periods with prognosis reassessed at each; patients may be discharged if prognosis improves and can re-enroll or revoke at any time.[1][9]
- Symptom-directed measures remain appropriate and are compatible with hospice — enteral stenting or venting gastrostomy for gastric outlet obstruction, EBRT or endoscopic therapy for bleeding, and standard analgesic and antiemetic management.[10]

Would you like to explore which prognostic tools best estimate 6-month survival in untreated advanced gastric cancer?

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Question 476

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?

A. Abdominal radiograph
B. ß-hCG
C. CT scan
D. Stool occult blood

https://openevidence.com/ask/07d71cd3-6ee1-48bd-b743-8a9cae314ba4

The correct answer is **B. β-hCG**.

This patient's presentation — **right lower quadrant pain, vomiting, low-grade fever, tachycardia, and a positive Rovsing sign** (RLQ pain reproduced by LLQ palpation) — is classic for **acute appendicitis**.[1] However, in any **woman of reproductive age** presenting with acute abdominal pain, the essential first step before imaging is to obtain a **β-hCG to establish pregnancy status**.[2][3]

This is critical for several reasons:

- **Ectopic pregnancy** can present with RLQ pain and mimic appendicitis. A positive β-hCG would prompt transvaginal ultrasonography and serial quantitative β-hCG levels to evaluate pregnancy location.[4]
- **Imaging strategy depends on pregnancy status.** The ACR Appropriateness Criteria for acute pelvic pain in reproductive-age women organizes all imaging recommendations by β-hCG result — CT abdomen/pelvis (the most accurate modality for appendicitis) involves

ionizing radiation and is not the preferred initial study in a pregnant patient. If β-hCG is negative, CT can proceed; if positive, ultrasound or MRI is preferred.[3][5][6][7]

- A JAMA review of acute appendicitis in adults specifically recommends that evaluation include a **urine β-hCG level** "to rule out uterine or ectopic pregnancy" as part of the standard workup.[1]

Why not the other options:

- **A (Abdominal radiograph):** Poor sensitivity for appendicitis and not part of the standard diagnostic pathway.[1]
- **C (CT scan):** Appropriate imaging after pregnancy has been excluded, but should not precede β-hCG testing in a reproductive-age woman.[5]
- **D (Stool occult blood):** Not relevant; the clinical picture points to appendicitis, not occult GI bleeding.

Would you like to explore the current evidence on clinical scoring systems and non-operative management of acute appendicitis?

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Question 477

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?

A. Bacterial Infection
B. Food
C. Medication
D. Idiopathic

https://openevidence.com/ask/077c3cd1-0649-447c-9fbe-a21d50644d82

The answer is **C. Medication**. This presentation is consistent with a **G6PD deficiency hemolytic crisis triggered by glipizide**, a sulfonylurea.

Why this is G6PD deficiency:

- **African-American male** — G6PD deficiency is an **X-linked disorder** with high prevalence in populations of African, Mediterranean, and Southeast Asian descent.[1]
- **Recurrent episodes since birth** — consistent with a hereditary enzymopathy that manifests episodically upon exposure to oxidative triggers.
- **Dark urine and fatigue** — hemoglobinuria from intravascular hemolysis and resulting anemia.

Why medication is the trigger:

- **Glipizide was started one week ago**, and symptoms began 3 days ago — a strong temporal association. The FDA label for glipizide explicitly warns: "Treatment of patients with glucose 6-phosphate dehydrogenase (G6PD) deficiency with sulfonylurea agents can lead to hemolytic anemia," and recommends that "a non-sulfonylurea alternative should be considered".[2][3]

- Sulfonylureas (including glibenclamide) are listed as having a **possible association** with hemolysis in G6PD-deficient patients in classic reference tables.[4]

Why not the other options:

- **Food (B)** — The Lebanese restaurant visit was **one month ago**. While fava beans (common in Lebanese cuisine) are a well-known G6PD trigger — and are actually the most common cause of major hemolysis in G6PD-deficient patients in real-world data (71.8% of cases in one large cohort) — favism typically causes hemolysis within **24–48 hours** of ingestion, not a month later.[5]
- **Bacterial infection (A)** — Infections can trigger G6PD hemolysis, but the patient had **no preceding URI or GI symptoms**.
- **Idiopathic (D)** — An identifiable trigger (the new medication) is present, making an idiopathic designation inappropriate.

It is worth noting that real-world evidence has questioned the clinical significance of sulfonylurea-induced hemolysis — a large Israeli cohort study found that glibenclamide and glimepiride were prescribed safely to hundreds of G6PD-deficient patients.[5] Nonetheless, the FDA labeling and the temporal relationship in this case make medication the best answer.

Would you like to review the recommended alternative diabetes medications for patients with known G6PD deficiency, or discuss the workup approach for confirming G6PD deficiency in this patient?

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Question 478

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?

A. Decreased lymphocyte count
B. Increased platelet count
C. Increased prothrombin time
D. Decreased gamma globulin

https://openevidence.com/ask/6817fabc-0aee-48b6-833b-d8fc189e4bbe

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The answer is **A. Decreased lymphocyte count**.

This vignette describes classic **systemic lupus erythematosus (SLE)**: a young woman with fatigue, arthralgias, **malar rash** (erythema with scaling on both cheeks sparing the nasolabial folds), and **oral ulcers** — all of which are EULAR/ACR classification criteria for SLE.[1][2]

Lymphopenia is the most characteristic hematologic finding among the answer choices. Leukopenia in SLE is primarily driven by lymphopenia, affecting approximately **22–42%** of patients.[3] Lymphopenia is included as a specific criterion item in the 2019 EULAR/ACR classification criteria (leukopenia defined as WBC <4 × 10^9/L).[1] The mechanism involves anti-lymphocyte antibodies and complement-mediated lymphocyte destruction.

Why the other options are incorrect:

- **B. Increased platelet count** — SLE causes **thrombocytopenia** (~20% of patients), not thrombocytosis, due to immune-mediated platelet destruction.[3]
- **C. Increased prothrombin time** — While the lupus anticoagulant (an antiphospholipid antibody) prolongs the **aPTT**, it does not typically prolong the PT. Moreover, the lupus anticoagulant is a prothrombotic state, not a bleeding diathesis.
- **D. Decreased gamma globulin** — SLE is characterized by B-cell hyperactivity and polyclonal **hypergammaglobulinemia**, the opposite of what this option suggests.

Would you like to explore the recommended initial laboratory workup for suspected SLE?

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Question 479

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?

A. Increase in capillary pressure
B. Decrease in plasma proteins
C. Increase in capillary permeability
D. Increase in interstitial fluid pressure

https://openevidence.com/ask/e0d2319c-2114-463b-be85-97a065dd3a20

The answer is **A. Increase in capillary pressure**.

This patient presents with classic findings of **congestive heart failure** — dyspnea on exertion, bilateral lower extremity pitting edema, and elevated JVP — in the setting of a prior myocardial infarction causing left ventricular dysfunction with resultant right-sided congestion.

The **primary mechanism** of peripheral edema in heart failure is **elevated capillary hydrostatic pressure**. The failing heart leads to neurohormonal activation and renal salt and water retention, which increases venous pressures throughout the circulatory system and drives efflux of fluid out of the vasculature into the interstitium.[1] Elevated central venous pressure (CVP) directly raises capillary hydrostatic pressure, increasing the rate of fluid filtration into the interstitial space (the "lymphatic load").[1][2] When sustained, lymphatics become overwhelmed, lymph vessels dilate, and lymphatic valves become incompetent — resulting in clinically apparent edema.[1]

Why not the other choices?

- **B (Decreased plasma proteins):** This mechanism underlies edema from nephrotic syndrome, malnutrition, or cirrhosis — conditions that reduce intravascular oncotic pressure. No such condition is suggested here.[3]
- **C (Increased capillary permeability):** This is the mechanism of edema in inflammatory states (e.g., sepsis, burns, anaphylaxis). While chronic heart failure does involve some degree of systemic inflammation and vascular permeability changes, this is a secondary contributor, not the primary mechanism.[2]

- **D (Increased interstitial fluid pressure):** Increased interstitial hydrostatic pressure would actually **oppose** further fluid accumulation per the Starling equation and would not explain edema formation.[4]

Would you like to explore guideline-directed medical therapy for heart failure with reduced ejection fraction in post-MI patients?

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Question 480

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?

A. Pancreatic adenocarcinoma
B. Esophageal varices
C. Porcelain gallbladder
D. Hepatic steatosis

https://openevidence.com/ask/ad3b807c-c9da-4522-a5ee-9fbbfd740802

The answer is **A. Pancreatic adenocarcinoma**. **Cigarette smoking is the leading modifiable risk factor** for pancreatic ductal adenocarcinoma, with a **relative risk of ~1.8** (95% CI 1.7–1.9) for current smokers compared with never smokers.[1] This patient's 25 pack-year smoking history confers a significantly elevated risk. Approximately **20–25% of all pancreatic cancers are attributable to smoking**, and the risk increases with greater intensity and duration of use.[2][3][4]

The other options are not supported by this patient's history:

- **Esophageal varices (B)** result from portal hypertension, most commonly due to cirrhosis. Two to three glasses of wine per week represents light alcohol consumption and does not pose a meaningful risk for cirrhosis or portal hypertension.
- **Porcelain gallbladder (C)** is calcification of the gallbladder wall associated with chronic cholecystitis/gallstones; smoking is not an established risk factor.
- **Hepatic steatosis (D)** is associated with obesity, metabolic syndrome, diabetes, and heavy alcohol use. This patient's modest alcohol intake is well below the threshold for alcohol-associated fatty liver disease.

Notably, the risk of pancreatic cancer associated with smoking persists for at least 10–15 years after cessation, although it does decline over time. After approximately 15–20 years of abstinence, risk approaches that of never smokers.[5][6] This underscores the importance of counseling this patient on smoking cessation as a modifiable cancer risk reduction strategy.

Would you like to explore current screening strategies for pancreatic cancer in high-risk individuals?

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Question 481

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?

A. Adrenalectomy
B. Polychemotherapy and radiation therapy
C. Transsphenoidal hypophysectomy
D. Partial nephrectomy

https://openevidence.com/ask/38b1a0c8-a0b0-4315-870b-7fbcbe59f1a9

The correct answer is **A. Adrenalectomy**.

This patient presents with classic **Cushing syndrome**: central obesity, dorsocervical fat pad (buffalo hump), purple striae, proximal myopathy, hirsutism, oligomenorrhea, hypertension, hyperglycemia, hypokalemia, and metabolic alkalosis. The critical distinguishing lab is the **ACTH of 2 pg/mL**, which is suppressed (normal 7–50 pg/mL), localizing the source of cortisol excess to the **adrenal gland** (ACTH-independent Cushing syndrome).[1][2]

Why ACTH matters here:

- **Suppressed ACTH (<10 pg/mL)** indicates autonomous adrenal cortisol production (adenoma, carcinoma, or bilateral hyperplasia), which suppresses pituitary ACTH via negative feedback.[1][3]
- **Normal or elevated ACTH** would suggest an ACTH-dependent cause — pituitary adenoma (Cushing disease) or ectopic ACTH secretion.[1][2]

Why the other options are incorrect:

- **Transsphenoidal hypophysectomy (C)** is the treatment for **Cushing disease** (pituitary ACTH-secreting adenoma), which would present with normal-to-elevated ACTH.[1][4]
- **Polychemotherapy and radiation (B)** could apply to an ectopic ACTH-secreting malignancy (e.g., small cell lung cancer), which would present with markedly elevated ACTH.[1]
- **Partial nephrectomy (D)** is not relevant to this presentation.

Adrenalectomy is the established first-line treatment for unilateral cortisol-producing adrenal tumors causing Cushing syndrome, with laparoscopic approach preferred for benign-appearing lesions and open surgery recommended when adrenocortical carcinoma is suspected.[1][5][6] Perioperative **glucocorticoid replacement** is required given contralateral adrenal suppression from chronic ACTH suppression.[1][7]

Would you like to explore how to differentiate adrenal adenoma from adrenocortical carcinoma in ACTH-independent Cushing syndrome?

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Question 482

A scientist observes a myocyte beating in cell culture. Which step is the most direct necessary component of relaxation for this cell?

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

https://openevidence.com/ask/6f03fe91-ec5a-48c3-9aca-8f4f5d7b1725

The answer is **D. Efflux of calcium ions**.

Relaxation of a spontaneously beating cardiac myocyte requires removal of calcium from the cytoplasm. A myocyte beating in cell culture is a cardiomyocyte, as these cells contract spontaneously. During contraction, intracellular calcium rises through L-type channel influx and calcium-induced calcium release from the sarcoplasmic reticulum (SR). For relaxation, calcium must be cleared from the cytoplasm via two primary mechanisms:[1][2]

- **SERCA2a** (SR Ca^{2+} -ATPase) pumps calcium back into the SR (~70% of cytoplasmic calcium removal in human cardiomyocytes)[3]
- **Na^{+} /Ca^{2+} exchanger (NCX)** extrudes calcium out of the cell (~28%)[3]

Both of these represent **efflux of calcium ions** from the cytoplasm — the most direct and necessary step for relaxation.[1][4]

Why the other options are incorrect:

- **A (Na^{+} influx)** — Sodium influx drives depolarization, initiating contraction, not relaxation.
- **B (Ca^{2+} influx from the SR)** — Ca^{2+} release from the SR into the cytoplasm via RyR2 channels is the amplification step of contraction, not relaxation.[1][5]
- **C (Ca^{2+} influx from outside)** — Extracellular calcium entry through L-type channels triggers contraction via calcium-induced calcium release.[2][6]

Would you like to explore how phospholamban regulates SERCA2a and its implications for cardiac relaxation?

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Question 483

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?

A. Delayed skeletal maturity
B. Short stature
C. Genu varum
D. Coarse facial features

https://openevidence.com/ask/a017268a-2292-45cf-a4ce-dcdd7f09a9c3

The answer is **B. Short stature**.

This 7-year-old girl with menarche and Tanner stage 3 breast and pubic hair development meets the definition of **central precocious puberty** (CPP) — onset of central puberty before age 8 in girls.[1] The key long-term consequence of untreated CPP is **reduced adult height** due to premature epiphyseal fusion from early estrogen exposure.[2][3]

Although children with CPP are initially tall for their age due to an accelerated growth spurt, sustained sex steroid levels cause **advanced bone maturation and early closure of the growth plates**, resulting in a paradoxically **short adult stature**.[4] In historical series of untreated girls, mean adult heights ranged from **150 to 154 cm**, corresponding to a loss of approximately **12 cm** compared to normal adult height.[3] Height loss is inversely correlated with the age at onset of puberty — the younger the onset, the greater the height compromise.[3][5]

> "Several studies have assessed adult height in people with a history of precocious puberty. 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 the other options are incorrect:

- **A. Delayed skeletal maturity** — The opposite occurs; CPP causes **accelerated** skeletal maturation with advanced bone age.[5]
- **C. Genu varum** — Bowlegs are associated with rickets or Blount disease, not precocious puberty.
- **D. Coarse facial features** — This finding is characteristic of conditions such as mucopolysaccharidoses or acromegaly, not CPP.

Treatment with **GnRH agonists** suppresses the HPG axis, slows bone age advancement, and preserves adult height potential, which is the primary indication for treating CPP.[1][6]

Would you like to explore the recommended diagnostic workup for central precocious puberty, including when brain MRI is indicated?

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Question 484

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?

A. Prednisone and albuterol
B. Albuterol and montelukast
C. Prednisone and tiotropium
D. Albuterol and theophylline

https://openevidence.com/ask/6c5039ca-fe6b-4c35-96bc-c3b9ca61a5eb

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A. Prednisone and albuterol.

This is an acute exacerbation of COPD (chronic productive cough ≥3 years, 60 pack-year smoking history, hyperinflation with flattened diaphragms and increased lucency on radiograph, wheezes, hypoxemia). GOLD recommends **short-acting inhaled beta$_2$-agonists, with or without a short-acting anticholinergic, as the initial bronchodilator** (Evidence C), combined with **systemic corticosteroids** — 40 mg prednisone equivalent daily for 5 days (Evidence A) — which shorten recovery time and improve FEV1 and oxygenation.[1] Adding a short-acting anticholinergic (ipratropium) to albuterol is standard practice and would be an equally acceptable adjunct.[1][2]

Why the other options are wrong

- **B. Albuterol and montelukast** — leukotriene receptor antagonists have no established role in COPD exacerbations; montelukast is an asthma controller medication and provides no acute benefit.
- **C. Prednisone and tiotropium** — tiotropium is a long-acting antimuscarinic for maintenance therapy. GOLD advises continuing or initiating long-acting bronchodilators around the exacerbation, but they are not the initial acute bronchodilator; ipratropium (short-acting) is the anticholinergic used acutely.[1]

- **D. Albuterol and theophylline** — methylxanthines are explicitly **not recommended** because of significant toxicity and a narrow therapeutic index.[1][3]

Additional management points in this case

- **Controlled oxygen therapy** targeting SpO_2 88–92%, with attention to CO_2 retention; obtain a blood gas.[1]
- **Antibiotics** (5 days) if sputum is purulent, there is a prior positive sputum culture, or ventilatory support is required.[1]
- Exclude mimics — pneumonia, pulmonary embolism, heart failure, pneumothorax — particularly given the focal-sounding crackles.[3]
- Consider **oral prednisone rather than IV**, which is equally effective, and note that even short steroid bursts carry risk of hyperglycemia, pneumonia, and sepsis, so use should be limited to significant exacerbations.[1]

Would you like to explore eosinophil-guided corticosteroid therapy in COPD exacerbations?

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Question 485

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?

A. Sulfosalicylic acid test
B. Urine sodium content
C. Fractional excretion of urea (FEUrea)
D. Nitrates in urine

https://openevidence.com/ask/10df1f78-a356-413d-a2ce-e1e6f695d3f0

The answer is **C. Fractional excretion of urea (FEUrea)**.

This patient presents with **acute decompensated heart failure** (orthopnea, JVD, displaced PMI, S4 gallop, pitting edema) in the setting of prior MI with likely ischemic cardiomyopathy. After 6 hours of furosemide therapy, persistent hypotension and a creatinine of 1.9 mg/dL raise concern for **acute kidney injury requiring differentiation between prerenal azotemia and intrinsic renal disease (ATN)**.

The pivotal clinical detail is that the patient is **receiving furosemide**, which blocks the NKCC2 cotransporter in the thick ascending limb, directly increasing urinary sodium excretion.[1] This renders both **urine sodium (option B)** and **FENa unreliable** — they become falsely elevated even in prerenal states, mimicking intrinsic renal disease.[2][3]

FEUrea is preferred in this setting because urea reabsorption occurs primarily through passive forces in the proximal tubule and collecting ducts and is **not significantly influenced by diuretic therapy**.[2][4] In the landmark prospective study by Carvounis et al., among prerenal AKI patients receiving diuretics, only **48% had FENa <1%**, whereas **89% had FEUrea <35%**.[2] FEUrea was

essentially identical between prerenal patients with and without diuretics (24.5% vs. 27.9%), and markedly different from ATN (58.6%).[2] A systematic review and meta-analysis confirmed that in patients on diuretics, FEUrea demonstrated **higher specificity (82% vs. 44%)** compared to FENa for diagnosing intrinsic AKI.[5]

Why the other options are incorrect:

- **A. Sulfosalicylic acid test** — Detects urinary protein including non-albumin proteins (e.g., Bence Jones proteins). Not useful for prerenal vs. intrinsic AKI differentiation.
- **B. Urine sodium** — Falsely elevated by furosemide use, making it unreliable in this clinical scenario.[3][4]
- **D. Nitrates in urine** — Urinary nitrites on dipstick detect nitrate-reducing bacteria (suggestive of UTI). Irrelevant to prerenal vs. intrinsic AKI differentiation.

Here is the FEUrea calculator for reference:

A **FEUrea ≤35%** supports prerenal azotemia, while **>35%** suggests intrinsic renal disease, though values in the indeterminate range should be interpreted alongside urine sediment, clinical trajectory, and response to volume or hemodynamic optimization.[2][6]

Would you like to explore management strategies for cardiorenal syndrome in the setting of acute decompensated heart failure?

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Question 486

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?

A. Janeway lesions
B. Diffuse maculopapular rash
C. Malar rash
D. Erythema nodosum

https://openevidence.com/ask/db880418-cca7-4ed2-a5ff-afde4d96df77

The answer is **B. Diffuse maculopapular rash**.

This presentation is consistent with **drug-induced acute interstitial nephritis (AIN)** from NSAID use (ibuprofen and diclofenac). The supporting findings include:

- **Acute kidney injury** with oliguria (<0.3 mL/kg/h) and elevated creatinine (1.9 mg/dL)
- **Peripheral eosinophilia** (0.9×10^9/L)
- **WBC casts** on urinalysis, indicating interstitial/tubular inflammation
- **Isosthenuria** (urine density 1.010), suggesting impaired tubular concentrating ability
- Systemic symptoms: fever, malaise, nausea, vomiting

The **classic triad** of drug-induced AIN is **fever, skin rash, and eosinophilia**.[1][2] The skin rash is characteristically a **diffuse maculopapular rash**, reflecting a type IV delayed hypersensitivity reaction.[1][3] This patient already demonstrates two components of the triad (fever and eosinophilia), making a maculopapular drug rash the expected cutaneous finding.

Notably, this full triad is seldom present in practice and is even less common with NSAID-induced AIN compared to antibiotic-induced AIN.[1][4] However, among the listed options, a diffuse maculopapular rash is the only skin manifestation associated with AIN.

Why the other options are incorrect:

- **Janeway lesions** — painless erythematous lesions on the palms and soles, characteristic of **infective endocarditis**, not supported by this presentation.
- **Malar rash** — butterfly-distribution facial rash associated with **systemic lupus erythematosus**; no features of SLE are present here.
- **Erythema nodosum** — tender subcutaneous nodules on the shins, associated with **sarcoidosis, inflammatory bowel disease, and infections** such as streptococcal pharyngitis, not with drug-induced AIN.

Would you like to explore the management of drug-induced AIN, including indications and timing for corticosteroid therapy?

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Question 487

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?

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

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The answer is **C. New York Heart Association Class III**.

The NYHA functional classification system categorizes heart failure into **four classes (I–IV)** based on patient-reported functional limitation.[1][2] Notably, **there are no subclasses "IIa" or "IIb"** — these are distractors (options A and B).

This patient's presentation maps to **Class III — marked limitation of physical activity; comfortable at rest, but less than ordinary activity causes symptoms**.[2][3] The key clinical features supporting this classification:

- **Less-than-ordinary activities** (e.g., getting dressed in the morning) now produce symptoms, which goes beyond Class II (symptoms only with ordinary activity).
- She is **comfortable at rest** — sitting down alleviates her symptoms — which distinguishes her from Class IV (symptoms at rest or inability to perform any physical activity without discomfort).[1][2]

Here is the NYHA classification calculator for reference:

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

Worsening NYHA functional class is associated with a **worse prognosis**, and any symptomatic patient (NYHA Class II–IV) should have further optimization of guideline-directed medical therapy.[4]

Would you like to explore guideline-directed medical therapy optimization for NYHA Class III heart failure?

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Question 488

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?

A. Multiple periventricular sclerotic plaques
B. Erythematous papules in the V2/V3 nerve distribution
C. Photophobia and phonophobia
D. Rhinorrhea, lacrimation, and ptosis

https://openevidence.com/ask/03984a31-a8ab-4b58-8ee9-83de263aa310

The answer is **A. Multiple periventricular sclerotic plaques**.

This presentation is classic for **multiple sclerosis (MS) presenting with secondary trigeminal neuralgia (TN)**. Several features distinguish this from classical or idiopathic TN and point strongly toward MS:

- **Young age (36 years)**: Typical TN onset is age 50–60; younger age is significantly associated with secondary TN.[1]
- **Bilateral TN**: Bilateral pain is very frequent in MS-related TN (~14%) but rare in classical TN, making it a strong predictor of MS as the underlying cause.[2][3]
- **Trigeminal sensory deficits (V2/V3 bilaterally)**: Sensory loss is significantly more common in secondary TN than in classical forms.[1][3]
- **Prior transient right arm weakness** lasting about one week: Consistent with a prior demyelinating relapse.

- **Left upper extremity weakness (3/5)** and **lower extremity spasticity with sustained clonus**: These upper motor neuron signs indicate corticospinal tract involvement at a separate CNS location.

The combination of relapsing neurological deficits affecting multiple CNS regions (brainstem/trigeminal pathways, right arm, left arm, bilateral corticospinal tracts) at different time points is highly suggestive of MS, and brain MRI would be expected to reveal characteristic **periventricular demyelinating plaques**.

> "In 15% of patients with typical pain attacks, trigeminal neuralgia is caused by multiple sclerosis or by benign tumors in the cerebellopontine angle. The risk of trigeminal neuralgia is increased by a factor of 20 among patients with multiple sclerosis, as compared with the general population."
>
> —Giorgio Cruccu, M.D. et al., Sapienza University of Rome. Trigeminal Neuralgia. N Engl J Med. August 20, 2020.
>
> Used under license from The New England Journal of Medicine.

MS-related TN is attributed to demyelinating plaques along the intrapontine trigeminal afferents, including at the trigeminal root entry zone.[1][4] MRI with gadolinium is advisable at initial TN diagnosis specifically to rule out MS and cerebellopontine angle masses.[1][5]

Why the other options are incorrect:

- **B (Erythematous papules in V2/V3)**: Would suggest herpes zoster, which does not explain the upper motor neuron signs, relapsing deficits, or bilateral involvement.
- **C (Photophobia and phonophobia)**: Would suggest migraine — the family history of migraines is a distractor, but migraines do not cause focal neurological deficits with spasticity and clonus.
- **D (Rhinorrhea, lacrimation, ptosis)**: Would suggest a trigeminal autonomic cephalalgia (e.g., cluster headache), which does not account for the multifocal neurologic findings.

Would you like to explore first-line pharmacotherapy for MS-related trigeminal neuralgia?

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Question 489

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?

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

https://openevidence.com/ask/bc2fe036-c3af-44d4-8ce1-7852a7abff4a

The answer is **B. Secondary active transporters fail to completely reabsorb glucose in the renal tubules**.

This patient has uncontrolled type 2 diabetes (HbA1c 9%) with evidence of end-organ damage including **diabetic retinopathy** (microaneurysms), **peripheral neuropathy** (loss of vibration sense), and **diabetic nephropathy** (proteinuria). The glucosuria (urine glucose 199 mg/dL) results from the filtered glucose load exceeding the reabsorptive capacity of the **sodium-glucose cotransporters (SGLT2 and SGLT1)** in the proximal tubule.

Why secondary active transport is the correct mechanism:

Glucose reabsorption in the proximal tubule is mediated by **SGLT2** (~90%, S1 segment) and **SGLT1** (~10%, S2/S3 segments), which are **secondary active transporters** — they couple glucose uptake to the sodium gradient generated by the basolateral Na+/K+ ATPase.[1][2] When plasma glucose exceeds the renal threshold (~180–200 mg/dL), the filtered load surpasses the tubular maximum reabsorptive capacity (TmG, ~375 mg/min), saturating these transporters and causing glucose to spill into the urine.[3][4]

Why the other options are incorrect:

- **A (Primary active transport):** The Na+/K+ ATPase is the primary active transporter, but it does not directly transport glucose. SGLT2/SGLT1 use the sodium gradient it creates — making glucose transport **secondary**, not primary.[2][3]
- **C (Passive transport):** Glucose exits tubular cells into blood via **GLUT2** (facilitated diffusion, basolateral side), but apical reabsorption from the tubular lumen is an active, sodium-coupled process, not passive.[2]
- **D (Increased GFR):** While a higher GFR would increase filtered glucose, the fundamental cause of glucosuria in diabetes is **transporter saturation** due to hyperglycemia, not a primary increase in GFR.[1][5]

Would you like to explore the role of SGLT2 inhibitors in managing this patient's diabetic nephropathy?

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Question 490

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?

A. Rotator cuff impingement
B. Adhesive capsulitis
C. Glenohumeral osteoarthritis
D. Subacromial bursitis

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The answer is **B. Adhesive capsulitis**.

The critical exam finding in this vignette is **decreased both passive and active range of motion**, which is the hallmark of adhesive capsulitis (frozen shoulder). This distinguishes it from the other answer choices:[1][2][3]

- **Rotator cuff impingement** and **subacromial bursitis** characteristically limit **active ROM only**; passive ROM is preserved because the examiner can move the joint without requiring the impinged or inflamed structures to generate force.[3]
- **Glenohumeral osteoarthritis** can restrict both passive and active ROM, but it typically presents with crepitus and is confirmed by radiographic joint-space narrowing; it lacks the strong association with diabetes seen here.[4]

The patient's risk factor profile is classic for adhesive capsulitis: **diabetes mellitus** confers a **3.7-fold increased odds** of developing the condition, and additional recognized associations include[5][6] **obesity, sedentary lifestyle, and age between 40 and 65**.[5][7] The pathophysiology involves inflammatory and fibrotic contracture of the glenohumeral joint capsule itself — not the bones, cartilage, tendons, or muscles — resulting in global restriction of motion.[1][7]

The **4/5 strength** is consistent with adhesive capsulitis, where mild weakness results from pain and mechanical restriction rather than true neuromuscular impairment. The clinical presentation of difficulty with overhead activities (combing hair, reaching high shelves) reflects the characteristic limitation in abduction and external rotation.[2][8]

Would you like to explore the management of adhesive capsulitis in diabetic patients, including considerations around corticosteroid injections and glycemic control?

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Question 491

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?

A. Medication side effect
B. Myeloproliferative neoplasm
C. Neuronal hyperexcitability
D. Toxic exposure

https://openevidence.com/ask/caad9d2e-5488-4070-9e7a-df6cde1ec383

D. Toxic exposure — this is subacute/chronic **carbon monoxide poisoning**, almost certainly from a faulty wood stove, furnace, or generator at the winter cabin. The diagnostic thread is that symptoms (headache, dizziness, nausea) abate whenever he leaves the cabin to shovel snow and he is asymptomatic in the office, and the marked erythrocytosis (Hgb 20 g/dL, Hct 60%) is the expected secondary erythropoietic response to chronic carboxyhemoglobinemia.[1][2][3] The SpO_2 of 98% is falsely reassuring: standard pulse oximetry cannot distinguish carboxyhemoglobin from oxyhemoglobin, so **diagnosis requires co-oximetry (blood COHb level)**.[4]

Why CO fits

- Chronic/intermittent CO exposure lasting weeks produces headache, vertigo, fatigue, cognitive complaints, and **polycythemia** — a specifically listed feature of long-term exposure.[1]
- CO binds hemoglobin with far greater affinity than oxygen and left-shifts the dissociation curve; the resulting functional tissue hypoxia drives erythropoiesis. Controlled low-dose CO inhalation raising COHb ~5% increased hemoglobin mass with a rise in reticulocytes and EPO. Smokers' polycythemia and chronic hookah-related carboxyhemoglobinemia are the classic clinical analogues.[3][5][6]
- Occult CO poisoning presents as a flu-like illness in cold weather, unresponsive to analgesics, and is classically source-linked — symptoms resolve away from the dwelling.[7]

Why not the others

- **A. Medication side effect** — none of amlodipine, metformin, glimepiride, or fluticasone/salmeterol cause erythrocytosis. The drug classes that do are SGLT2 inhibitors, testosterone/anabolic steroids, and exogenous EPO.[2][8]
- **B. Myeloproliferative neoplasm** — polycythemia vera would not remit on stepping outdoors. Expected features (pruritus, splenomegaly, leukocytosis/thrombocytosis in ~half, subnormal EPO, JAK2 variant in >95%) are absent here; his WBC and platelets are normal.[9]
- **C. Neuronal hyperexcitability** — migraine or seizure disorder does not explain Hct 60%.

Clinical follow-through

- Obtain **co-oximetry COHb** promptly and start **high-flow 100% oxygen by non-rebreather** rather than waiting on the result; CO half-life is ~5 hours on room air versus ~85 minutes on high-flow oxygen, so a level drawn after hours away from the source can be misleadingly low and does not exclude poisoning.[7]
- **Remove him from the source**: cabin inspection by the fire department/utility, CO detectors, and evaluation of any co-inhabitants.
- Involve poison control/hyperbaric consultation for high-risk features — loss of consciousness, neurologic deficits or persistent cognitive abnormality, cardiac ischemia, metabolic acidosis, pregnancy — rather than relying on current asymptomatic status alone. Screen for cardiac injury and counsel about delayed neuropsychiatric sequelae, which can emerge 2–40 days after exposure.[7][10]

- Do not assume the Hct 60% is fully explained until it corrects. Repeat the CBC after exposure removal; if erythrocytosis persists, pursue serum **EPO and JAK2** testing and consider other secondary causes (OSA, occult tobacco use, altitude).[2][11]

Would you like to explore the indications and thresholds for hyperbaric oxygen therapy in CO poisoning?

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Question 492

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?

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

https://openevidence.com/ask/a6a3a342-e502-48da-a971-e75953d9f288

The correct answer is **B: Intravenous cefotetan and doxycycline with inpatient admission**.

This patient's presentation — **cervical motion tenderness, purulent vaginal discharge, fever, and a tender adnexal mass** — is consistent with **pelvic inflammatory disease (PID) complicated by a probable tubo-ovarian abscess (TOA)**.[1][2] She meets multiple CDC criteria for hospitalization:[3]

- **Tubo-ovarian abscess** (tender adnexal mass)
- **Severe illness with nausea and vomiting** (vomited three times, unlikely to tolerate oral medications)
- **Surgical emergency cannot be excluded** (right lower quadrant tenderness overlapping with appendicitis)

The CDC 2021 STI Treatment Guidelines recommend **parenteral regimens** for inpatient PID, including **cefotetan 2 g IV every 12 hours plus doxycycline 100 mg orally or IV every 12 hours**.[3] For patients with TOA, **>24 hours of inpatient observation** is recommended, with transition to oral therapy (doxycycline plus metronidazole for anaerobic coverage) to complete 14 days of treatment.[3]

Why the other options are incorrect:

- **A (IM ceftriaxone + oral doxycycline, outpatient):** This is the appropriate outpatient regimen for **mild-to-moderate PID without complicating features**. It is inadequate here given the TOA, active vomiting precluding oral intake, and severity of illness.[1][4]
- **C (Oral vancomycin, outpatient):** This treats *Clostridioides difficile* colitis. Although the patient had recent ciprofloxacin use and an episode of diarrhea, the dominant findings (cervical motion tenderness, purulent discharge, adnexal mass, fever) point decisively to PID/TOA.
- **D (Methotrexate, outpatient):** This is used for **ectopic pregnancy**. While the 6-week LMP and adnexal mass warrant an urgent **β-hCG and transvaginal ultrasound** to exclude ectopic pregnancy, the purulent cervical discharge, cervical motion tenderness, and fever strongly favor an infectious etiology over ectopic pregnancy.

Would you like to explore the indications for interventional drainage versus surgery in tubo-ovarian abscess?

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Question 493

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?

A. Antibody to soluble factor
B. Inhibitor of microtubule polymerization
C. Inhibitor of proximal tubule reabsorption
D. Inhibitor of xanthine oxidase

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The answer is **D. Inhibitor of xanthine oxidase**.[1][2]

This vignette describes **podagra** — acute gout of the first MTP joint — in a patient with risk factors including obesity, hypertension, and alcohol use. After resolution of the acute flare, **allopurinol**, a xanthine oxidase inhibitor and the first-line urate-lowering therapy for gout prophylaxis, is the most likely drug prescribed.[3]

The critical clue explaining the **pancytopenia** is the patient's **inflammatory bowel disease (IBD)**. IBD is commonly treated with **azathioprine**, a thiopurine immunomodulator that the patient may be taking among her unrecalled medications. Xanthine oxidase is one of the major pathways for inactivation of azathioprine; when allopurinol inhibits this enzyme, azathioprine metabolism is shunted toward increased production of **6-thioguanine nucleotides**, the active but myelotoxic metabolite, resulting in severe bone marrow suppression.[4][5] The FDA label for azathioprine explicitly warns that concomitant allopurinol use requires dose reduction to **one-third to one-quarter** of the usual azathioprine dose, with close CBC monitoring.[2][4] This is a classic and potentially **life-threatening drug interaction**.[6][7]

Why not the other options:

- **A (Antibody to soluble factor)** — This describes canakinumab (anti-IL-1β), used for refractory gout flares but not standard first-line prophylaxis.
- **B (Inhibitor of microtubule polymerization)** — This describes colchicine, used for acute flares and short-term flare prophylaxis but not for long-term urate lowering. While colchicine can cause cytopenias, the IBD medication interaction makes the xanthine oxidase inhibitor the intended answer.
- **C (Inhibitor of proximal tubule reabsorption)** — This describes probenecid, a uricosuric agent that is not first-line and does not characteristically cause pancytopenia through drug interactions.

Would you like to explore safe co-prescribing strategies for allopurinol and azathioprine, including required dose adjustments?

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Question 494

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?

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

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The correct answer is **B. Thumb spica cast and repeat X-rays in 2 weeks**.

This presentation — **fall on outstretched hand (FOOSH), anatomical snuffbox tenderness, decreased grip strength, and negative initial radiographs** — is the classic scenario for a **clinically suspected occult scaphoid fracture**. Up to **16% of scaphoid fractures are missed on initial X-rays**.[1] Because delayed diagnosis risks **nonunion and avascular necrosis** (given the scaphoid's retrograde blood supply), the standard practice is to **presume a fracture and immobilize** despite normal radiographs.[1][2][3]

Why thumb spica cast (B) over rest and ice alone (C)?

The critical distinction between these two options is **immobilization**. The scaphoid requires rigid immobilization to protect against displacement and to promote healing. Rest and ice alone do not adequately protect the scaphoid, and failure to immobilize a true fracture significantly increases the risk of nonunion and subsequent osteoarthritis.[1][4] At 2 weeks, bone resorption at the fracture site makes the fracture line more visible on repeat radiographs; if repeat films

remain negative but clinical suspicion persists, advanced imaging (MRI or CT) should be pursued. [5][6]

Why not the other options?

- **A. Corticosteroid injections** — Not indicated in acute fracture management; would be considered for inflammatory conditions like de Quervain tenosynovitis (which is excluded here by the negative Finkelstein test).
- **D. Percutaneous pinning** — A surgical intervention reserved for confirmed displaced or unstable fractures, not appropriate when no fracture has been visualized.[2][7]

Would you like to explore the role of early MRI versus CT in diagnosing radiographically occult scaphoid fractures?

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Question 495

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?

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

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The answer is **A. Periductal concentric scarring and fibrosis**.

This presentation is classic for **primary sclerosing cholangitis** **(PSC)**: a middle-aged man with ulcerative colitis, positive pANCA, cholestatic liver biochemistry (elevated alkaline phosphatase, conjugated hyperbilirubinemia), pruritus, and MRCP demonstrating **multifocal intrahepatic bile duct strictures alternating with dilation** (the characteristic "beaded" appearance).[1]

The hallmark histologic finding of PSC is **concentric "onion skin" periductal fibrosis**, where layers of fibrotic tissue surround and progressively obliterate the bile ducts.[1][2][3] While this finding is nearly pathognomonic for PSC, it is actually seen infrequently on needle biopsy (reported in only ~14% of cases), as it predominantly affects medium-sized septal bile ducts that may not be sampled.[4][5] Other compatible histologic features include bile duct loss, ductular reaction, and cholate stasis in periportal hepatocytes.[2][6]

Why the other options are incorrect:

- **B. Periportal lymphocytic infiltration and piecemeal necrosis** — describes **autoimmune hepatitis** (lymphoplasmacytic interface hepatitis), not PSC.

- **C. Irregular ductal glands lined by atypical and pleomorphic cells** — describes **cholangiocarcinoma**, a complication of PSC but not the expected biopsy finding here.
- **D. Ductopenia and fibrotic degeneration of periportal hepatocytes** — more consistent with **primary biliary cholangitis (PBC)**, which is associated with antimitochondrial antibodies and destruction of small interlobular bile ducts, not the large-duct pattern seen on MRCP here.

Over **70% of patients with PSC have concomitant IBD**, most commonly ulcerative colitis, making the clinical association in this vignette strongly supportive of the diagnosis.[1][2]

Would you like to explore the cholangiocarcinoma surveillance strategy in PSC?

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Question 496

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?

A. Diazepam
B. Ramelteon
C. Buspirone
D. Alprazolam

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The correct answer is **C. Buspirone**.[1][2]

This patient's presentation — **excessive, uncontrollable worry about daily tasks, restlessness, insomnia, muscle tension, and autonomic symptoms persisting for over 6 months** — is consistent with **generalized anxiety disorder (GAD)**. Among the listed options, buspirone is the best choice for several reasons:

Why buspirone: Buspirone is a **5-HT1A partial agonist FDA-approved for GAD** with demonstrated efficacy in randomized trials.[1] Critically, it carries **no abuse or dependence potential**, making it appropriate in a patient with a history of prior illicit drug use (cocaine and heroin). It is also listed by the **AGS Beers Criteria** as a recommended alternative for anxiety in older adults.[3]

Why not benzodiazepines (diazepam or alprazolam): Both diazepam (A) and alprazolam (D) are effective anxiolytics but carry significant risks of **misuse and dependence**.[2] Expert guidelines recommend benzodiazepines only in patients without current or past substance use history.[4] Additionally, the **AGS Beers Criteria explicitly recommends avoiding benzodiazepines in older**

adults due to increased risks of falls, cognitive impairment, and dependence.[3] At age 67 — particularly with symptoms of near-syncope — benzodiazepines pose additional safety concerns.

Why not ramelteon: Ramelteon (B) is a **melatonin receptor agonist FDA-approved exclusively for insomnia** characterized by difficulty with sleep onset.[5] While this patient has sleep disturbance, the primary disorder is GAD; treating the underlying anxiety is the appropriate approach rather than targeting insomnia alone.

Would you like to explore first-line pharmacotherapy and dosing for GAD in older adults?

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Question 497

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?

A. Normal anion gap metabolic acidosis
B. Hyperkalemia
C. Hyperglycemia
D. Hyponatremia

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The answer is **D. Hyponatremia**.

This patient is experiencing an **adrenal crisis due to glucocorticoid-induced adrenal insufficiency** precipitated by surgical stress. Chronic prednisolone use suppressed her hypothalamic-pituitary-adrenal (HPA) axis, as confirmed by **both low cortisol and low ACTH**.[1] The surgical stress of cholecystectomy demanded an increase in cortisol that her suppressed adrenal glands could not mount, resulting in hemodynamic collapse.[2][3]

The key to distinguishing the expected electrolyte findings lies in the **intact mineralocorticoid axis** in secondary/glucocorticoid-induced adrenal insufficiency. Aldosterone secretion is primarily regulated by the renin-angiotensin-aldosterone system, not ACTH, and is therefore **preserved**:[1][4]

- **Hyponatremia (correct)** — Occurs in both primary and secondary adrenal insufficiency, but through different mechanisms. In secondary adrenal insufficiency, cortisol deficiency removes the normal inhibition of pituitary vasopressin (ADH) release, leading to **increased vasopressin secretion, impaired free water excretion, and dilutional hyponatremia**.[5][6]
- **Hyperkalemia (B) — not expected** — Hyperkalemia is a feature of **primary** adrenal insufficiency (Addison disease) where aldosterone is deficient. Because aldosterone is preserved in secondary adrenal insufficiency, potassium handling remains intact.[4][5][7]

- **Normal anion gap metabolic acidosis (A) — not expected** — This results from impaired renal hydrogen ion excretion due to aldosterone deficiency (type 4 RTA), again a feature of primary, not secondary, adrenal insufficiency.[5]
- **Hyperglycemia (C) — not expected** — Cortisol is a counter-regulatory hormone that raises blood glucose. Its deficiency leads to **hypoglycemia**, not hyperglycemia.[2][8]

  "Although hyponatremia occurs in both primary and secondary adrenal insufficiency, its pathophysiology in the two disorders differs. In primary adrenal insufficiency it is mainly due to aldosterone deficiency and sodium wasting, whereas in secondary adrenal insufficiency it is due to cortisol deficiency, increased vasopressin secretion, and water retention."

  —Wolfgang Oelkers, M.D., Freie Universität Berlin. Adrenal Insufficiency. N Engl J Med. October 17, 1996.

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Would you like to explore perioperative stress-dose glucocorticoid protocols for patients with adrenal insufficiency?

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Question 498

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?

A. Atrophy of G cells
B. Anti-intrinsic factor antibodies
C. Decreased methylmalonic acid levels
D. Antithrombotic state

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The answer is **B. Anti-intrinsic factor antibodies**.

This presentation is classic **pernicious anemia**: megaloblastic anemia (hematocrit 29%, **hypersegmented neutrophils** with 7 lobes, **macro-ovalocytes**), **glossitis** (sore tongue), and **subacute combined degeneration** of the spinal cord (decreased position sense and loss of vibratory sensation from posterior column involvement). The history of **Hashimoto's thyroiditis** further supports this diagnosis, as pernicious anemia is well known to cluster with autoimmune thyroiditis as part of polyglandular autoimmune syndromes.[1][2]

Anti-intrinsic factor antibodies are **>95% specific** for pernicious anemia and are nearly diagnostic of the condition.[2][3][4] They block intrinsic factor from binding vitamin B12, impairing intestinal B12 absorption and leading to the clinical syndrome described.

Why the other options are incorrect:

- **A. Atrophy of G cells** — In pernicious anemia, **parietal cells** (not G cells) are destroyed by autoimmune attack. G cells in the gastric antrum actually undergo **hyperplasia** due to loss of acid-mediated negative feedback, resulting in elevated serum gastrin levels.[5]
- **C. Decreased methylmalonic acid levels** — MMA is **increased**, not decreased, in B12 deficiency. B12 is a cofactor for methylmalonyl-CoA mutase; without it, methylmalonyl-CoA cannot be converted to succinyl-CoA, causing MMA accumulation. Elevated MMA is in fact a specific diagnostic marker for B12 deficiency.[3][6][7]

- **D. Antithrombotic state** — B12 deficiency causes **elevated homocysteine** (because B12 is also a cofactor for methionine synthase), which is associated with a **prothrombotic**, not antithrombotic, state.[3][7]

Would you like to explore the treatment regimens and monitoring approach for pernicious anemia?

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Question 499

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?

A. Precontemplation
B. Contemplation
C. Maintenance
D. Relapse

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The correct answer is **D. Relapse**.

In the **Transtheoretical Model (TTM)** of behavioral change, this patient had successfully quit smoking for 1 year — placing him in the **maintenance stage** (abstinence sustained >6 months).[1][2] However, he has now resumed smoking, which represents **relapse**, defined as movement backward through the stages after previously achieving action or maintenance.[3][4]

The five core stages of the TTM are:[1][2]

- **Precontemplation** — No intention to change behavior; often unaware of the problem.
- **Contemplation** — Aware of the problem and intending to change within 6 months, but not yet committed to action.
- **Preparation** — Intending to take action within the next month, with early behavioral steps.
- **Action** — Active behavior modification for less than 6 months.

- **Maintenance** — Sustained behavior change for more than 6 months, working to prevent relapse.

Relapse is not always listed as a formal sixth stage but is a well-recognized component of the model, describing the return to a prior unhealthy behavior after a period of successful change.[3] Progression through the stages is not necessarily linear, and cycling through relapse is common — particularly with tobacco addiction, where relapses can occur even after prolonged abstinence.[5]

This patient's 65-pack-year smoking history, COPD exacerbation with hypoxemia (SpO2 87%), bilateral rales, and altered mental status underscore the clinical consequences of his relapse and the importance of re-engaging cessation strategies tailored to his current stage.[6]

Would you like to explore evidence-based strategies for managing smoking cessation after relapse?

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Question 500

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?

A. Displacement
B. Dissociation
C. Projection
D. Repression

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The answer is **C. Projection**.

Projection is the defense mechanism in which an individual **attributes their own unacceptable thoughts, feelings, or impulses to another person**.[1][2] In this vignette, the man is the one flirting with co-workers and questioning his commitment — yet he accuses his wife of flirtatious behavior and infidelity. He externalizes his own unacceptable desires onto her, thereby avoiding the guilt and shame of acknowledging them as his own.

Projection involves at least three cognitive steps: differentiating internal from external experience, comparing a thought or feeling with internal standards of acceptability, and then attributing that unacceptable thought to an external source.[1] By accusing his wife of the very behavior he is engaging in, the man avoids responsibility for his own impulses.[2][3]

The other options differ in important ways:

- **Displacement** involves redirecting an emotion (typically toward a less threatening target) but the feeling is still recognized as one's own. A classic example is expressing anger at a safe target rather than the original source.[3]
- **Dissociation** involves a disconnection from one's thoughts, feelings, identity, or surroundings — not an attribution of one's feelings to someone else.

- **Repression** involves unconsciously blocking unacceptable thoughts or impulses from awareness entirely, rather than attributing them outward. In this scenario, the man's desires are clearly expressed (through flirting), not suppressed from consciousness.[4][5]

Would you like to explore the distinction between projection and projective identification?

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Question 501

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?

A. Dilatation and evacuation (D&E)
B. Oxytocin-induced labor
C. Manual uterine aspiration
D. Oral mifepristone + misoprostol

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The correct answer is **D. Oral mifepristone + misoprostol**.

Gestational age estimation: The patient missed her period 4 weeks ago, and with regular 28–35 day cycles, her gestational age (counted from the last menstrual period) is approximately **8–9 weeks at initial presentation and 9–10 weeks (63–70 days) when she returns 1 week later**. This places her within the **FDA-approved window for medication abortion (up to 70 days / 10 weeks)**.[1]

The recommended regimen is **mifepristone 200 mg orally followed by misoprostol 800 mcg buccally 24–48 hours later**.[2][3] This approach has an overall **success rate of 95–97%** with a major complication rate of **<0.5%**.[4][5] ACOG and the Society of Family Planning endorse combined mifepristone–misoprostol as the **preferred regimen** for medication abortion because it is significantly more effective than misoprostol-only regimens.[1]

Why the other options are incorrect:

- **A. Dilatation and evacuation (D&E)** — Reserved for **second-trimester** terminations (typically >13–14 weeks gestation); it is not indicated at this early gestational age.

- **B. Oxytocin-induced labor** — Used for later gestational ages. Guidelines explicitly recommend **against oxytocin-based regimens** unless mifepristone/misoprostol is unavailable or contraindicated.[6]
- **C. Manual uterine aspiration** — This is a valid first-trimester surgical option with slightly higher complete abortion rates (~97%). However, at ≤10 weeks gestation in an uncomplicated patient requesting elective termination, **medication abortion is the preferred noninvasive approach** and is the most appropriate initial choice, avoiding the procedural risks, anesthesia, and instrumentation associated with aspiration.[1][7][8]

Would you like to explore the contraindications and special considerations for medication abortion with mifepristone and misoprostol?

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Question 502

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?

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

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The answer is **C. Increased residual volume and decreased 1 second forced expiratory volume**.

This patient presents with classic findings of **COPD/emphysema**: a heavy smoking history (55 pack-years), progressive exertional dyspnea, pursed-lip breathing, decreased breath sounds, barrel chest (increased AP diameter), and hyperresonance to percussion — all hallmarks of hyperinflation and air trapping.

Decreased FEV1 is the defining physiologic abnormality in COPD, resulting from increased airway resistance due to small airway narrowing, inflammation, and loss of elastic recoil.[1][2] The 2026 GOLD Report states that patients with COPD "typically show a decrease in both FEV1 (due to airflow obstruction)".[2]

Increased residual volume reflects gas trapping, one of the earliest and most characteristic pathophysiologic features of the disease. As the GOLD guidelines note:

The ERS/ATS Technical Standard similarly identifies an **increase in RV or RV/TLC** as one of the earliest manifestations of small airway disease, driven by premature airway closure and air trapping.[3]

The other answer choices are incorrect because they include a decreased or normal residual volume, which would be inconsistent with the obstructive physiology and air trapping seen in emphysema.

Would you like to explore the GOLD criteria for classifying COPD severity?

References

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Question 503

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?

A. Congestive heart failure
B. Liver cirrhosis
C. Lymphoma
D. Nephrotic syndrome

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The answer is **C. Lymphoma**.

This patient's pleural fluid meets **Light's criteria for an exudative effusion**:[1][2]

- **Pleural fluid protein/serum protein ratio = 5.8/7.0 = 0.83**, which exceeds the 0.5 threshold
- **Pleural fluid LDH = 258 U/L**, which exceeds the 200 U/L threshold

Meeting even one of these criteria classifies the effusion as exudative.[1][3]

Why lymphoma is correct:

Lymphoma is a well-established cause of **exudative** pleural effusions, classified under neoplastic etiologies alongside lung cancer, breast cancer, and mesothelioma.[1] The patient's constitutional symptoms — progressive dyspnea, fatigue, and headaches — are also consistent with a lymphoproliferative disorder.

Why the other options are incorrect:

All three alternatives — **congestive heart failure, liver cirrhosis, and nephrotic syndrome** — are classic causes of **transudative** effusions, driven by hydrostatic or oncotic pressure imbalances rather than pleural inflammation or invasion.[1][2] A transudate would be expected to have a protein ratio ≤0.5 and LDH ≤200 U/L, which does not match this patient's fluid analysis.

Would you like to explore the recommended diagnostic workup for a suspected malignant pleural effusion?

References

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Question 504

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?

A. Alpha-adrenergic antagonism
B. Beta-adrenergic antagonism
C. Relative lipophobicity
D. Serotonergic antagonism

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The answer is **C. Relative lipophobicity**.

Fexofenadine, a second-generation H1-antihistamine, is **non-sedating because it poorly penetrates the blood-brain barrier (BBB)** due to its lipophobic chemical properties. As described in a key NEJM review:

> "Second-generation H1-antihistamines are specific for H1-receptors and penetrate the central nervous system poorly, owing to their lipophobicity and affinity for P-glycoprotein that is expressed on vascular endothelial cells in the central nervous system. Their propensity to occupy central nervous system H1-receptors varies from none for fexofenadine to 30 percent for cetirizine."
>
> —F. Estelle R. Simons, M.D., University of Manitoba. Advances in H1-Antihistamines. N Engl J Med. November 18, 2004.

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In contrast, first-generation antihistamines like **diphenhydramine are highly lipophilic**, have relatively low molecular weight, and are not recognized by the P-glycoprotein (P-gp) efflux pump, allowing them to freely cross the BBB and occupy 50–90% of central H1-receptors, causing sedation.[1] PET studies confirm that fexofenadine achieves essentially **0% brain H1-receptor occupancy** (−8.0% to −0.1%), compared to 56.4% for diphenhydramine 30 mg.[2]

Two complementary mechanisms explain fexofenadine's lack of CNS penetration:

- **Lipophobicity** — Second-generation antihistamines are large, lipophobic molecules with charged side chains and high albumin binding, making passive diffusion across the BBB difficult.[3]
- **P-glycoprotein efflux** — Fexofenadine is a substrate for the P-gp efflux pump at the BBB, which actively transports it back out of the CNS.[4]

Why the other choices are incorrect:

- **A (Alpha-adrenergic antagonism)** and **D (Serotonergic antagonism)** are off-target effects of some first-generation antihistamines that contribute to their side-effect profiles, not mechanisms that reduce sedation.[3]
- **B (Beta-adrenergic antagonism)** is not a relevant pharmacologic property of either antihistamine class.

Would you like to explore the optimal management of allergic rhinitis in patients with comorbid asthma, as in this case?

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Question 505

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?

A. Pneumothorax
B. Pleural effusion
C. Systemic inflammatory response syndrome
D. Bronchioalveolar carcinoma

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The answer is **B. Pleural effusion**. **Pleural effusion is the most common clinical finding** in malignant pleural mesothelioma, present in approximately **60% of patients at diagnosis** and seen on CT in up to **74% of cases**.[1][2] The NCCN algorithm for pleural mesothelioma begins with the clinical presentation of **recurrent pleural effusion and/or pleural thickening**.[3]

This patient's history of **naval shipyard work** during his twenties is classic for occupational asbestos exposure, the primary risk factor for mesothelioma (latency typically 20–40 years).[4][5] His presenting symptoms of **chest pain and exertional dyspnea** align with the two most common symptoms, each occurring in ~60% of patients — breathlessness caused by the effusion and chest pain from chest wall invasion.[1]

> "The most common presenting symptoms at diagnosis include breathlessness caused by a pleural effusion or tumor encasement of the lung and the more sinister chest pain due to direct invasion into the chest wall or mediastinum."
>
> —Sam M. Janes, M.D., Ph.D. et al., University College London and other institutions. Perspectives on the Treatment of Malignant Pleural Mesothelioma. N Engl J Med. September 23, 2021.
>
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The other answer choices are not characteristic findings of mesothelioma:

- **A. Pneumothorax** — not a typical association with mesothelioma.

- **C. Systemic inflammatory response syndrome** — not a recognized presenting feature.
- **D. Bronchoalveolar carcinoma** — while asbestos exposure does increase lung cancer risk, a concurrent second primary malignancy would not be "most likely" present.

Would you like to explore the current first-line treatment options for malignant pleural mesothelioma?

References

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Question 506

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?

A. Endoscopic sclerotherapy
B. Metoprolol
C. Nadolol
D. Repeat endoscopy

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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** requiring primary prophylaxis, and **nonselective beta-blockers (NSBBs)** are the recommended first-line therapy in this setting.[1][2][3]

The AASLD, EASL, Baveno consensus, and UK guidelines all recommend NSBBs (e.g., **nadolol, propranolol, or carvedilol**) for patients with small varices that have red wale marks or in patients with Child-Pugh B/C cirrhosis.[1][2][4] The AASLD Practice Guidance specifically notes that when high-risk varices are small, **NSBB administration is the only technically feasible method** of prophylaxis, as endoscopic variceal ligation (EVL) is difficult to perform on small varices.[2]

> "In patients with small varices that are associated with a high risk of hemorrhage (varices with red wale marks or varices in a patient with Child class B or C disease), nonselective beta-blockers are recommended."
>
> —Guadalupe Garcia-Tsao, M.D. et al., Yale University School of Medicine and other institutions. Management of Varices and Variceal Hemorrhage in Cirrhosis. N Engl J Med. March 04, 2010.

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Why the other options are incorrect:

- **A. Endoscopic sclerotherapy** — Has **no role in primary prophylaxis** of variceal bleeding per AASLD guidelines.[1]
- **B. Metoprolol** — This is a **cardioselective (beta-1 selective)** beta-blocker. Only **nonselective** beta-blockers reduce portal pressure through both decreased cardiac output (beta-1) and splanchnic vasoconstriction (beta-2 blockade). Metoprolol lacks the beta-2 blockade essential for reducing portal inflow.[5][6]
- **D. Repeat endoscopy** — Would be inappropriate here because the high-risk features have already been identified. Surveillance endoscopy without intervention would delay necessary prophylaxis.

Nadolol is typically initiated at **20–40 mg/day** and titrated to a resting heart rate of approximately **55–60 bpm**, with monitoring for contraindications such as bronchospasm, symptomatic hypotension, or heart block.[6][7]

Would you like to explore how carvedilol compares to traditional NSBBs like propranolol and nadolol for variceal bleeding prophylaxis?

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Question 507

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?

A. Levothyroxine therapy during pregnancy
B. Dietary restriction of phenylalanine
C. Daily allopurinol intake
D. Avoidance of fasting states

https://openevidence.com/ask/b2452881-c4d2-42d5-b1fe-45b7987e56be

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B. Dietary restriction of phenylalanine. This is untreated classic phenylketonuria (PAH deficiency), missed because the boy was born at home in Romania with no newborn screening. Every feature fits: **seizure, developmental delay, eczema, hypopigmentation (pale skin, blue eyes), and a musty/mouse-like body odor** from excreted phenylalanine metabolites.[1][2][3] Initiating a low-phenylalanine diet in the neonatal period — before irreversible brain injury accrues — is the intervention that would have prevented these manifestations.[4]

Why the findings point to PKU

- **Musty odor** reflects excretion of phenylalanine and its metabolites (phenylpyruvate, phenyllactate, phenylacetate).[3][5]
- **Hypopigmentation** results from tyrosinase inhibition by high phenylalanine plus low blood tyrosine, limiting melanin synthesis.[3][6]
- **Neurologic phenotype**: infants appear normal for the first few months, then develop progressive encephalopathy with intellectual disability, seizures, microcephaly, and behavioral/autistic features such as poor eye contact.[2][7]
- **Eczema** is a recognized feature of untreated disease.[8][9]

Why dietary restriction is preventive rather than therapeutic here

Restriction of natural protein with phenylalanine-free amino acid supplementation, started within the first weeks of life, prevents or substantially reduces learning disability; cohort data indicate benefit when initiated within the first ~20 days.[4] Once persistent severe hyperphenylalaninemia has caused neurocognitive impairment, treatment may improve behavior and motor findings but **does not reverse the intellectual disability**.[3] Classic PKU requires roughly 200–500 mg/day of phenylalanine, adjusted to plasma levels.[9]

Why the other options are wrong

- **A. Levothyroxine in pregnancy** — congenital hypothyroidism causes developmental delay but presents with macroglossia, umbilical hernia, hypotonia, constipation, and prolonged jaundice, not musty odor or hypopigmentation with eczema. Maternal levothyroxine would not treat fetal thyroid dysgenesis.
- **C. Allopurinol** — used in Lesch-Nyhan for hyperuricemia; that disorder features self-mutilation, dystonia/choreoathetosis, and gout, and allopurinol does not prevent the neurologic phenotype.
- **D. Avoidance of fasting** — the strategy for fatty acid oxidation defects (e.g., MCAD deficiency), which present with hypoketotic hypoglycemia, vomiting, and lethargy during intercurrent illness or fasting, without odor of this type or hypopigmentation.

Practical next steps in this child

Send plasma amino acids (quantitative phenylalanine and tyrosine) and urine organic acids; classic PKU is defined by phenylalanine >1200 μmol/L on normal protein intake.[2] Also test for BH4 (tetrahydrobiopterin) cofactor defects, which account for ~2% of hyperphenylalaninemia and are not corrected by diet alone.[2] Refer urgently to metabolic genetics and a metabolic dietitian, evaluate the seizure, and screen the older sibling — maternal PKU should also be considered in the mother's future pregnancies.

Would you like to explore how BH4 cofactor defects are distinguished from classic PAH deficiency in newly detected hyperphenylalaninemia?

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Question 508

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?

A. Osteosarcoma
B. Osteochondroma
C. Ewing sarcoma
D. Osteoid osteoma

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The answer is **C. Ewing sarcoma**. This presentation is classic, with every feature pointing to this diagnosis:

- **Age and sex**: Ewing sarcoma predominantly affects children and young adults, with a peak incidence around age 15 and a slight male predilection.[1]
- **Diaphyseal location**: Ewing sarcoma has a predilection for the **diaphysis (shaft)** of long bones, whereas osteosarcoma favors the metaphysis.[2][3]
- **X-ray findings**: Multiple **lytic ("moth-eaten") lesions** with **several layers of new bone** (the classic **"onion peel" lamellated periosteal reaction**) are hallmark radiographic features of Ewing sarcoma. Osteosarcoma, in contrast, more typically produces a "sunburst" or "hair-on-end" spiculated periosteal reaction with osteoid matrix.[1][4]
- **Biopsy showing small round blue cells**: Histologically, Ewing sarcoma reveals sheets of **small, round, blue cells** with a prominent nucleus and scant cytoplasm. Osteosarcoma is distinguished by malignant mesenchymal cells producing osteoid.[1][2][5]

- **Systemic findings**: The elevated **WBC (21,000)** and **ESR (68)** are consistent with Ewing sarcoma, which can present with fever and elevated inflammatory markers mimicking infection.[1][6]

The other options are incorrect:

- **Osteosarcoma (A)**: Metaphyseal, produces osteoid on biopsy, and has spiculated (not lamellated) periosteal reaction.
- **Osteochondroma (B)**: A benign cartilage-capped bony exostosis; does not cause lytic lesions or small round blue cells.
- **Osteoid osteoma (D)**: A small benign tumor (<2 cm) that classically **responds to NSAIDs** (particularly at night), features a characteristic nidus on imaging, and does not produce lytic destruction or periosteal layering.

Would you like to explore the current treatment approach for localized Ewing sarcoma?

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Question 509

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?

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.

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The answer is **D**.[1] **Suppression** is a **mature defense mechanism** classified at the highest adaptive level, defined as **intentionally avoiding thinking about disturbing problems, wishes, feelings, or experiences**.[1] It is the **conscious** counterpart of repression.[2] The patient in option D demonstrates this precisely: he acknowledges awareness of the stressor (pending colonoscopy results) but **deliberately chose** not to dwell on it, reasoning that worrying would not be productive. The distressing content remains accessible to consciousness — it is the **postponement of attending to it** that characterizes suppression.[1]

The other options illustrate different mechanisms:

- **A — Sublimation (or altruism):** Channeling anxiety about cancer into volunteering for the Cancer Society redirects distressing impulses into a socially valued activity. Altruism involves gaining vicarious gratification from giving others what one would like to receive. Both are mature defenses but distinct from suppression.[1][3]
- **B — Idealization (with denial):** Attributing exaggerated curative powers to the physician ("I just know you've cured my cancer") and dismissing the need for ongoing surveillance reflects **idealization** of the physician and **denial** of ongoing risk — a narcissistic-level and disavowal-level defense, respectively.[1][3]

- **C — Passive aggression:** Arriving late and failing to complete requested labs represents indirect expression of resistance or hostility toward the medical process, an action-level (immature) defense.[1]

Would you like to explore the recommended post-surgical surveillance schedule for this patient's stage I colon cancer?

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Question 510

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?

A. Diabetic ketoacidosis
B. Diuretic overdose
C. Hyperventilation
D. Opioid overdose

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The answer is **D. Opioid overdose**.

This presentation is the **classic opioid toxidrome**: unresponsiveness, **miosis** (constricted pupils), and **respiratory depression** (respiratory rate of 7/min with shallow breathing).[1][2] The ABG demonstrates an **acute respiratory acidosis** — elevated PCO2 (70 mmHg) with a near-normal bicarbonate (26 mEq/L) — indicating acute hypoventilation without renal compensation, consistent with an acute central nervous system depressant effect on respiratory drive.[3][4]

> "A respiratory rate of 12 breaths per minute or less in a patient who is not in physiologic sleep strongly suggests acute opioid intoxication, particularly when accompanied by miosis or stupor."
>
> —Edward W. Boyer, M.D., Ph.D., University of Massachusetts Medical Center. Management of Opioid Analgesic Overdose. N Engl J Med. July 12, 2012.
>
> Used under license from The New England Journal of Medicine.

Why the other options are incorrect:

- **A. Diabetic ketoacidosis** — DKA produces a **metabolic acidosis** with low bicarbonate and an elevated anion gap. Respiratory compensation would drive PCO2 down (Kussmaul respirations), not up. The ABG here shows the opposite pattern.
- **B. Diuretic overdose** — Diuretics (especially loop and thiazide) typically cause a **metabolic alkalosis** (contraction alkalosis with elevated bicarbonate and pH), not respiratory acidosis. They also would not explain miosis, coma, or respiratory depression.
- **C. Hyperventilation** — Hyperventilation produces a **respiratory alkalosis** (low PCO2, elevated pH), the direct opposite of the ABG findings here (PCO2 of 70 mmHg with acidemia).

The combination of **stupor, miotic pupils, respiratory depression, and acute hypercapnic respiratory acidosis** in a patient found unresponsive without obtainable history is highly characteristic of opioid overdose.[1][5] Immediate management priorities include securing ventilation/oxygenation and administering **naloxone**.[6]

Would you like to explore naloxone dosing strategies and administration routes for opioid overdose reversal?

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Question 511

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?

A. Decrease medication dosage
B. Reassurance
C. Ocular examination under anesthesia
D. Slit-lamp examination

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D. Slit-lamp examination. The best first step is a complete, non-invasive ophthalmic evaluation beginning with slit-lamp biomicroscopy (followed by dilated fundoscopy with a fundus lens), because chronic phenothiazine (low-potency typical antipsychotic) therapy is a recognized cause of insidious, painless visual decline — corneal and anterior lens pigmentary deposits with chlorpromazine, and pigmentary retinopathy with impaired night vision with thioridazine.[1][2][3]

Why slit lamp fits this presentation

- **Chlorpromazine ocular changes** occur in patients treated usually ≥2 years at ≥300 mg/day and consist of fine particulate deposits in the lens and cornea, with star-shaped anterior lens opacities in advanced cases; some patients have visual impairment, and epithelial keratopathy and pigmentary retinopathy have also been reported. The label explicitly advises periodic ocular examinations for long-term patients on moderate-to-high doses.[1][4]
- **Thioridazine pigmentary retinopathy** — seen primarily above recommended doses — produces diminished acuity, brownish discoloration of vision, and **impaired night vision**, with pigment deposits on fundus examination. This is the option that best explains difficulty with night driving, and it can be irreversible with photoreceptor outer-segment and RPE loss.[2][5]

- Reported cases of gradual-onset blurred vision on long-term chlorpromazine were diagnosed at the slit lamp, showing creamy-white or yellowish deposits on the corneal endothelium/Descemet membrane and anterior lens capsule.[6][7]

Why the other options are inferior

- **A. Decrease medication dosage** — premature. The offending agent, dose, and the actual ocular finding are not yet established, and empirically altering a well-controlled regimen risks psychotic relapse. That said, if examination does demonstrate retinal toxicity, coordinate promptly with psychiatry rather than waiting for exhaustive confirmatory testing, since injury may be irreversible or progress after withdrawal. Corneal/lens deposits appear largely irreversible in one long-term series, while the chlorpromazine label notes lesions may regress after withdrawal.[1][2][5][8]
- **B. Reassurance** — unsafe with 6 months of progressive deterioration; phenothiazine retinopathy is vision-threatening and patients with psychiatric illness often under-report symptoms, which is why screening is advocated.[9][10]
- **C. Examination under anesthesia** — reserved for children or uncooperative patients; this patient is cooperative and compliant.

What follows the initial exam

- Dilated fundus examination for nummular hypopigmented/choroidal atrophic lesions of phenothiazine retinopathy.[5]
- Color vision, visual fields, and, if retinopathy is suspected, OCT, fundus autofluorescence, and ERG.
- Review cumulative dose and duration — retinal effects track with total drug exposure over time; annual slit-lamp screening has been recommended for patients on long-term thioridazine or chlorpromazine.[3][11]
- Keep the differential open: age-related or other cataract, anticholinergic/mydriasis-related angle narrowing with low-potency agents, and non-drug retinal dystrophy.[3]

Would you like to explore the recommended ophthalmologic screening schedule for patients on long-term phenothiazines?

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Question 512

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?

A. Hypothyroidism
B. Folate deficiency
C. Vitamin B12 deficiency
D. Parvovirus infection

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The answer is **C. Vitamin B12 deficiency**.

This patient presents with the hallmarks of **severe vitamin B12 (cobalamin) deficiency**: megaloblastic anemia (Hb 6.1 g/dL, MCV 109 fL), **pancytopenia** (low platelets, WBC 3,000), a **low reticulocyte count** (0.8%), **hypersegmented neutrophils** on peripheral smear, and prominent **neuropsychiatric symptoms** (behavioral changes, paranoia, delusions, wide-based ataxic gait).[1][2][3] His **vegetarian diet** is a major risk factor, as vitamin B12 is found only in animal-source foods.[4][5] Studies show 7% of vegetarians and 52% of vegans have B12 deficiency.[1]

Why negative anti-intrinsic factor antibodies do not exclude B12 deficiency

The negative anti-intrinsic factor antibodies are a key distractor. These antibodies are highly specific for **pernicious anemia** but have only about **60–70% sensitivity** — meaning they are negative in 30–40% of patients with pernicious anemia.[3][6][7] More critically, pernicious anemia is only one cause of B12 deficiency. In this vegetarian patient, **dietary insufficiency** is the most likely etiology, and anti-IF antibodies would not be expected to be positive.[4][8]

Why neuropsychiatric symptoms distinguish B12 from folate deficiency

Both B12 and folate deficiency produce identical hematologic findings (megaloblastic anemia, hypersegmented neutrophils, pancytopenia). However, **B12 deficiency characteristically causes neuropsychiatric disease** — including psychosis ("megaloblastic madness"), personality changes, paranoia, ataxia, and subacute combined degeneration of the cord — whereas folate deficiency does so far less frequently.[2][9][10][11] This patient's prominent psychiatric and gait abnormalities strongly favor B12 over folate. Additionally, vegetarian diets are typically **rich in folate** from leafy greens and legumes, making folate deficiency less likely in this context.

Why not the other options

- **A. Hypothyroidism** — Can cause macrocytic anemia but does not produce hypersegmented neutrophils, pancytopenia, or this neuropsychiatric constellation.
- **B. Folate deficiency** — Produces identical hematologic findings but rarely causes the degree of neuropsychiatric involvement seen here. Vegetarians generally have adequate folate intake.
- **D. Parvovirus B19 infection** — Causes **pure red cell aplasia** with selective suppression of erythropoiesis, not megaloblastic anemia with hypersegmented neutrophils and pancytopenia.

Would you like to explore the treatment approach for severe B12 deficiency with neurological manifestations?

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Question 513

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?

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

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The answer is **C. Testing for serum ESR and autoantibodies**.

This patient's presentation — **warm, swollen wrist and PIP joints**, **morning stiffness lasting ≥30 minutes**, and **pain that improves with activity** — is characteristic of **inflammatory arthritis**, with rheumatoid arthritis (RA) being the leading consideration. The 2010 ACR/EULAR classification criteria incorporate joint distribution, serology (**rheumatoid factor and anti-CCP antibodies**), **acute phase reactants (ESR/CRP)**, and symptom duration.[1] Initial assessment of suspected RA requires serologic testing for autoantibodies and acute phase reactants, alongside clinical joint examination.[1][2]

Specific features supporting an inflammatory arthritis workup include:

- **Symmetric small-joint polyarthritis** of the wrists and PIPs with effusion, warmth, and swelling — a hallmark RA distribution[2][3]

- **Prolonged morning stiffness** (≥30 minutes), which distinguishes inflammatory from mechanical arthritis[1][4]
- **Improvement with activity**, characteristic of inflammatory rather than degenerative joint disease

Notably, the back pain beginning around age 39 with inflammatory features (morning stiffness, improvement with movement) could also raise consideration for **axial spondyloarthritis**, which would further support obtaining inflammatory markers and potentially HLA-B27 as part of the autoantibody panel.[5]

Why not the other options:

- **A (Ca/PTH):** Relevant for hyperparathyroidism or metabolic bone disease, but does not address the prominent inflammatory synovitis on exam.
- **B (Calcium/Vitamin D):** Appropriate for osteoporosis management (as in the mother), but does not explain or evaluate warm, swollen joints with inflammatory features.
- **D (Ferritin):** Could screen for hemochromatosis, which can cause arthropathy (classically affecting 2nd–3rd MCP joints), but hemochromatosis typically produces a degenerative pattern rather than warm, swollen joints with prolonged morning stiffness. The clinical picture here is far more consistent with inflammatory autoimmune arthritis.

Anti-CCP antibodies have **higher specificity (95%) for RA** compared to rheumatoid factor (85%) and better predict erosive disease, making them a key component of the serologic workup.[6][7]

Would you like to explore the initial treatment approach once RA is confirmed, including methotrexate and treat-to-target strategies?

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Question 514

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?

A. Cefazolin
B. Ceftriaxone
C. Levofloxacin
D. Penicillin

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The answer is **C. Levofloxacin**.

This patient presents with a **severe acute exacerbation of COPD (AECOPD)** — he has all three Anthonisen cardinal symptoms (increased dyspnea, increased sputum volume, and **purulent sputum**), fever, hypoxemia (SpO2 85%), and signs of impending respiratory failure (thoracoabdominal asynchrony, difficulty speaking). He is already appropriately receiving bronchodilators and systemic corticosteroids.

Why antibiotics are indicated: The 2026 GOLD guidelines recommend antibiotics for AECOPD patients with at least two cardinal symptoms (including sputum purulence as one of them), prior

positive sputum cultures, or those requiring mechanical ventilation.[1][2] This patient meets these criteria with purulent sputum, increased dyspnea, and increased sputum volume.

Why levofloxacin specifically:

- This patient is a **frequent exacerbator** with 4 hospitalizations in the past year. Per GOLD 2026, initial empirical treatment is typically an aminopenicillin with clavulanic acid, a macrolide, or a tetracycline, with **quinolones reserved for selected patients** — specifically those with repeated exacerbations or suspected bacterial resistance.[1]
- A JAMA review similarly notes that first-line agents (TMP-SMX, doxycycline, macrolides) are appropriate for initial presentations, while **quinolones or ampicillin-clavulanate are considered for patients with repeated exacerbations** or suspected resistant organisms.[3]
- **Levofloxacin** is FDA-approved for acute bacterial exacerbation of chronic bronchitis, covering the key pathogens: S. pneumoniae, H. influenzae, H. parainfluenzae, M. catarrhalis, and methicillin-susceptible S. aureus.[4]

Why not the other choices:

- **Cefazolin (A):** First-generation cephalosporin with inadequate gram-negative coverage for typical AECOPD pathogens (H. influenzae, M. catarrhalis).
- **Ceftriaxone (B):** While it has reasonable gram-negative coverage, it is not the standard recommended agent for AECOPD and lacks atypical coverage.
- **Penicillin (D):** Too narrow a spectrum for the polymicrobial bacterial pathogens typical of AECOPD.

Would you like to explore the indications and evidence for noninvasive ventilation in severe COPD exacerbations like this one?

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Question 515

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?

A. Anti-citrullinated protein antibodies
B. Erythrocyte sedimentation rate
C. Anti-histone bodies
D. Antineutrophil cytoplasmic antibodies

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The answer is **D. Antineutrophil cytoplasmic antibodies (ANCA)**.

This presentation is classic for **granulomatosis with polyangiitis (GPA)**, which manifests with the characteristic triad of **upper airway involvement** (bloody nasal secretions, nasal ulcers), **lower respiratory tract involvement** (dyspnea, diffuse bilateral crackles suggesting pulmonary hemorrhage or infiltrates), and **renal involvement** (creatinine 3.09 mg/dL).[1][2] Supporting

features include constitutional symptoms (weight loss), arthralgias, elevated inflammatory markers (ESR, CRP), and failure to improve with antibiotics — all consistent with a systemic vasculitis rather than infection.

Why ANCA confirms the diagnosis:

- Approximately **90% of patients** with GPA are ANCA-positive, most commonly **c-ANCA/anti-PR3** (cytoplasmic pattern targeting proteinase 3).[2][3]
- In the 2022 ACR/EULAR classification criteria for GPA, **c-ANCA or anti-PR3 positivity carries the highest weight (+5 points)** among all criteria items.[4]
- The KDIGO 2024 guidelines state that a clinical presentation compatible with small-vessel vasculitis in combination with positive PR3- or MPO-ANCA serology supports a diagnosis of AAV and should prompt initiation of immunosuppressive therapy.[3]

Why the other options are incorrect:

- **A. Anti-citrullinated protein antibodies (anti-CCP)** — specific for rheumatoid arthritis, not vasculitis. While this patient has joint pain, the multisystem presentation with nasal ulcers, pulmonary disease, and renal failure points away from RA.
- **B. ESR** — already obtained (35 mm/h) and is a nonspecific inflammatory marker; it cannot confirm a specific diagnosis.
- **C. Anti-histone antibodies** — associated with drug-induced lupus, which does not present with this triad of upper airway, pulmonary, and renal disease.

Would you like to explore the recommended induction therapy for GPA with renal involvement?

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Question 516

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?

A. Abdominal radiograph
B. Contrast enema
C. Upper gastrointestinal series
D. Sweat testing

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The correct answer is **A. Abdominal radiograph**.

This 3-day-old presents with classic signs of **distal neonatal bowel obstruction**: delayed meconium passage, abdominal distension, absent bowel sounds, and moderate distress. The differential includes **Hirschsprung disease**, **meconium ileus** (strongly associated with cystic fibrosis, which has increased carrier frequency in Ashkenazi Jewish populations), **small left colon syndrome**, and **intestinal atresia**.[1] The ACR–SPR guidelines and Cystic Fibrosis Foundation consensus both state that **evaluation of neonatal bowel obstruction begins with plain abdominal radiographs**, which confirm obstruction and help localize it as proximal versus distal, guiding subsequent imaging.[1][2][3]

Why not the other options:

- **B. Contrast enema** — This is the appropriate *subsequent* step once radiographs confirm a distal obstruction pattern (multiple dilated loops, paucity of distal gas). The ACR

Appropriateness Criteria designate contrast enema as "the diagnostic imaging procedure of choice when there is a **suspected** distal obstruction" confirmed on radiographs. It should not precede radiography, in part because findings such as pneumoperitoneum (suggesting perforation) on the initial film would contraindicate contrast enema.[1][3][4]

- **C. Upper GI series** — Used when malrotation with midgut volvulus is suspected, typically after radiographs suggest a proximal obstruction pattern. The presentation here (distension, absent bowel sounds, no bilious vomiting described) is more consistent with distal obstruction.[2][5]

- **D. Sweat testing** — While CF evaluation is essential in any neonate with suspected meconium ileus, sweat testing does not address the acute obstruction and is generally unreliable in the first weeks of life; it requires the infant to be at least ~36 weeks corrected gestational age, >2 kg, and well-hydrated (typically performed after ~2 weeks of age). Newborn screening (IRT) should be confirmed, and CFTR genetic testing can be pursued, but this is not the immediate priority over imaging.[3]

Would you like to explore how to differentiate meconium ileus from Hirschsprung disease on imaging?

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Question 517

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?

A. TMP-SMX
B. Nitrofurantoin
C. Levofloxacin
D. No treatment is necessary

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D — no treatment is necessary. This is asymptomatic bacteriuria: >100,000 CFU of Enterobacter with pyuria, positive leukocyte esterase, and positive nitrites in a patient with no dysuria, frequency, urgency, suprapubic or flank pain, no fever, and normal vital signs. The IDSA 2019 guideline strongly recommends against screening for or treating ASB in older community-dwelling persons, including those who are functionally impaired, because there is high certainty of harm and low certainty of any benefit.[1]

Why the reported memory complaint does not change this

- Difficulty locating the remote, keys, and purse in a woman with established Alzheimer's dementia represents her baseline chronic cognitive impairment, not an acute change. She is afebrile and hemodynamically stable with no localizing genitourinary findings.
- Even if this were an acute mental status change, IDSA recommends **assessment for other causes and careful observation rather than antimicrobial treatment** in cognitively impaired older adults with bacteriuria, delirium, and no localizing GU symptoms or systemic signs. Observational data suggest the delirium–bacteriuria association reflects shared host factors rather than causation, and the one randomized comparison (norfloxacin vs placebo in bacteriuric long-term care residents) showed no improvement in behavioral scores.[1]
- **Pyuria does not convert ASB into UTI.** ASB is defined by bacteriuria without signs or symptoms of infection, irrespective of pyuria.[2]
- The important exception: a bacteriuric patient with **fever, hemodynamic instability, or other systemic signs of sepsis without a localizing source** should receive broad-spectrum empiric therapy covering urinary and nonurinary sources. None of that is present here.[1]

Why each antibiotic option is wrong

The decisive reason to withhold TMP-SMX, nitrofurantoin, and levofloxacin is simply that there is no indication to treat. Unnecessary therapy carries documented harm: a retrospective study found >8.5-fold higher risk of *C. difficile* infection within 3 months among bacteriuric patients treated without meeting minimum diagnostic criteria, and treatment drives selection of multidrug-resistant gram-negative organisms.[1] Secondary considerations if therapy were ever indicated: Enterobacter species are frequently resistant to first-line agents and often harbor inducible AmpC β-lactamases; nitrofurantoin has poor efficacy against Enterobacter and requires adequate renal function; TMP-SMX with lisinopril raises hyperkalemia risk; and fluoroquinolones in a 78-year-old carry risks of tendinopathy, QT prolongation, CNS effects, and *C. difficile*.

Only two populations warrant screening and treatment of ASB: pregnant women and patients undergoing endourologic procedures with anticipated mucosal trauma.[2][3][4] Diabetes mellitus — present in this patient — is explicitly not an indication.[3][4] The USPSTF likewise recommends against screening nonpregnant adults (D recommendation).[5]

Incidental finding worth addressing separately

The 3/6 holosystolic murmur at the left sternal border with an S3 and bibasilar crackles merits characterization in its own right — the location is more consistent with tricuspid regurgitation or

a ventricular septal defect than mitral regurgitation, though radiation can be misleading. With her known CHF, an echocardiogram and volume-status assessment are reasonable, but this is a separate issue from the urinalysis and does not by itself establish acute decompensation given normal vitals and absence of symptoms.

Would you like to explore how to diagnose UTI in older adults with dementia who cannot reliably report symptoms?

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Question 518

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?

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

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B. PCR positive for *Chlamydia trachomatis* — this is **lymphogranuloma venereum (LGV)**, caused by *C. trachomatis* serovars L1–L3.[1][2] A chlamydia NAAT performed on a bubo aspirate, lesion swab, or genital specimen will be positive, and LGV-specific PCR genotyping is the definitive test.[1]

Why LGV fits

- The classic triphasic course is present: a **small, painless, self-limited genital ulcer/papule at the inoculation site** (her labial ulcer 3 weeks ago that resolved), followed **2–6 weeks later by tender inguinal/femoral lymphadenopathy**, typically unilateral, with bubo formation that spontaneously ruptures in roughly 30% of cases.[1][2][3]
- Acquisition during travel in Southeast Asia is consistent with the geographic distribution of LGV.[4]
- Absence of systemic symptoms and the sequence ulcer → resolution → suppurative adenitis distinguish this from a synchronous ulcer-plus-adenitis presentation.

Diagnostic caveat: commercially available chlamydia NAATs detect LGV serovars but cannot distinguish L1–L3 from serovars D–K, and no NAAT is FDA-cleared for genital ulcer specimens.[3][5] Diagnosis is therefore usually presumptive — based on clinical suspicion, epidemiology, a positive *C. trachomatis* NAAT at the symptomatic site, and exclusion of syphilis, HSV, and chancroid.[1] Chlamydia serology should not be used routinely, though microimmunofluorescence titers ≥256 with a compatible presentation support LGV when NAAT material cannot be obtained.[1][5]

Why the other options are wrong

- **A. "School of fish" gram-negative rods** — chancroid (*Haemophilus ducreyi*). Chancroid produces **deep, painful, non-indurated ulcers concurrent with** tender suppurative adenopathy, not a painless ulcer that heals weeks before the bubo appears. Culture is required for definitive diagnosis and has <80% sensitivity.[1][6]
- **C. Positive RPR, VDRL, and FTA-ABS** — syphilis. The primary chancre is painless and self-resolving, but syphilitic inguinal adenopathy is **non-tender, rubbery, and non-suppurative**; it does not ulcerate or rupture. Serologies should still be sent, since syphilis must be excluded and coinfection is common.[1]
- **D. Tzanck smear with multinucleated giant cells** — HSV, which causes **painful grouped vesicles progressing to shallow ulcers** with tender but non-suppurative adenopathy; the initial lesion here was painless and there is no vesicular phase.

Management: doxycycline 100 mg PO BID for **21 days** is the recommended regimen; buboes may require aspiration or incision and drainage to prevent inguinal/femoral ulceration. Test for HIV and other STIs, and treat sex partners from the preceding 60 days.

Would you like to explore treatment regimens for LGV, including options in pregnancy?

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Question 519

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?

A. Infliximab
B. Anakinra
C. Methotrexate
D. High-dose prednisone for 60 days

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C. Methotrexate.

The presentation — symmetric polyarthritis of the MCP/PIP joints and wrists spreading to elbows and knees over weeks, morning stiffness improving with activity, fatigue, weight loss, and loss of NSAID responsiveness — is rheumatoid arthritis. Methotrexate is the anchor first-line DMARD, and both ACR (2021) and EULAR (2022) endorse starting a conventional synthetic DMARD as soon as the diagnosis is made ("window of opportunity"), with methotrexate strongly recommended over other csDMARDs in DMARD-naive patients with moderate-to-high disease activity.[1][2] Target dose is escalated rapidly toward 25 mg weekly, with folic acid supplementation to reduce nausea, stomatitis, alopecia, and hepatotoxicity.[2] It is contraindicated in pregnancy, significant hepatic disease, and severe renal impairment; monitor CBC, transaminases, and creatinine.

Why the other options are wrong

- **Infliximab (A)** — TNF inhibitors are added after inadequate response to csDMARD therapy, particularly in patients with poor prognostic factors (autoantibodies, high disease activity,

early erosions, failure of 2 csDMARDs), and are combined with methotrexate rather than used as initial monotherapy. Insufficient evidence supports greater efficacy of biologics as first-line, and costs are substantially higher.[1][2]

- **Anakinra (B)** — FDA-labeled for RA only after failure of one or more DMARDs, and it has been shown to be less effective than other biologics in RA.[3][4]
- **High-dose prednisone for 60 days (D)** — Glucocorticoids are used as short-term bridging therapy at low-to-moderate dose alongside a DMARD, tapered and stopped as rapidly as feasible (ideally within 3 months; ACR caps at ≤10 mg/day for a maximum of 3 months) — not as high-dose monotherapy. High-dose steroid monotherapy leaves the disease unmodified and carries cumulative toxicity, and it would be particularly problematic here given poorly controlled type 2 diabetes.[1][2][5]

Practical point for this patient: the difficult-to-control diabetes makes steroid-sparing strategy more important, favoring prompt methotrexate initiation with the shortest feasible bridging steroid course (or intra-articular/intramuscular steroid instead) and close glucose monitoring. Confirm the diagnosis with RF, anti-CCP, ESR/CRP, and hand/wrist radiographs before committing to therapy; also consider hepatitis B/C serologies, tuberculosis screening, and baseline LFTs/CBC prior to methotrexate. If anti-CCP and RF are negative and the arthropathy proves to be MCP-predominant with hook-like osteophytes in a patient with diabetes, hemochromatosis arthropathy would be an alternative consideration, though the symmetric inflammatory pattern with morning stiffness described here fits RA.

Would you like to explore the pre-treatment screening and monitoring schedule for methotrexate?

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Question 520

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?

A. Abstain from breastfeeding
B. Administer ampicillin intrapartum
C. Perform amniocentesis at 37 weeks
D. Administer intravenous immune globulin postpartum

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B. Administer ampicillin intrapartum.

The described isolate — bacitracin-resistant, beta-hemolytic gram-positive cocci on rectovaginal culture — is **Streptococcus agalactiae (group B streptococcus)**. Vertical transmission occurs during labor or after rupture of membranes, and **targeted intravenous intrapartum antibiotic prophylaxis is the only intervention proven to reduce early-onset neonatal GBS disease**.[1][2] Approximately 50% of colonized women transmit GBS to the neonate, and 1–2% of those newborns develop early-onset disease without prophylaxis.[1]

Regimen

- **Intravenous penicillin G is the agent of choice; intravenous ampicillin is an acceptable alternative** — penicillin is preferred only because of its narrower spectrum and lower likelihood of inducing resistance in other vaginal flora.[2][3]
- β-lactams cross the placenta rapidly, achieving cord-blood levels above the GBS MIC within 1–2 hours. Administration **≥4 hours before delivery is most effective**, though 2 hours reduces vaginal colony counts and clinical neonatal sepsis; **obstetric interventions should not be delayed solely to complete 4 hours of antibiotics**.[1][3][4]
- Neither antepartum nor intrapartum **oral or intramuscular** regimens are effective, and antenatal eradication of colonization does not work.[2][4]

- **Penicillin allergy**: cefazolin if low risk of anaphylaxis or uncertain severity; clindamycin only if the isolate is documented susceptible (vancomycin otherwise) — clindamycin and vancomycin are less effective at preventing early-onset disease. ACOG encourages penicillin allergy testing in pregnancy.[2][4]
- **Exception**: prophylaxis is not required for prelabor cesarean birth with intact membranes.[2]

Why the others are wrong

- **A. Abstain from breastfeeding** — breast milk is not a meaningful route of GBS vertical transmission; transmission is intrapartum via the colonized genital tract. Breastfeeding remains recommended.[1]
- **C. Amniocentesis at 37 weeks** — no diagnostic or preventive role; invasive and carries infection risk.
- **D. IVIG postpartum** — not a recommended strategy; prevention guidance rests on culture-based intrapartum prophylaxis. (Maternal GBS vaccines remain investigational.)[4]

One practice-point caveat on the vignette: current ACOG guidance recommends universal vaginal–rectal screening at **36 0/7–37 6/7 weeks**, not 35 weeks, since culture results predict colonization reliably for about 5 weeks.[2] A culture obtained at 35 weeks in a patient delivering after 40 weeks would fall outside that window and warrant repeat screening.

Would you like to explore management of GBS prophylaxis when the patient has a severe penicillin allergy and susceptibility data are unavailable?

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Question 521

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?

A. Air embolization
B. Tension pneumothorax
C. Disseminated intravascular coagulation
D. Coagulopathy of trauma

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The answer is **C. Disseminated intravascular coagulation (DIC)**. This vignette presents the classic findings of trauma-induced DIC: an underlying trigger (massive tissue injury from high-energy MVC with ejection and multiple long bone fractures), **consumption of platelets and clotting factors** (thrombocytopenia at 48,000/mm³, prolonged PT and aPTT), and the characteristic bleeding pattern of **petechiae, purpura, and oozing from venipuncture sites**.[1][2]

Why DIC and not the other options:

- **Air embolization (A)** and **tension pneumothorax (B)** would present with acute cardiopulmonary collapse (cardiovascular instability, absent breath sounds, JVD), not a consumptive coagulopathy with diffuse microvascular bleeding.
- **Coagulopathy of trauma (D)** is the main competing answer. In a board context, this term typically refers to the multifactorial coagulopathy driven by the "**lethal triad**" of hypothermia, acidosis, and hemodilution. This patient is **not hypothermic** (37.5°C), and there is no mention of massive crystalloid resuscitation or acidosis. The specific findings of **petechiae and purpura** — reflecting microvascular thrombosis and platelet consumption —

along with **oozing from IV sites** are the hallmark clinical presentation that distinguishes DIC from the broader coagulopathy of trauma.[1][2][3]

Pathophysiology in this case:

Massive tissue injury releases **tissue factor**, activating the coagulation cascade systemically. This leads to widespread thrombin generation, fibrin deposition in the microvasculature, and consumption of both platelets and clotting factors.[4][5] The NEJM describes the resulting clinical picture:

> "In fulminant disseminated intravascular coagulation, the consumption and diminished supply of platelets and coagulation proteins usually results in oozing at vascular access sites and wounds but occasionally causes profuse hemorrhage."
>
> —Beverley J. Hunt, M.D., King's College London and other institutions. Bleeding and Coagulopathies in Critical Care. N Engl J Med. February 27, 2014.
>
> Used under license from The New England Journal of Medicine.

The ISTH diagnostic criteria for DIC rely on exactly the parameters described: **thrombocytopenia, prolonged PT, and elevated fibrin degradation products** in the setting of an underlying disorder known to cause DIC.[3] Trauma is one of the most common triggers, alongside sepsis, malignancy, and obstetric emergencies.[5]

Would you like to explore the acute management of trauma-induced DIC, including transfusion strategies and adjunctive therapies?

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Question 522

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?

A. Alcohol
B. Cocaine
C. Diphenhydramine
D. Haloperidol

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B. Cocaine. The constellation of hyperthermia (38.3°C), hypertension (173/97), tachycardia (105), mydriasis (7 mm), psychomotor agitation with combativeness, and **warm, diaphoretic skin** is a classic sympathomimetic toxidrome, which cocaine produces through catecholamine reuptake blockade at both peripheral adrenergic and central dopaminergic/serotonergic synapses.[1][2] The subsequent emergence of suicidal ideation as the acute effects wane fits the post-binge "crash," in which depressive symptoms with suicidal thoughts are the most serious feature of stimulant withdrawal.[3]

Why the other options are wrong

- **Diphenhydramine (C)** — the strongest distractor, given the seasonal-allergy note and the shared mydriasis, hyperthermia, tachycardia, and agitated delirium. The discriminator is the skin: anticholinergic poisoning produces **dry, flushed skin** (plus dry mucous membranes, urinary retention, absent bowel sounds), whereas this patient is **sweaty**, which is cholinergically mediated and preserved in sympathomimetic toxicity. Antihistamine

overdose also more often produces sedation/CNS depression, with atropine-like fixed dilated pupils and flushing rather than frank diaphoresis.[1][4]

- **Alcohol (A)** — acute intoxication causes CNS depression, ataxia, and slurred speech without hyperthermia, hypertensive surge, or mydriasis. Alcohol withdrawal could reproduce the autonomic hyperactivity, but would be expected to feature tremor, and there is no history of dependence or cessation.

- **Haloperidol (D)** — the IM medication was given after the vital-sign abnormalities were recorded, so it cannot explain them. Neuroleptic malignant syndrome would present with **lead-pipe rigidity and altered consciousness** rather than preserved spontaneous movement, and antipsychotics do not cause mydriasis. Acute dystonia or akathisia would also not produce this degree of hypertension and fever.

Management implication: benzodiazepines are first-line for the agitation, hypertension, and hyperthermia of cocaine toxicity; prolonged physical restraint should be minimized because it can worsen hyperthermia, acidosis, and rhabdomyolysis.[1][5] Pure beta-blockade is generally avoided because of concern for unopposed alpha stimulation, with calcium channel blockers, alpha-1 antagonists (phentolamine), or nitrates preferred for persistent severe hypertension.[1][5] The suicidal statement warrants continuous observation and formal psychiatric reassessment once intoxication resolves, since stimulant-induced depressive symptoms typically remit within days but confer real short-term risk.[3][6]

Would you like to explore the ED management algorithm for cocaine-induced hyperthermia and severe agitation?

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Question 523

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?

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.

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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 apnea and hypopnea events divided by hours of sleep: **(12 + 30) / 7 = 6 events/hour**, which exceeds 5. An AHI ≥5 events/hour defines obstructive sleep apnea (OSA), with severity classified as **mild (5–15)**, **moderate (16–30)**, and **severe (>30)**.[1][2][3] This patient's AHI of 6 places him in the **mild OSA** category.

Why the other options are incorrect:

- **B — Deeper stages of NREM sleep:** Obstructive respiratory events are **more prominent during REM sleep**, not deeper NREM stages. REM sleep atonia reduces upper airway muscle tone, increasing pharyngeal collapsibility, and apneas during REM are typically **longer and associated with greater oxygen desaturation**. During deep NREM sleep (N3), breathing tends to be more stable.[4][5]
- **C — Mouth opening relieving obstruction:** Mouth opening during sleep actually **worsens** airway obstruction. It allows the mandible to drop posteriorly, the tongue to fall backward,

and breaks the palatal seal — all of which increase pharyngeal collapse rather than relieve it.

- **D — Gynoid obesity: Central (android/visceral) obesity** is the pattern most strongly associated with OSA, not gynoid obesity. Increased adipose tissue within the tongue, pharynx, and parapharyngeal fat pads from central fat distribution increases mechanical loading and airway collapsibility. Peripheral (gynoid) adiposity may actually be **protective** against OSA development.[2][6][7]

Would you like to explore first-line treatment options for mild obstructive sleep apnea?

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Question 524

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?

A. Adverse effect of medication
B. Malignant hyperthermia
C. Urinary tract infection
D. Transfusion reaction

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The answer is **D. Transfusion reaction** — specifically, a **febrile non-hemolytic transfusion reaction (FNHTR)**. This patient's presentation of **high fever (39.5°C) and chills within 2 hours** of receiving packed red blood cells is classic for FNHTR, which occurs in approximately 1–3% of transfused units.[1][2]

Why transfusion reaction fits best:

- FNHTRs present as a **temperature rise ≥1°C accompanied by chills, rigors, and sometimes transient hypertension**, occurring during or up to 4 hours after transfusion. This matches the clinical timeline and findings precisely.[1][3]
- The mechanism involves **recipient antibodies against donor leukocyte antigens** or pro-inflammatory cytokines (IL-1, IL-6, TNF) accumulated in stored blood products.[1][3]
- The history of **hysterectomy for leiomyomata** implies prior pregnancies, which would have sensitized her immune system to foreign HLA antigens — a known risk factor for developing anti-leukocyte antibodies that drive FNHTR.[1][4]

Why the other options are less likely:

- **A (Adverse effect of medication):** Cephalexin can cause drug fever, but this typically develops over days, not acutely within 2 hours with rigors.
- **B (Malignant hyperthermia):** This occurs during or immediately after exposure to triggering agents (volatile anesthetics, succinylcholine) and presents with **muscle rigidity, hypercarbia, rhabdomyolysis, and metabolic acidosis** — none of which are described here. It would also manifest intraoperatively, not 2 hours postoperatively.
- **C (Urinary tract infection):** A catheter-associated UTI would not cause fever within 2 hours of placement; these infections require days to develop.

Would you like to explore the workup and management algorithm for suspected febrile non-hemolytic transfusion reactions?

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Question 525

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?

A. Oral morphine therapy
B. Intravenous ampicillin and gentamicin combination therapy
C. Oral methimazole therapy
D. Dextrose infusion

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The answer is **A. Oral morphine therapy**.

This newborn presents with classic features of **neonatal opioid withdrawal syndrome (NOWS)**: high-pitched cry, poor feeding, diaphoresis, hyperreflexia, tremors, and excessive startle response — in the context of maternal codeine use without prenatal care.[1] Normal labs (glucose, calcium, bilirubin, CBC) effectively rule out metabolic and infectious etiologies, making the other answer choices incorrect:

- **Ampicillin/gentamicin (B)** would address neonatal sepsis, but the normal CBC and clinical picture (tremors, hyperreflexia, startle) are more consistent with withdrawal than infection.
- **Methimazole (C)** treats neonatal hyperthyroidism, which can present with tachycardia and irritability but is not supported here without thyroid pathology or maternal Graves disease.
- **Dextrose infusion (D)** treats hypoglycemia, which has been excluded by normal serum glucose.

Management of NOWS

Per AAP guidelines, **nonpharmacologic care** (swaddling, low-stimulation environment, skin-to-skin contact) is the foundation for all opioid-exposed infants.[2] When these measures are insufficient — as in this case where the infant has severe withdrawal signs — **pharmacologic therapy with an opioid is first-line**.[2][3] **Oral morphine is the most commonly used agent** in the United States, typically dosed at **0.3–1.0 mg/kg/day divided every 3–4 hours**.[4] Methadone and buprenorphine are alternatives that may shorten length of stay, though morphine remains the standard first-line agent at most centers.[2][3] Clonidine or phenobarbital may be added as second-line agents if opioid therapy alone does not adequately control symptoms.[2]

Would you like to explore how the Eat, Sleep, Console approach compares with Finnegan-based scoring for assessing withdrawal severity in NOWS?

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Question 526

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?

A. Endoplasmic reticulum (ER)
B. Ribosomes
C. Lysosomes
D. Mitochondria

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The answer is **C. Lysosomes**.

Heart failure cells are hemosiderin-laden alveolar macrophages that form in the setting of chronic pulmonary congestion from CHF. Elevated pulmonary capillary pressures cause extravasation of red blood cells into alveolar spaces, where alveolar macrophages **phagocytose** them.[1][2] The critical step in hemosiderin formation occurs when the **phagosome fuses with lysosomes** to form a phagolysosome, providing the acidic, hydrolytic environment necessary for degrading the engulfed erythrocytes and their hemoglobin.[3][4]

Within the **lysosomal compartment**, iron released from heme is sequestered and ultimately converted to **hemosiderin** — an insoluble iron-storage complex that gives these macrophages their characteristic golden-brown, Prussian blue–positive granules.[4][5][6] This intralysosomal hemosiderin formation has been described as a protective strategy to suppress iron-catalyzed redox reactions.[5]

Why not the other options:

- **Endoplasmic reticulum** — involved in protein synthesis and folding, not in the degradation of phagocytosed material.
- **Ribosomes** — sites of protein translation; not involved in intracellular digestion of engulfed cells.

- **Mitochondria** — responsible for oxidative phosphorylation and energy production; not the organelle that processes phagocytosed erythrocytes into hemosiderin.

Would you like to explore the clinical use of Golde scoring for hemosiderin-laden macrophages in BAL?

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Question 527

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?

A. Decreased prostaglandin synthesis
B. Erosion of tortuous submucosal arteriole
C. Bacterial colonization of the gastric antrum
D. Decreased gastric blood flow

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D. Decreased gastric blood flow. This is a Curling ulcer — stress-related mucosal disease from splanchnic hypoperfusion after major thermal injury. Massive burns cause plasma loss, hypovolemia, reduced cardiac output, and catecholamine-driven splanchnic vasoconstriction, which lower gastric mucosal blood flow and produce ischemic erosions/ulcers within the first 24 hours.[1] The resulting mucosal injury impairs bicarbonate secretion and mucus barrier function, permits acid back-diffusion, and can bleed briskly enough to cause melena, hypotension, and tachycardia.[1][2]

Endoscopic evidence of stress-related mucosal disease is present in 75–100% of critically ill patients within 24 hours of ICU admission, with decreased blood flow, mucosal ischemia, and ischemia–reperfusion injury as the dominant mechanisms.[3] Clinically important bleeding occurs in roughly 1–4% of at-risk patients not receiving prophylaxis.[1][3]

Why the other options are wrong

- **A. Decreased prostaglandin synthesis** — the mechanism of NSAID-induced ulceration via COX-1 inhibition, reducing mucus/bicarbonate secretion and mucosal blood flow. Reduced prostaglandin production is a downstream contributor in stress ulceration, but the initiating insult in a burn patient is hypoperfusion, and there is no NSAID exposure described.[1][4]

- **B. Erosion of tortuous submucosal arteriole** — Dieulafoy lesion, a congenital caliber-persistent artery causing sudden massive hematemesis/melena, unrelated to burn injury and far less likely than stress ulceration in this setting.
- **C. Bacterial colonization of the gastric antrum** — *H. pylori*, which causes chronic peptic ulcer disease over months to years, not acute bleeding 20 hours after admission in a previously healthy patient.[1]

Clinical corollary: this presentation is the rationale for stress ulcer prophylaxis in high-risk ICU patients. The 2024 SCCM/ASHP guideline suggests prophylaxis with either a PPI or H2RA as first-line in critically ill adults with risk factors; early enteral nutrition also appears to reduce bleeding, likely by preserving barrier function and mucosal blood flow.[1][5] Note the ongoing debate about PPI-associated mortality signals in higher-severity patients.[1]

Would you like to explore stress ulcer prophylaxis and early enteral feeding protocols specifically in major burn patients?

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Question 528

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?

A. Alkaline phosphatase
B. RNase
C. Superoxide dismutase
D. Telomerase

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The answer is **D. Telomerase**.[1][2][3]

Telomerase is a ribonucleoprotein reverse transcriptase that maintains telomere length, conferring **replicative immortality** — one of the hallmarks of cancer. In most differentiated somatic cells, telomerase expression is repressed, and telomeres progressively shorten with each cell division until the cell reaches replicative senescence.[4][5] Malignant cells bypass this checkpoint by reactivating telomerase, which is detected in approximately **85–90% of all human cancers**.[1][6][7]

This question tests the fundamental distinction between benign and malignant neoplasms at the molecular level. In the specific context of lipomatous tumors:

- **Telomerase activity was detected in ~69% of malignant lipomatous tumors** but was absent in benign lipomatous neoplasms.[8]
- In soft tissue sarcomas broadly, telomerase was found in **52% of sarcomas and 0% of benign soft tissue tumors**.[9]

- Higher telomerase activity and hTERT expression correlate with **tumor progression** in liposarcomas, with the highest levels seen in higher-grade subtypes (e.g., myxoid/round-cell).[10][11]

Why not the other options:

- **A. Alkaline phosphatase** — Associated with osteoblastic activity, hepatobiliary disease, and bone-forming tumors (e.g., osteosarcoma), but not a general marker of malignant transformation.
- **B. RNase** — Degrades RNA; no established association with malignant transformation.
- **C. Superoxide dismutase** — An antioxidant enzyme that neutralizes reactive oxygen species; not a hallmark enzyme of cancer cells.

Would you like to explore the role of alternative lengthening of telomeres (ALT) versus telomerase in sarcoma prognosis?

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Question 529

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?

A. Elevated TSH
B. High Patient Health Questionnaire-9 (PHQ-9) score
C. Positive anti-CCP antibodies
D. Positive urine toxicology

https://openevidence.com/ask/387c4648-5edd-43e5-81b2-be252fbcd006

A. Elevated TSH. The constellation of fatigue, difficulty concentrating, 15-lb weight gain, constipation, arthralgia, bradycardia (55/min), diastolic hypertension (127/98), slowed speech and movement, and **delayed relaxation of deep tendon reflexes** is classic overt primary hypothyroidism — most likely Hashimoto thyroiditis, which causes up to 85% of primary hypothyroidism in iodine-sufficient regions.[1][2] The episode 6 months earlier of palpitations, increased stool frequency, and tremor represents the **transient thyrotoxic phase (hashitoxicosis)** from destructive release of preformed hormone, followed by hypothyroidism as stores deplete.[3][4]

Why the exam findings fit

- **Delayed relaxation of tendon reflexes** occurs in ~75% of hypothyroid patients and has a specificity around 93% for hypothyroidism by Achilles reflex time.[1][5]

- **Bradycardia (12%–19%) and diastolic hypertension** are recognized cardiovascular manifestations.[1][2]
- **Fatigue (74%–86%), weight gain (24%–59%), constipation (33%–41%), and cognitive impairment (45%–48%)** match her presenting symptoms.[1]
- **Joint pain and muscle cramps** are listed musculoskeletal manifestations of hypothyroidism.[1]
- Maternal rheumatoid arthritis reflects the familial clustering of autoimmunity; Hashimoto thyroiditis frequently coexists with RA, type 1 diabetes, and other autoimmune disease.[3]

Why the other options are less likely

- **B — High PHQ-9:** Depression can produce fatigue, poor concentration, weight change, and psychomotor slowing, and depression is a recognized feature of hypothyroidism itself. It does not explain bradycardia, delayed reflex relaxation, or the preceding thyrotoxic episode.[1][3]
- **C — Positive anti-CCP:** Her joint complaints are tenderness without described synovitis, morning stiffness, or symmetric small-joint swelling; arthralgia is common in hypothyroidism. RA would not account for the bradycardia, weight gain, reflex findings, or biphasic thyroid symptoms. A maternal history alone does not outweigh the thyroid picture.[1]
- **D — Positive urine toxicology:** A single LSD exposure 6 years ago would not be detectable and explains none of the findings.

Confirmatory testing and management

Order **serum TSH with reflex free T4**; a high TSH with low free T4 confirms overt primary hypothyroidism, whereas a normal free T4 indicates subclinical disease.[1][6] TPO antibodies, positive in ~95% of Hashimoto thyroiditis, establish the autoimmune etiology but are not needed to make the diagnosis.[3][4] Treat overt hypothyroidism with levothyroxine — full weight-based replacement is appropriate in a young patient without cardiac disease, with **TSH rechecked 6–8 weeks after initiation or any dose change**, then annually once at goal.[1] Confirm biochemistry before committing to full replacement dosing, since subclinical hypothyroidism with TSH below 10 mU/L does not always warrant treatment.[7]

Would you like to explore levothyroxine initiation and titration in a young adult with newly diagnosed overt hypothyroidism?

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Question 530

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?

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

https://openevidence.com/ask/f2c7f689-d667-4216-b6ce-c58ef9549092

The answer is **B. A septal hematoma causing a perforation**.

Nasal whistling is a hallmark symptom of a septal perforation, which is a recognized complication of rhinoplasty (reported incidence **0–2.6%**).[1] The pathophysiology involves a post-operative **septal hematoma** that compromises blood supply to the underlying cartilage, leading to avascular necrosis and eventual perforation of the septum.[2] Anterior perforations in particular cause turbulent airflow through the defect, producing a characteristic **whistling sound**, along with crusting, epistaxis, and nasal obstruction.[3][4]

The other options are less likely:

- **A. Post-operative swelling** — By 3 months post-rhinoplasty, significant swelling has typically resolved. Swelling causes congestion and obstruction rather than a whistling noise.[5]
- **C. A straightened deviated septum** — Correction of a deviated septum improves nasal airflow and would not produce whistling.
- **D. Excessive columellar show** — This is a cosmetic concern related to the visibility of the columella; it does not alter intranasal airflow dynamics in a way that generates whistling.

Would you like to explore management options for post-rhinoplasty septal perforations?

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Question 531

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?

A. Superfical epidermis
B. Hair follicles
C. Papillary dermis
D. Eccrine sweat glands

https://openevidence.com/ask/5fb3112b-5fb8-45da-a91c-8f8285463e92

B. Hair follicles.

This is Pseudomonas aeruginosa "hot tub" folliculitis — the classic presentation of pruritic erythematous papules and papulopustules on the trunk and areas covered by swimwear, appearing 8–48 hours (up to ~5 days) after exposure to an inadequately chlorinated whirlpool, hot tub, or pool, often with clustering among co-exposed contacts.[1][2][3] The organism enters through the **hair follicle** (facilitated by high water pH, low free chlorine, and maceration/abrasion of the stratum corneum), and the inflammation begins as a **suppurative folliculitis centered on the follicular ostium and pilar canal**, with neutrophilic infiltration of the follicle and perifollicular tissue; biopsies may show extension to dermal abscess formation.[1][4][5][6]

Why the other options are wrong:

- **Superficial epidermis** — would suggest impetigo or an irritant/contact dermatitis; lesions here are follicularly based papulopustules, not subcorneal bullae or erosions.
- **Papillary dermis** — the site of urticarial/vasculitic or lichenoid interface processes; in Pseudomonas folliculitis dermal involvement is secondary spread from the follicle, not the origin.

- **Eccrine sweat glands** — the target in neutrophilic eccrine hidradenitis (chemotherapy-associated) and miliaria (ductal occlusion), neither of which produces follicular pustules after whirlpool exposure.

Management is supportive: the eruption is self-limited and resolves in 7–10 days without antibiotics in immunocompetent hosts.[2][6] Systemic therapy (e.g., a fluoroquinolone) is reserved for severe, persistent, or systemically symptomatic disease, or concomitant Pseudomonas otitis externa.[4][7]

Would you like to explore when systemic antibiotics are warranted in Pseudomonas folliculitis and which agents to use?

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Question 532

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?

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

https://openevidence.com/ask/6d10d7bf-5c38-4e36-93d5-f83ec272a2fc

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The answer is **B. Lateral aspect of the shoulder**.

This vignette describes a classic **anterior glenohumeral dislocation** — the humeral head is palpated below the coracoid process, the arm is externally rotated and abducted, and the normal rounded deltoid contour is lost. The nerve most vulnerable in this injury is the **axillary nerve** (C5–C6), which passes just inferior to the glenohumeral joint capsule and is stretched or compressed by the dislocating humeral head. It is injured in up to **40% of anterior shoulder dislocations**.[1]

The axillary nerve provides sensory innervation to the **lateral aspect of the shoulder**, known as the **"regimental badge" or "regimental patch" area** — the skin overlying the lateral deltoid.[1][2] Axillary neuropathy presents with **lateral shoulder sensory disturbance in the regimental patch**, along with weakness in shoulder abduction and external rotation.[1]

The other options correspond to different nerves:

- **A (Medial upper arm)** — medial cutaneous nerve of the arm (medial cord, C8–T1)
- **C (Skin above clavicle)** — supraclavicular nerves (cervical plexus, C3–C4)
- **D (Dorsal forearm and hand)** — posterior cutaneous nerve of the forearm (radial nerve) and superficial branch of the radial nerve

Would you like to explore the management of axillary nerve injury following anterior shoulder dislocation?

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Question 533

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?

A. Decreased production of PGE2
B. Buildup of a toxic metabolite due to kidney disease
C. Increased stimulation of the vagus nerve
D. Hypovolemia

https://openevidence.com/ask/827930cd-0727-4748-96a2-dd76c2d47ab9

A. Decreased production of PGE2.

Massive ingestion of a nonselective NSAID or aspirin in a suicide attempt causes acute gastroduodenal mucosal injury that can progress to ulceration and perforation. The mechanism is inhibition of COX-1, which normally generates the constitutive prostaglandins (chiefly PGE2 and PGI2) that maintain the gastric mucosal barrier.[1][2][3] Loss of these prostaglandins reduces mucus and bicarbonate secretion, decreases mucosal blood flow, and suppresses epithelial proliferation and restitution, leaving the mucosa exposed to acid, pepsin, and bile salts.[1][4][5][6] Aspirin/NSAIDs are also directly topically injurious — disrupting the surface phospholipid layer and uncoupling mitochondrial oxidative phosphorylation — which acts synergistically with prostaglandin depletion, particularly with the enormous intraluminal drug concentrations seen in overdose.[4][7][8] NSAIDs including aspirin are the classic drug-related risk factor listed for perforated peptic ulcer.[9]

Clinically the case fits: acute severe epigastric pain with peritonism, and crepitus/free air on CT confirming perforation.

Why the other options are wrong

- **B. Toxic metabolite accumulating from kidney disease** — this describes accumulation of agents such as meperidine's normeperidine or metformin in renal failure; neither pattern

causes acute gastric perforation, and there is nothing to suggest underlying renal disease in a 25-year-old.

- **C. Increased vagal stimulation** — vagal drive increases acid secretion (the basis for vagotomy in ulcer surgery) but is not an acute perforating mechanism after a single ingestion.
- **D. Hypovolemia** — splanchnic hypoperfusion produces stress-related mucosal disease in critically ill patients (shock, sepsis, burns, mechanical ventilation); this patient is hemodynamically normal (BP 135/86, HR 86).[4]

Management points

Beyond the mechanism, an intentional overdose with gastric perforation warrants: emergent surgical consultation for operative repair, broad-spectrum antibiotics and IV fluids, IV PPI, and — critically — identification of the ingestant. Check acetaminophen and salicylate levels, an ABG/VBG with electrolytes and anion gap, and an ECG, since co-ingestants are common and a salicylate level with mixed respiratory alkalosis/metabolic acidosis would change management substantially. Activated charcoal is contraindicated once perforation is documented. Psychiatric evaluation and one-to-one observation are required once medically stabilized.

Would you like to explore the management thresholds for acute salicylate toxicity, including when to alkalinize versus dialyze?

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Question 534

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?

A. Blocking reuptake of dopamine and norepinephrine
B. Inhibiting breakdown of biogenic amines
C. Antagonizing the NMDA receptor
D. Inhibiting the GABA receptor

https://openevidence.com/ask/5d37a38c-078d-4bbc-8297-827afc4338c3

The answer is **A. Blocking reuptake of dopamine and norepinephrine**.

This vignette describes a classic presentation of **cocaine-induced STEMI**. The key clinical clues are the combination of acute chest pain with ST elevation, sympathomimetic signs (hypertension, tachycardia, mydriasis, agitation), and a **perforated nasal septum** — a hallmark of chronic intranasal cocaine use resulting from vasoconstriction-mediated tissue ischemia.[1][2] The patient denies illicit drug use despite overwhelming physical evidence, which is not uncommon.

Cocaine blocks the reuptake of norepinephrine and dopamine at presynaptic adrenergic terminals, causing accumulation of catecholamines at the postsynaptic receptor and producing a powerful sympathomimetic state.[3][4] This leads to increased heart rate, blood pressure, and myocardial contractility (raising oxygen demand) while simultaneously causing coronary vasoconstriction (reducing oxygen supply), enhanced platelet aggregation, and accelerated atherosclerosis — a multifactorial mechanism for myocardial ischemia and infarction.[3][5]

Why the other options are incorrect:

- **B (Inhibiting breakdown of biogenic amines)** — This describes **monoamine oxidase (MAO) inhibitors**, which prevent enzymatic degradation of catecholamines rather than blocking reuptake.
- **C (Antagonizing the NMDA receptor)** — This describes **ketamine** or **PCP (phencyclidine)**. While PCP can cause agitation and sympathomimetic-like effects, it does not cause nasal septum perforation or this classic sympathomimetic toxidrome.
- **D (Inhibiting the GABA receptor)** — This is not the primary mechanism of any common recreational drug associated with this presentation. GABA antagonism would produce excitatory effects but is not the mechanism of cocaine.

Would you like to explore the acute management of cocaine-induced STEMI, particularly the beta-blocker controversy?

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Question 535

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?

A. Abnormal coagulation and fibrinolysis
B. Capillary leakage
C. Decreased cardiac output
D. Pseudocyst formation

https://openevidence.com/ask/9a9852c1-85d9-4af3-b0f3-dee78543de26

The answer is **B. Capillary leakage**.

This patient has **acute pancreatitis** — epigastric pain radiating to the back, nausea, elevated amylase (250 U/L) — with **hypotension (84/58 mmHg) and tachycardia (115/min)**. The underlying cause of these vital sign abnormalities is **inflammatory capillary leakage with third-space fluid sequestration**.

In acute pancreatitis, the systemic inflammatory response causes release of proinflammatory cytokines and vasoactive mediators (TNF-α, IL-1, IL-6, bradykinin, endothelin) that **increase capillary permeability**, leading to extravasation of plasma from the intravascular space into the interstitium and peritoneum.[1][2][3] The American College of Gastroenterology guidelines note that patients with acute pancreatitis have "marked systemic endothelial injury and increased

vascular permeability leading to fluid shifts into the interstitial space and peritoneum," resulting in decreased intravascular volume.[2]

Several findings in this case support capillary leak as the mechanism:

- **Hematocrit of 48%** (hemoconcentration) — plasma is extravasating while cellular elements remain intravascular, concentrating the blood. Hemoconcentration is a well-established marker of third-space losses and is associated with higher risk of pancreatic necrosis and organ failure.[1][4][5]
- **BUN of 32 mg/dL** (elevated) — consistent with prerenal azotemia from intravascular volume depletion, a marker of decreased renal perfusion that parallels decreased pancreatic perfusion.[2]
- **Warm extremities** — consistent with a distributive/inflammatory process rather than cardiogenic shock, which would produce cool, clammy extremities.

Why not the other options:

- **A (Abnormal coagulation/fibrinolysis):** While coagulopathy can occur in severe pancreatitis, this patient's platelet count is normal (175,000/mm^3), and the primary mechanism of hemodynamic compromise is capillary leak, not DIC.[6]
- **C (Decreased cardiac output):** The warm extremities and hemodynamic profile are inconsistent with cardiogenic shock. Acute pancreatitis typically produces a high cardiac index with decreased systemic vascular resistance.[7]
- **D (Pseudocyst formation):** Pseudocysts require **weeks** to develop (typically ≥4 weeks after onset) and would not explain acute hemodynamic instability 8 hours into presentation.

Would you like to explore current evidence-based fluid resuscitation strategies in acute pancreatitis?

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Question 536

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?

A. Gastric adenocarcinoma
B. Astrocytoma and cardiac rhabdomyoma
C. Esophageal adenocarcinoma
D. Acute lymphocytic leukemia

https://openevidence.com/ask/383a3c8d-a90c-4c3f-bdea-f019f8ffd11c

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The answer is **D. Acute lymphocytic leukemia (ALL)**. Down syndrome (trisomy 21) confers a well-established **10- to 20-fold increased risk of ALL** and an even greater (up to 150-fold) risk of acute myeloid leukemia, particularly before age 5.[1][2][3] Of the options listed, ALL is the only neoplasm with a recognized association with Down syndrome.

Why the other options are incorrect:

- **A. Gastric adenocarcinoma** and **C. Esophageal adenocarcinoma** — Down syndrome is actually associated with **decreased** incidence of most solid tumors, including digestive system malignancies (OR 0.39 in one large study). Neither GI adenocarcinoma has a known association with Down syndrome.[4]
- **B. Astrocytoma and cardiac rhabdomyoma** — This pairing is the classic neoplasm association with **tuberous sclerosis complex** (TSC), not Down syndrome. Brain tumors, including astrocytomas, are notably rare in Down syndrome.[5]

Key points on Down syndrome cancer predisposition:

- **Hematologic malignancies** are markedly increased: both ALL (20-fold risk) and AML (up to 500-fold before age 5, particularly acute megakaryoblastic leukemia).[2][6]

- **Solid tumors overall are decreased**, with significantly lower rates of breast, prostate, lung, colorectal cancers, and melanoma.[2][7]
- **Testicular cancer** is the notable exception among solid tumors, occurring at higher rates (SIR ~4.3).[2][7]
- Leukemia develops in approximately **2–3%** of all individuals with Down syndrome, independent of transient abnormal myelopoiesis.[1]

Would you like to explore current screening and surveillance recommendations for malignancies in Down syndrome?

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Question 537

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?

A. TH1 cells
B. TH2 cells
C. TH17
D. T0 cells

https://openevidence.com/ask/6d2f8371-8489-4c79-bbb7-b6de9d50ae07

The correct answer is **B. TH2 cells**.

The clinical scenario describes **Enterobius vermicularis (pinworm) infection** — classic presentation with perianal pruritus, sleep disturbance, positive scotch tape test, and treatment with mebendazole. As a helminth, pinworm infection drives naïve CD4+ T cells (TH0) to differentiate into **TH2 cells**.

Helminth infections are the prototypical stimulus for TH2 polarization. Epithelial cells exposed to helminths produce alarmins (IL-25, IL-33, TSLP), which promote innate immune activation and support TH2 differentiation.[1] Activated TH2 cells produce the canonical type 2 cytokines **IL-4, IL-5, IL-9, and IL-13**, which drive the characteristic effector responses: **eosinophilia, IgE production, goblet cell hyperplasia, increased mucus secretion, and smooth muscle contraction** — all of which facilitate worm expulsion.[1][2][3] Pinworm infections specifically have been shown to elicit type 2 activity with elevated IgG1 and eosinophil counts.[4]

Why not the other options:

- **TH1 cells** — Associated with intracellular pathogens (viruses, intracellular bacteria, protozoa) via IFN-γ and macrophage activation. A TH1-dominated response during helminth infection actually compromises protective immunity.[5]
- **TH17 cells** — Primarily involved in defense against extracellular bacteria and fungi, driven by IL-6 and TGF-β.

- **T0 cells** — TH0 refers to naïve, undifferentiated T helper cells; the question asks what they differentiate into, not what they remain as.

Would you like to explore the pharmacologic management of pinworm infection, including mebendazole versus albendazole?

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Question 538

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?

A. Left middle cerebral
B. Right vertebral
C. Left posterior inferior cerebellar
D. Left penetrating

https://openevidence.com/ask/d8fc12d1-ec48-4d2d-b37d-43a5fea2bb10

A. Left middle cerebral. The vignette describes **conduction aphasia** — fluent speech, intact comprehension, but disproportionately impaired repetition with **phonemic paraphasias and repeated self-correction attempts** (conduite d'approche).[1][2] This localizes to the **left (dominant) perisylvian cortex** — the supramarginal gyrus (area 40), posterior planum temporale/area Spt, and the underlying arcuate fasciculus — territory supplied by **cortical branches of the left MCA**.[1][3][4]

Why the lesion is MCA-branch territory

- **Damasio's classic description**: conduction aphasia arises from damage at one of two dominant loci — the left supramarginal gyrus (area 40) ± white matter beneath the insula, or the left primary auditory cortices (areas 41/42) with insula and underlying white matter. Both are perisylvian and MCA-supplied.[1]
- Lesion-overlap and fMRI aggregate analyses place the critical zone at **area Spt** in the posterior left planum temporale, at the temporoparietal junction.[3]

- Cadaveric and tractography work confirms the **arcuate/superior longitudinal fasciculus lies in direct 3D relation to MCA branches**, from the bifurcation through the medullary branches.[4]

- A **discrete cortical branch occlusion** (typically inferior division/parietal branches) accounts for an isolated language deficit without hemiparesis or hemianopia; motor signs are characteristically absent in conduction aphasia apart from possible right facial weakness.[1]

Why not the other options

- **Right vertebral** — posterior circulation; produces brainstem/cerebellar findings, and the right side is non-dominant in a right-handed patient, so aphasia would not occur.

- **Left PICA** — lateral medullary (Wallenberg) syndrome: vertigo, ipsilateral Horner, crossed sensory loss, dysphagia, **dysarthria rather than aphasia**.

- **Left penetrating (lenticulostriate)** — lacunar syndromes (pure motor hemiparesis, pure sensory stroke, ataxic hemiparesis, dysarthria–clumsy hand). These small-vessel branches supply internal capsule, caudate, and globus pallidus, not the perisylvian language cortex. [5][6]

Clinical caveat beyond the exam item: the stated 3-month history of speech difficulty warrants clarification of onset. If the deficit was sudden and static, a prior small left MCA-branch infarct fits. If it has been **gradually progressive**, the differential shifts toward a structural mass lesion or the **logopenic variant of primary progressive aphasia**, which likewise features impaired repetition and phonologic errors with preserved comprehension. MRI with vascular imaging is the appropriate next step in either case.

Would you like to explore how logopenic variant PPA is distinguished from vascular conduction aphasia?

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Question 539

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?

A. Clostridium botulinum
B. Clostridium tetani
C. Group B streptococcus
D. Listeria monocytogenes

https://openevidence.com/ask/8c4dd8b3-ac41-4a77-897d-35ce32c0711f

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The answer is **B. *Clostridium tetani*** — this presentation is classic **neonatal tetanus**.

Key features pointing to the diagnosis:

- **Timing**: Symptom onset at **day 6–7 of life** falls squarely within the typical median incubation period of **5–7 days** (range 3–24 days) for neonatal tetanus, with ~90% of cases presenting between days 3–14.[1][2]
- **Risk factors**: Traditional **home birth** (potential for unsterile umbilical cord cutting) and an **unvaccinated mother** (no transplacental transfer of protective anti-tetanus antibodies) are the hallmark predisposing factors.[2][3]
- **Clinical findings**: **Trismus** (clenched jaw preventing latching), **increased tone**, **clenched hands**, and **absent head lag** (reflecting generalized hypertonia rather than the expected head lag of a normal neonate) are the cardinal manifestations. Neonates classically present with inability to suck/feed as the first symptom, followed by generalized rigidity.[1][2]

- **Normal bloodwork**: Tetanus is a **clinical diagnosis**; routine laboratory studies are characteristically normal because the pathology is toxin-mediated (blockade of inhibitory GABA/glycine neurotransmission), not due to bacteremia or systemic inflammation.[4]

Why not the other options:

- **A. *C. botulinum***: Infant botulism causes **descending flaccid paralysis** (hypotonia, "floppy baby"), constipation, and weak cry — the opposite of the hypertonia and rigidity seen here.[3][5]
- **C. Group B streptococcus**: GBS neonatal sepsis/meningitis typically presents with fever/hypothermia, lethargy, respiratory distress, and abnormal screening labs (elevated WBC, CRP, or positive blood cultures) — not isolated hypertonia with normal labs.
- **D. *Listeria monocytogenes***: Neonatal listeriosis presents similarly to GBS sepsis with systemic signs of infection and abnormal labs, not with the specific pattern of trismus and generalized rigidity.

Would you like to explore the acute management of neonatal tetanus?

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Question 540

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?

A. Renal failure
B. Hepatomegaly
C. Chorea
D. Pleural effusion

https://openevidence.com/ask/1fdda8a4-73cb-4e98-a9a4-58b459ad80a2

The answer is **C. Chorea**.

This presentation is classic **acute rheumatic fever (ARF)** following Group A Streptococcal (GAS) pharyngitis. The patient already demonstrates two major Jones criteria: **painless subcutaneous nodules** over extensor surfaces and **arthritis** of the lower extremities.[1][2] Among the answer choices, **Sydenham's chorea** is the only recognized major manifestation of ARF and thus the most likely additional finding.

Why chorea fits this case:

- **Sydenham's chorea** occurs in **10–30% of ARF cases**, presenting as purposeless, involuntary movements of the extremities and trunk that disappear during sleep. It characteristically has a **latent period of 1–6 months** after GAS infection, consistent with this patient's 3-month timeline.[1][3]
- Chorea is one of the **five major Jones criteria** alongside carditis, arthritis, erythema marginatum, and subcutaneous nodules.[1][2]

Why the other options are incorrect:

- **Renal failure (A)** — a feature of **post-streptococcal glomerulonephritis**, which is a separate, non-rheumatic sequela of GAS infection and does not overlap with ARF.
- **Hepatomegaly (B)** — not a recognized manifestation of ARF.

- **Pleural effusion (D)** — not a typical feature. While carditis (valvulitis, pericarditis) occurs in 50–70% of ARF cases, isolated pleural effusion is not among the Jones criteria manifestations.[2]

Notably, **subcutaneous nodules** are almost never the sole major manifestation of ARF and are strongly associated with concurrent **carditis**, so echocardiographic evaluation for valvulitis would also be essential in this patient.[1][2]

Would you like to explore the recommended secondary prophylaxis regimen for preventing recurrent ARF and rheumatic heart disease?

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Question 541

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?

A. Slit-lamp examination
B. Electrocardiogram
C. Prolactin level
D. Complete blood count

https://openevidence.com/ask/a5e9dc4f-410e-4f10-a91c-15a1064cebe6

The answer is **D. Complete blood count**.

Clozapine carries a risk of severe neutropenia and agranulocytosis, a rare but potentially fatal adverse effect that mandates regular monitoring of the **absolute neutrophil count (ANC)**, obtained via a **complete blood count (CBC)**.[1] Per the FDA-approved Clozapine REMS program, the monitoring schedule is:[1]

- **Weeks 1–26 (first 6 months): weekly** ANC
- **Months 7–12: every 2 weeks**
- **Month 13 onward: monthly**

Since this patient started clozapine only **2 weeks ago**, he is well within the highest-risk period — the risk of severe neutropenia is greatest during the **first 18 weeks** of treatment.[1][2] A CBC with ANC should be obtained weekly at this stage before clozapine can be dispensed.

Why not the other options?

- **A. Slit-lamp examination** — Associated with **quetiapine** (lens opacities in animal studies) and long-term use of **chlorpromazine/thioridazine** (corneal and lenticular deposits). Not a standard clozapine monitoring requirement.

- **B. Electrocardiogram** — A baseline ECG is reasonable before clozapine initiation, and clozapine can cause myocarditis and ECG changes. However, **ongoing mandatory monitoring** for clozapine is hematologic, not electrocardiographic.[3]
- **C. Prolactin level** — Hyperprolactinemia is most associated with **typical antipsychotics** and **risperidone/paliperidone**. Clozapine has relatively minimal prolactin-elevating effects and does not require routine prolactin monitoring.

Would you like to explore the monitoring and early detection of clozapine-induced myocarditis?

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Question 542

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?

A. Human immunodeficiency virus infection
B. Hypertrophic cardiomyopathy
C. Adrenocortical insufficiency
D. Pheochromocytoma

https://openevidence.com/ask/aaf40abc-0882-40b6-a7f0-3f646e744292

The correct answer is **C. Adrenocortical insufficiency**.

This presentation — a child with a URI prodrome, rapid deterioration with loss of consciousness, **petechial rash**, **neck rigidity**, fever, and **hemodynamic collapse** — is classic for **fulminant meningococcal septicemia** (meningococcemia).[1] The most likely cause of his hypotension is **Waterhouse-Friderichsen syndrome**, characterized by **bilateral hemorrhagic infarction of the adrenal glands** resulting in acute adrenocortical insufficiency and cardiovascular collapse.[2][3]

Meningococcal endotoxin triggers massive disseminated intravascular coagulation (DIC), and the highly vascular adrenal glands are particularly susceptible to hemorrhagic necrosis during endotoxemia, especially when the adrenal cortex is already stimulated by the stress of infection.[4] This leads to an abrupt loss of cortisol production, contributing to refractory hypotension. Studies in children with meningococcal sepsis have confirmed that nonsurvivors have significantly lower cortisol-to-ACTH ratios, indicating inadequate adrenal response.[5] Corticosteroid replacement is a component of treatment.[6]

Why not the other options:

- **A (HIV):** While HIV can cause chronic adrenal insufficiency, it would not cause this acute presentation with petechial rash and meningismus.
- **B (Hypertrophic cardiomyopathy):** Causes outflow obstruction and syncope but does not explain the infectious syndrome with petechiae and neck rigidity.
- **D (Pheochromocytoma):** Characteristically causes **hypertension** (from catecholamine excess), not hypotension, and does not fit this clinical picture.

Would you like to explore the empiric antibiotic regimen and role of adjunctive dexamethasone in pediatric bacterial meningitis?

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Question 543

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?

A. Ketamine
B. Midazolam
C. Propofol
D. Etomidate

https://openevidence.com/ask/6a793f20-c11c-4a11-a060-a42946a30cd1

The correct answer is **A. Ketamine**.

Ketamine, an **NMDA receptor antagonist**, is the agent that reduces the risk of postoperative opioid-induced hyperalgesia (OIH) when administered intraoperatively.[1][2] This clinical scenario describes a chronic opioid user experiencing intense pain despite adequate PCA dosing — a hallmark of OIH, in which prolonged opioid exposure paradoxically enhances pain sensitivity through NMDA receptor-mediated central sensitization.

Mechanism: Low-dose ketamine blocks NMDA receptors, which play a central role in the wind-up phenomenon, central sensitization, and OIH.[1] By antagonizing these receptors, ketamine attenuates the development of opioid tolerance and hyperalgesia — effects demonstrated in both animal models and clinical trials.[2][3]

Clinical evidence: Consensus guidelines from the American Society of Regional Anesthesia specifically recommend consideration of ketamine for **opioid-tolerant and opioid-dependent patients** undergoing surgery.[4][5] A meta-analysis of 9 RCTs (802 opioid-using patients) found that perioperative ketamine reduced cumulative opioid consumption by ~97 mg at 24 hours and ~186 mg at 48 hours, and was described as a "useful anti-hyperalgesic adjuvant" in this population.[6] In a blinded RCT of 147 opioid-dependent patients undergoing lumbar fusion, intraoperative ketamine (0.5 mg/kg bolus + 0.25 mg/kg/h infusion) significantly reduced 24-hour morphine consumption (79 vs. 121 mg, $p < 0.001$) without increased hallucinations or nightmares.[3]

Why not the other choices:

- **Midazolam** (B) — a benzodiazepine with no anti-hyperalgesic properties
- **Propofol** (C) — a GABA-ergic sedative-hypnotic; does not target NMDA-mediated hyperalgesia
- **Etomidate** (D) — a GABA-ergic induction agent; no role in preventing OIH

Would you like to explore specific ketamine dosing protocols for perioperative use in opioid-tolerant patients?

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Question 544

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?

A. Antibiotics
B. Carotid massage
C. Clonazepam
D. Propranolol

https://openevidence.com/ask/43b156dd-a963-4b69-81b7-cf32fbb5f494

The answer is **D. Propranolol**.

This presentation is classic for **thyroid storm** — a life-threatening decompensation of thyrotoxicosis. The key features include a patient with known Graves' disease (goiter, exophthalmos, methimazole use) who **discontinued antithyroid medication** ~1 week ago and developed an **intercurrent infection** (URI), both recognized precipitants.[1][2] The clinical picture of **high fever (105°F), tachycardia (145/min), hypotension, altered mentation, agitation, diaphoresis, vomiting, and tremor** fulfills diagnostic criteria for thyroid storm.[1][3]

Why propranolol?

Among the answer choices, **propranolol** is the cornerstone of immediate symptomatic management. Per the 2016 American Thyroid Association (ATA) guidelines, propranolol (60–80 mg every 4 hours) is recommended to counteract the adrenergic hyperactivation driving the tachycardia, agitation, tremor, and diaphoresis.[2] Propranolol is preferred over other beta-blockers in this setting because it also **inhibits peripheral T4-to-T3 conversion** at high doses, providing an additional therapeutic benefit.[2][4]

Why not the other choices?

- **A. Antibiotics** — While the precipitating URI should be addressed, antibiotics alone do not treat the thyrotoxic crisis itself and are not the best initial intervention.
- **B. Carotid massage** — This is a vagal maneuver for supraventricular tachycardia, which is not the mechanism of this patient's sinus tachycardia driven by thyroid hormone excess.
- **C. Clonazepam** — Benzodiazepines may address agitation but do not treat the underlying hyperadrenergic state or reduce thyroid hormone effects.

Complete thyroid storm management also includes **thionamides** (propylthiouracil preferred), **inorganic iodine** (given ≥1 hour after thionamides), **glucocorticoids** (hydrocortisone 300 mg IV load, then 100 mg every 8 hours), and **ICU-level supportive care**.[2][3][5] Acetaminophen rather than salicylates should be used for fever, as salicylates increase free T3/T4 by displacing them from binding proteins.[4]

Would you like to explore the complete stepwise pharmacologic protocol for thyroid storm management?

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Question 545

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?

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

https://openevidence.com/ask/94450253-830f-4fb8-b1de-b35be55975cc

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The answer is **A. Constriction of afferent arteriole and no effect on efferent arteriole**.

This vignette describes **Reye syndrome** — a biphasic illness in which a child develops a viral prodrome (fever, cough), receives **aspirin** (an OTC salicylate), and then presents with profuse vomiting, encephalopathy (lethargy, confusion), and **hepatomegaly** from acute hepatic steatosis.[1][2] The strong epidemiological association between aspirin use during viral illness in children and Reye syndrome led to public health warnings beginning in the 1980s, after which incidence declined dramatically.[2][3]

Aspirin's renal effect stems from its inhibition of cyclooxygenase (COX), which reduces synthesis of vasodilatory prostaglandins (PGE2 and PGI2). These prostaglandins normally **dilate the afferent arteriole** to maintain renal blood flow, particularly in states of reduced perfusion.[4][5] By blocking their synthesis, aspirin causes **unopposed vasoconstriction of the afferent arteriole**, reducing glomerular perfusion pressure and GFR.[6][7] Aspirin has **no direct effect on the efferent arteriole**, which is primarily regulated by angiotensin II.

The other choices can be eliminated by understanding the distinct nephron pharmacology:

- **B** (afferent dilation) — describes the prostaglandin effect itself, not the result of blocking it
- **C** (efferent constriction) — describes the action of **angiotensin II**
- **D** (efferent dilation) — describes the action of **ACE inhibitors or ARBs**

Would you like to explore the clinical staging and management of Reye syndrome?

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Question 546

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?

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

https://openevidence.com/ask/e826fb46-9c28-4bcf-acd7-9691c4e60b95

The correct answer is **D. It competes with acetylcholine for binding sites in the neuromuscular junction**.

Atracurium is a **nondepolarizing neuromuscular blocking agent** used as an adjunct to general anesthesia to facilitate endotracheal intubation and provide skeletal muscle relaxation during surgery. Per the FDA label, nondepolarizing agents "antagonize the neurotransmitter action of acetylcholine by **binding competitively with cholinergic receptor sites on the motor end-plate**". [1][2] This competitive antagonism is reversible with acetylcholinesterase inhibitors such as neostigmine.[1] A review in the NEJM similarly describes that nondepolarizing agents "compete with acetylcholine to bind to an α subunit" of the nicotinic receptor, preventing ion channel opening and producing flaccid paralysis.[3]

The other answer choices describe different drug classes:

- **A (reduces neuron and muscle tissue excitability)** — describes local anesthetics (Na^+ channel blockers), not neuromuscular blockers.
- **B (increases GABA-linked chloride channel opening)** — describes the mechanism of barbiturates or benzodiazepines, which are CNS depressants, not neuromuscular blockers.
- **C (acts on pain centers in the spinal cord and brain)** — describes opioid analgesics, which modulate nociception centrally. Atracurium has no analgesic properties.

In this anesthesia protocol, **nitrous oxide** and **desflurane** serve as the inhaled anesthetics (providing amnesia, analgesia, and unconsciousness), while **atracurium** provides the skeletal muscle paralysis necessary for surgical access during hysterectomy.[1][4]

Would you like to explore the unique organ-independent metabolism of atracurium via Hofmann elimination and its clinical implications?

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Question 547

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?

A. Chediak-Higashi syndrome
B. Wiskott-Aldrich syndrome
C. Paroxysmal nocturnal hemoglobinuria
D. Hereditary angioedema

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The correct answer is **D. Hereditary angioedema (HAE)**.

This presentation is classic for **HAE with C1-inhibitor deficiency (Type I)**. Every feature aligns:

- **Recurrent, nonpruritic angioedema** affecting the face, hands, and neck, with episodes lasting **2–3 days** — typical attack duration peaks at ~24 hours and resolves over 48–72 hours.[1][2]
- **Abdominal pain** from submucosal intestinal edema, which can mimic acute abdomen.[1][3]
- **Oropharyngeal involvement** (difficulty eating and swallowing) — laryngeal/oropharyngeal attacks occur in over 50% of patients during their lifetime and represent the most life-threatening manifestation.[1][4]
- **Onset in childhood with worsening in young adulthood** — HAE typically manifests in childhood and worsens around puberty.[1][5]

- **Autosomal dominant inheritance** — the mother and maternal aunt are affected, consistent with the inheritance pattern. The unaffected father supports maternal transmission of the SERPING1 mutation.[5]
- **Extremely low C1-inhibitor levels** — the hallmark laboratory finding of Type I HAE (~85% of cases), which results from mutations in the SERPING1 gene leading to reduced production of functional C1-inhibitor protein.[5][6]

The other choices are not consistent with this presentation:

- **Chediak-Higashi syndrome** — an autosomal recessive disorder of lysosomal trafficking characterized by partial oculocutaneous albinism, recurrent pyogenic infections, and giant granules in leukocytes.
- **Wiskott-Aldrich syndrome** — an **X-linked** disorder presenting with thrombocytopenia, eczema, and immunodeficiency; would not present in a female with this pattern.
- **Paroxysmal nocturnal hemoglobinuria** — an acquired complement-mediated hemolytic anemia with hemoglobinuria and thrombosis; not hereditary and not associated with angioedema or C1-inhibitor deficiency.

Would you like to explore the current treatment options for acute attacks and long-term prophylaxis in hereditary angioedema?

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Question 548

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?

A. Urge incontinence
B. Vesicovaginal fistula
C. Fecal incontinence
D. Stress incontinence

https://openevidence.com/ask/06755e4e-52b2-4bc2-8efd-4a323a7120e2

The answer is **C. Fecal incontinence**.

A **third-degree perineal laceration** involves the **anal sphincter complex** — specifically, the external anal sphincter (and potentially the internal anal sphincter depending on subclassification 3a–3c).[1] A midline laceration at the 6 o'clock position extending into the perineum is the classic trajectory for obstetric anal sphincter injury (OASIS). The most clinically significant long-term consequence of this injury is **anal/fecal incontinence** due to disruption of the sphincter mechanism.[2][3]

Supporting this case, the patient has multiple risk factors for OASIS: **nulliparity, macrosomia** (90th percentile, gestational diabetes), and **operative vaginal delivery** (vacuum-assisted).[4][5] Long-term follow-up data estimate that **more than 50% of women** experience some form of anal incontinence following OASIS, and incontinence rates are directly related to the severity of the sphincter defect.[3][6]

Why the other options are less likely:

- **A. Urge incontinence** — Results from detrusor overactivity; not a direct consequence of perineal/anal sphincter disruption.
- **B. Vesicovaginal fistula** — Classically associated with prolonged obstructed labor causing pressure necrosis of the vesicovaginal septum, not perineal lacerations.

- **D. Stress incontinence** — Related to urethral hypermobility and pelvic floor laxity; while pelvic floor trauma from vaginal delivery can contribute, a third-degree laceration specifically damages the **posterior** perineal structures (anal sphincter), making fecal incontinence the more direct and characteristic complication.

Would you like to explore the recommended repair techniques and postpartum management for obstetric anal sphincter injuries?

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Question 549

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?

A. Phyllodes tumor
B. Fibroadenoma
C. Fibrocystic disease of the breast
D. Invasive lobular carcinoma

https://openevidence.com/ask/1e17a345-92df-4100-8d73-cc6caf01eb70

The answer is **A. Phyllodes tumor**.

The constellation of findings in this case is classic for a phyllodes tumor:

- **Rapid growth** of a large (5 cm) breast mass is a hallmark clinical feature. Phyllodes tumors typically present as a rapidly enlarging, previously stable mass, with an average size of 4–5 cm.[1][2]
- **Age of 45** aligns with the median age of presentation of 40–45 years, which is 1–2 decades later than fibroadenomas.[2]
- **Smooth polylobulated mass on mammography** is characteristic; these tumors appear as round or lobulated, well-circumscribed, benign-appearing opacities.[3][4]
- **Biopsy showing papillary projections of epithelial-lined stroma with hyperplasia and atypia** describes the defining histological feature: **leaf-like (phyllodes) architecture** in which hypercellular stromal fronds lined by epithelium project into cystically dilated spaces, with stromal hypercellularity and atypia.[1][5][6]

Why not the other choices:

- **Fibroadenoma (B):** Typically presents in women in their 20s–30s, is smaller, grows slowly, and lacks the pronounced stromal hypercellularity, leaf-like fronds, and atypia seen here.[1] [7]
- **Fibrocystic disease (C):** Presents with diffuse lumpiness and tenderness rather than a discrete, rapidly growing multinodular mass, and has entirely different histology (cysts, apocrine metaplasia, fibrosis).
- **Invasive lobular carcinoma (D):** Characterized by single-file infiltration of small neoplastic epithelial cells with loss of E-cadherin, not a biphasic fibroepithelial pattern with stromal fronds.

Would you like to explore surgical management and margin recommendations for phyllodes tumors?

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Question 550

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?

A. Gastroesophageal reflux disease
B. Esophageal candidiasis
C. Meckel's diverticulum
D. Zenker's diverticulum

https://openevidence.com/ask/e7fc2902-5edc-4e16-a3b1-6c33751980d2

The answer is **D. Zenker's diverticulum**.

Zenker's diverticulum is a posterior pharyngoesophageal pulsion pseudodiverticulum that forms through Killian's triangle — the area of relative weakness between the oblique fibers of the inferior pharyngeal constrictor and the horizontal fibers of the **cricopharyngeus muscle**.[1][2] The pathophysiology directly involves **cricopharyngeal dysfunction**: decreased compliance and incomplete relaxation of the upper esophageal sphincter creates a high-pressure zone, leading to mucosal herniation posteriorly.[1][3]

This presentation is classic for Zenker's diverticulum:

- **Demographics**: Most commonly affects elderly individuals (7th–8th decade), with a male predominance.[1][2]
- **Dysphagia**: The most common symptom, present in 80–90% of patients, caused by incomplete UES opening and extrinsic compression by the enlarging pouch.[1]
- **Halitosis**: Results from food debris accumulating and decomposing within the diverticulum.[2][4]
- **Cricopharyngeal muscle dysfunction**: The central pathophysiologic mechanism — fibroadipose replacement of normal muscle and connective tissue compromises sphincter elasticity and opening.[1]

Why the other options are incorrect:

- **A. GERD** — Can cause dysphagia but is not associated with cricopharyngeal dysfunction as a primary mechanism. Notably, GERD may be a contributing factor to Zenker's formation but is not the diagnosis this vignette describes.[5][6]
- **B. Esophageal candidiasis** — Causes odynophagia and dysphagia, typically in immunocompromised patients, and is unrelated to cricopharyngeal dysfunction.
- **C. Meckel's diverticulum** — A true diverticulum of the ileum (a remnant of the vitelline duct), entirely unrelated to the esophagus or cricopharyngeus.

Would you like to explore the current endoscopic treatment approaches for Zenker's diverticulum?

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Question 551

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?

A. Intravenous immunoglobulin (IVIG)
B. Prednisone
C. Botulism antitoxin
D. Gabapentin

https://openevidence.com/ask/9416c07a-0628-4932-b506-a37e6bca2647

The answer is **A. Intravenous immunoglobulin (IVIG)**.

This presentation is classic for **Guillain-Barré syndrome (GBS)**: a preceding upper respiratory infection ~3 weeks prior, **acute ascending bilateral lower extremity weakness**, distal paresthesias, and **areflexia** (absent knee and ankle jerks). The CSF demonstrates **albuminocytologic dissociation** — elevated protein (91 mg/dL) with a normal cell count (2/mm³) — which is the hallmark laboratory finding of GBS, present in ~70% of patients.[1] The normal creatine kinase argues against a primary myopathic process.

IVIG (2 g/kg over 2–5 days) is first-line therapy for GBS, and is particularly preferred over plasma exchange in children due to ease of vascular access and better tolerability.[2][3] Both IVIG and plasma exchange are equally effective in adults, but IVIG is used in ~92% of treated GBS patients overall.[4] In pediatric GBS, IVIG accelerates recovery compared to supportive care alone.[5]

Why the other options are incorrect:

- **Prednisone (B):** Corticosteroids alone are **not effective** in GBS. Methylprednisolone as an add-on to IVIG has shown only marginal short-term benefit, and steroids are not standard monotherapy.[6]
- **Botulism antitoxin (C):** Botulism causes **descending** paralysis beginning with cranial nerves (diplopia, dysphagia), not ascending weakness with areflexia and albuminocytologic dissociation.
- **Gabapentin (D):** Addresses neuropathic pain only and does not treat the underlying autoimmune demyelination driving the progressive weakness.

Would you like to explore the criteria for ICU admission and respiratory monitoring in pediatric GBS?

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Question 552

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?

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

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D. Blocks reuptake of norepinephrine and serotonin.

Clomipramine is a tricyclic antidepressant that inhibits presynaptic reuptake of both serotonin and norepinephrine by blocking SERT and NET, though its affinity for the serotonin transporter is far greater than for the norepinephrine transporter — the property that distinguishes it from other TCAs and underlies its efficacy in OCD.[1][2] Its active metabolite, desmethylclomipramine, is a relatively potent norepinephrine reuptake inhibitor, so both transporters are affected in vivo.[3][4] The FDA label attributes the anti-obsessional effect specifically to serotonin reuptake inhibition, while noting the precise neurochemical mechanism is unknown.[3]

Why the other options are wrong

- **A. Decreased degradation** describes monoamine oxidase inhibitors (phenelzine, tranylcypromine), which block enzymatic breakdown of monoamines rather than reuptake.
- **B. Alpha-2 antagonism** describes mirtazapine, a noradrenergic and specific serotonergic antidepressant that antagonizes α2-autoreceptors and heteroreceptors plus 5-HT2/5-HT3 receptors.[5]

- **C. Norepinephrine reuptake only** describes secondary amine TCAs such as desipramine and nortriptyline, or selective NRIs like reboxetine and atomoxetine. Notably, desipramine was inferior to clomipramine in OCD, which is the classic evidence that serotonergic activity is required for anti-obsessional efficacy.[1][6]

Clinical points relevant to the vignette

- Clomipramine is the only TCA FDA-approved for OCD, dosed from 25 mg daily titrated to a maximum of 250 mg/day in adults.[3][7]
- Because of anticholinergic burden, orthostatic hypotension, quinidine-like cardiac conduction slowing, and dose-dependent seizure and arrhythmia risk above 200 mg/day, SSRIs are generally preferred first-line, with clomipramine reserved for SSRI non-responders.[7][8]
- All antidepressants carry a boxed warning for increased suicidality in patients under 25 — directly applicable to this 27-year-old only at the margin, but worth monitoring early in treatment.
- CBT with exposure and response prevention is at least as effective as clomipramine monotherapy and should be emphasized: in the Foa trial, response rates were 62% for ERP, 42% for clomipramine, and 70% for combination.[9]

Would you like to explore augmentation strategies for treatment-refractory OCD?

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Question 553

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?

A. Lorazepam
B. Naltrexone
C. Methadone
D. Naloxone

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C. Methadone is the correct answer. The presentation — 3 days of anxiety, nausea, vomiting, abdominal cramping, and diarrhea with mydriasis, diaphoresis, piloerection, tachycardia, hypertension, and restlessness in a young man with chronic back pain who has relocated (losing access to his opioid prescriptions) — is classic opioid withdrawal.[1][2][3] Opioid agonists (methadone or buprenorphine) are first-line: the American Society of Addiction Medicine recommends methadone or buprenorphine over abrupt cessation, and both are more effective than α2-adrenergic agonists for reducing withdrawal severity, retaining patients, and completing withdrawal management.[4]

Why the other options are wrong

- **Lorazepam** — benzodiazepines are only adjunctive for anxiety and insomnia in opioid withdrawal and do not treat the syndrome. This would be the answer for alcohol or sedative-hypnotic withdrawal, which is not supported here (no tremor, no confusion, no alcohol history).[1][4]
- **Naltrexone** — a μ-opioid antagonist; administering it to an opioid-tolerant patient precipitates severe withdrawal. It is used for relapse prevention only after withdrawal is

complete, typically ≥7 days off short-acting and 10–14 days off long-acting opioids.[1][2][3][4]

- **Naloxone** — an antagonist for reversal of overdose (which presents with miosis, respiratory depression, and depressed consciousness — the opposite of this picture) and would likewise precipitate withdrawal.[1][4]

Practical points that the vignette simplifies

- **Setting restriction for methadone:** by federal regulation, methadone for opioid withdrawal management must be delivered in an opioid treatment program or an acute care setting; it cannot be prescribed from a general office for this indication. In an office-based encounter, **buprenorphine** is the practical equivalent choice (initial 2–4 mg once objective withdrawal signs are present, titrated to 4–16 mg/day), withheld until objective withdrawal to avoid precipitated withdrawal.[4]
- **Methadone dosing:** ASAM specifies an initial dose of 20–30 mg/day for withdrawal from short-acting opioids with taper over ~6–10 days. Dosing should be titrated to observed response given methadone's delayed accumulation, respiratory depression, and QTc-prolongation risks.[4]
- **Withdrawal management alone is not treatment.** ASAM explicitly advises against detoxification without ongoing pharmacotherapy because of relapse and overdose-death risk from lost tolerance. This patient needs assessment for opioid use disorder, linkage to maintenance treatment, a chronic pain plan, and take-home naloxone.[4]
- **Adjuncts:** loperamide for diarrhea, ondansetron for nausea, NSAIDs for myalgias.[1][5]

Quantifying severity with the COWS score guides dosing decisions and, if buprenorphine is chosen, the timing of induction:

Computed value for COWS Score: 17

Moderate withdrawal. A score between 13 and 24 indicates moderate withdrawal. Patients may require more active management to alleviate symptoms.[6]

Based on the findings described (pulse 110, observable diaphoresis, restlessness, moderately dilated pupils, vomiting/diarrhea, obvious anxiety, palpable piloerection; bone/joint aches not scored separately given baseline chronic back pain), the estimated COWS is in the moderate range (13–24), which is well above the threshold at which buprenorphine induction can be safely undertaken if that route is chosen.[1][4]

Would you like to explore how to manage this patient's chronic back pain once he is on buprenorphine or methadone?

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Question 554

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?

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

https://openevidence.com/ask/13dc5b40-a002-4d86-a8d4-cab0cfde6595

The answer is **D. Degenerative disease of the joints**.

This presentation is classic for **osteoarthritis (OA)** of the hand. OA is characterized by **cartilage degradation, bone remodeling, osteophyte formation, and synovial inflammation**, leading to pain, stiffness, swelling, and loss of joint function.[1] Several features confirm this diagnosis:

- **Distribution**: The **DIP joints and first CMC/MCP joints** are the most commonly affected sites in hand OA. Rheumatoid arthritis, by contrast, typically involves the MCP and PIP joints symmetrically, sparing the DIP joints.[2]
- **Heberden's nodes**: The discrete, hard, mildly tender nodules over the DIP joints are **pathognomonic for OA**. These firm bony swellings are strongly associated with underlying radiographic changes including osteophytes and joint space narrowing.[3][4][5]
- **Radiographic findings**: Joint space narrowing, subchondral sclerosis, and osteophytes are the hallmark radiographic features of OA.[6][7]
- **Stiffness pattern**: Stiffness **worse at the end of the day** (after activity) is characteristic of OA, in contrast to the prolonged morning stiffness (>30–60 minutes) seen in inflammatory arthritis like RA.

- **Risk factors**: Age >50, female sex, and repetitive joint use (28 years as a typist) are established risk factors.[2][8]

The other options are incorrect:

- **A (Bacterial infection)**: Septic arthritis presents acutely with a hot, swollen joint — not a 6-month progressive course affecting multiple joints.
- **B (Autoimmune-mediated cartilage erosion)**: RA characteristically involves MCP and PIP joints (not DIP), presents with prolonged morning stiffness, and shows periarticular erosions rather than osteophytes on imaging.
- **C (CPPD crystal precipitation)**: Pseudogout typically presents with acute inflammatory episodes in larger joints (knee, wrist) and shows chondrocalcinosis on imaging, not the pattern described here.

Would you like to explore the current evidence-based management of hand osteoarthritis?

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Question 555

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?

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

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A. Increased Ca^{2+} influx in phase 4.

The clinical picture — urticaria, stridor, hypotension, and abdominal pain within minutes of peanut ingestion — is anaphylaxis, and the drug given is **epinephrine**, the only first-line pharmacotherapy.[1][2][3] In the hospital setting with persistent hypotension despite IM dosing and fluids, a continuous epinephrine infusion is used.[4]

Why increased phase 4 Ca^{2+} influx

- Epinephrine stimulates **β₁ receptors** → Gs → adenylyl cyclase → ↑cAMP → PKA activation in sinoatrial nodal cells.
- The result is a **steeper slope of phase 4 (spontaneous diastolic depolarization)**, so threshold is reached sooner and heart rate rises (positive chronotropy). In the SA node, phase 4 depolarization is driven by inward currents rather than fast Na^{+} channels, and β-adrenergic stimulation augments the depolarizing Ca^{2+} -dependent currents during diastole.[5][6]
- Mechanistically this involves ↑**T-type and L-type Ca^{2+} current** availability in the diastolic voltage range plus PKA-mediated enhancement of sarcoplasmic reticulum Ca^{2+} release through ryanodine receptors, which generates inward Na^{+} /Ca^{2+} exchanger current that

accelerates late diastolic depolarization. Blockade of the slow inward Ca^{2+} current abolishes epinephrine's ability to steepen diastolic depolarization. cAMP also directly shifts activation of the funny current (I_f) to more positive voltages, contributing to the same effect.[6][7][8][9][10]

Why the other options are wrong

- **B. Increased Na^{+} influx in phase 3** — Phase 3 in pacemaker cells is repolarization driven by K^{+} efflux with Ca^{2+} channel inactivation; there is no significant Na^{+} influx, and fast Na^{+} channels are largely absent/inactivated in SA nodal cells.
- **C. Decreased Ca^{2+} influx in phase 0** — Phase 0 of the pacemaker action potential is generated by L-type Ca^{2+} current. Epinephrine **increases** this current (raising upstroke velocity and conduction); **decreasing** it is the effect of non-dihydropyridine calcium channel blockers or β-blockers.[5]
- **D. Decreased K^{+} efflux during phase 3** — β-adrenergic stimulation actually **accelerates repolarization** (increased I_Ks/I_K). Decreased K^{+} efflux prolonging phase 3 describes class III antiarrhythmics.[5][6]

Note that epinephrine's benefit in anaphylaxis is not primarily chronotropic: **α_1-mediated vasoconstriction** reverses hypotension and mucosal edema, **β_2 activation** produces bronchodilation and inhibits further mast cell mediator release, and **β_1 effects** provide inotropy and chronotropy. Antihistamines and corticosteroids are adjunctive only and do not interrupt mast cell degranulation.[1][11]

Would you like to explore dosing and titration of continuous IV epinephrine infusions in refractory pediatric anaphylaxis?

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Question 556

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?

A. Complete blood count
B. Cranial ultrasonography
C. Head CT
D. MRI of the head

https://openevidence.com/ask/6695aca4-d16c-456c-a784-0ffe062a3df6

B. Cranial ultrasonography.

This is a 31-week, 1400 g infant on day 3 of life with a catastrophic neurologic syndrome — seizures, stupor with decreased spontaneous and elicited movement, hypotonia, bulging fontanelle, hypotension, bradycardia, and hypoventilation. That constellation is the classic presentation of **severe germinal matrix–intraventricular hemorrhage (GMH-IVH)**, and bedside cranial ultrasound through the anterior fontanelle is the diagnostic study of choice.

Why cranial ultrasound

- **cUS is the primary diagnostic modality for IVH** in preterm infants, allowing detection, Papile grading, and serial monitoring for post-hemorrhagic ventricular dilatation.[1][2]
- It is **portable, radiation-free, and performed at the bedside**, which matters in a hemodynamically unstable, hypoventilating 1400 g infant who should not be transported to CT or MRI.[3]
- The American College of Radiology practice parameter lists **seizures and other signs of CNS disorder, suspected hemorrhage, and ventriculomegaly** as explicit indications for neurosonography in neonates.[4]

- Timing fits: GMH-IVH onset clusters at **24–48 hours after birth**, with most events in the first 3 days of life.[2][5]

Why not the others

- **Head CT (C):** The AAP states CT is **no longer part of routine imaging of the preterm brain** and should be avoided in most instances, given ionizing radiation and the need for transport.[3]
- **MRI (D):** More sensitive than cUS for small, posterior fossa, and cerebellar hemorrhages and for white matter injury, but it requires transport and prolonged imaging in an unstable neonate; it is a **later, prognostic study (typically at term-equivalent age)**, not the acute diagnostic step.[1][3]
- **CBC (A):** Reasonable adjunctively — a **falling hematocrit** supports acute hemorrhage, and sepsis/coagulopathy are in the differential for a decompensating neonate — but it does not establish the diagnosis or grade the lesion.

Concurrently, not instead of imaging

Stabilize the airway and blood pressure, treat seizures (phenobarbital remains first-line in most NICUs), check glucose, electrolytes, calcium, blood gas, coagulation studies, and obtain blood culture with empiric antibiotics if sepsis or meningitis is plausible. Note that the AAP notes routine screening cUS at 7–10 days for infants ≤30 weeks, but **earlier scanning is indicated when clinical signs suggest significant brain injury**, as here.[3]

Would you like to explore management of post-hemorrhagic ventricular dilatation after severe IVH?

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Question 557

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?

A. Aortic stenosis
B. Cardiac tamponade
C. Hypertrophic cardiomyopathy
D. Third-degree heart block

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The answer is **C. Hypertrophic cardiomyopathy (HCM)**. This presentation is classic for obstructive HCM, with three cardinal findings pointing to this diagnosis:

Systolic ejection murmur augmented by Valsalva — "Forceful expiration against a closed airway" describes the Valsalva maneuver. The Valsalva decreases venous return (preload), which worsens dynamic left ventricular outflow tract (LVOT) obstruction and makes the HCM murmur louder. This is a key distinguishing feature: **most murmurs decrease in intensity with Valsalva, but HCM is one of only two exceptions** (the other being mitral valve prolapse).[1][2] In contrast, the murmur of **aortic stenosis decreases** with Valsalva.[3] The murmur of HCM is classically a harsh crescendo-decrescendo systolic murmur heard best between the apex and left sternal border, exactly as described.[4][5]

Pulsus bisferiens on carotid palpation — The two closely spaced systolic pulses represent a **bisferiens pulse**, which occurs in obstructive HCM due to dynamic LVOT obstruction. The arterial pulse has a rapid upstroke and downstroke, followed by a palpable reflected wave when obstruction transiently relieves.[6] This results from transient mid-systolic obstruction of the LVOT creating two distinct pressure peaks.[7][8] This contrasts with aortic stenosis, which produces **pulsus parvus et tardus** (a weak, slow-rising pulse).

Syncope and exertional dyspnea in a young patient — These are hallmark symptoms of obstructive HCM, resulting from LVOT obstruction that worsens with exertion (decreased preload, increased contractility).[5][9]

The other choices are incorrect:

- **Aortic stenosis** — murmur decreases with Valsalva and produces pulsus parvus et tardus, not bisferiens
- **Cardiac tamponade** — presents with hypotension, muffled heart sounds, and pulsus paradoxus, not a systolic ejection murmur
- **Third-degree heart block** — presents with bradycardia and hemodynamic compromise, not this murmur pattern

Would you like to explore the current treatment approach for symptomatic obstructive HCM, including the role of mavacamten?

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Question 558

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?

A. Prescribe levothyroxine 50 mcg daily
B. No specific management required
C. Recommend additional anti-TPO test
D. Recommend additional T3 assessment

https://openevidence.com/ask/e947e0b9-2712-45c6-bde5-3de88e4e7012

The answer is **B. No specific management required**.[1][2][3]

This patient's thyroid profile is entirely consistent with **normal physiological changes of pregnancy** at 18 weeks gestation:

- **TSH 0.3 mU/L** — Pregnancy physiologically lowers TSH due to hCG stimulation of the TSH receptor. A TSH below 0.4 mU/L is observed in ~10% of healthy women in the second trimester. This value is not indicative of hyperthyroidism given the normal free T4.[3]
- **Total T4 160 nmol/L** — Expected to be elevated. Per ACOG and ATA guidelines, TBG rises significantly by week 16 of gestation, and the **total T4 upper reference limit should be increased by ~50%** after 16 weeks. A US population study confirmed a second-trimester total T4 reference range of **66.6–176.0 nmol/L**, placing 160 nmol/L well within normal.[1][2]
- **Free T4 13 pmol/L** — Normal. Second-trimester free T4 reference ranges from the same US population study were **10.2–16.6 pmol/L**. Free T4 is the most clinically meaningful value here, and it is mid-range.[2]

Why the other options are incorrect:

- **A (Levothyroxine)** — Levothyroxine is indicated for hypothyroidism (elevated TSH ± low free T4). This patient's TSH is low-normal and free T4 is normal, so there is no indication.
- **C (Anti-TPO testing)** — Anti-TPO antibodies are clinically relevant when subclinical hypothyroidism is detected (elevated TSH with normal free T4), as TPO positivity increases the risk of progression and adverse pregnancy outcomes. With a normal thyroid profile, anti-TPO testing is not indicated.[4]
- **D (T3 assessment)** — T3 measurement is useful when hyperthyroidism is suspected (suppressed TSH with elevated free T4) to evaluate for T3-predominant thyrotoxicosis. This patient's profile does not suggest hyperthyroidism.[1]

The fatigability and depressed mood, while warranting clinical attention (including screening for perinatal depression and evaluation for anemia), are **not explained by thyroid dysfunction** based on these results.

Would you like to explore when levothyroxine treatment is indicated for subclinical hypothyroidism in pregnancy?

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Question 559

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?

A. Advise the patient to stop masturbating
B. Measure serum testosterone level
C. Reassure the mother
D. Prescribe sertraline

https://openevidence.com/ask/efbfcc8d-d8ca-4273-a71c-c2094e5fc09e

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C. Reassure the mother. Masturbation in a 15-year-old boy is a normal, expected component of adolescent sexual development, and this teen has no red flags — he is functioning well academically, holds a leadership position on his wrestling team, and has a normal physical examination. The only "abnormality" is that the behavior occurred in his bedroom, a private space, and was discovered by his mother.

Why reassurance is correct

- Masturbation is the most common adolescent sexual behavior in males. In a nationally representative US sample, 73.8% of males aged 14–17 reported ever masturbating, with 62.6% of 14-year-olds reporting at least one prior occurrence.[1]
- The American Academy of Pediatrics and ACOG explicitly recognize masturbation as **a normal component of child and adolescent development**, and recommend that clinicians educate and reassure patients and families about it during preventive visits.[1]
- It carries **no risk of pregnancy or sexually transmitted infection** and is associated with normal, and in males higher, condom-use rates — it is not a marker of pathology.[1]

Practical management at the visit

- Normalize the behavior for the mother, and counsel on **respecting the adolescent's privacy** (knocking before entering) — framing the issue as one of household boundaries rather than the son's behavior.
- Spend part of the visit **alone and confidentially with the patient**, using a HEADSS-type framework, both to avoid shaming him and to screen sexual activity, mood, and substance use. Confidentiality policy should ideally have been reviewed with both patient and parent.[2]
- Use the encounter for age-appropriate male sexual and reproductive health anticipatory guidance — STI/HIV risk, condom use, HPV vaccination status — which is under-delivered to adolescent males.[3]

Why the other options are wrong

- **A. Advise him to stop** — instructing an adolescent to stop a normal developmental behavior induces guilt and shame and has no medical basis; negative attitudes toward masturbation have been linked to worse subsequent sexual experiences.[1]
- **B. Serum testosterone** — there is nothing here suggesting a pubertal or endocrine disorder; masturbation frequency in a normally developing 15-year-old is not an indication for hormonal testing.
- **D. Sertraline** — no psychiatric diagnosis is present. An SSRI would be inappropriate and would risk iatrogenic sexual dysfunction.

When further evaluation would be warranted: masturbation that is **public, compulsive, interferes with school/social functioning or sleep, causes genital injury**, or occurs alongside other concerning behaviors, developmental disability with boundary issues, or signs of sexual abuse. In those settings, behavioral strategies (redirection to private space, structured boundaries, behavior therapy) rather than prohibition are recommended.[4] None of these features are present here.

Would you like to explore how to structure the confidential HEADSS interview and its legal limits with adolescent patients?

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Question 560

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?

A. Etanercept
B. Moxonidine
C. Sacubitril
D. Aliskiren

https://openevidence.com/ask/cc8af849-61e6-4c35-9ad4-4cf7271e21e1

The answer is **C. Sacubitril**.

This patient presents with **heart failure with preserved ejection fraction (HFpEF)** based on exertional dyspnea, paroxysmal nocturnal dyspnea, bibasilar crackles, tender hepatomegaly, elevated BNP, enlarged left atrium, and an **EF of 55%** in the setting of longstanding hypertension. **Sacubitril** is a neprilysin inhibitor that, when combined with valsartan as a fixed-dose ARNI (sacubitril/valsartan), reduces cardiovascular and HF hospitalization events in HFpEF.[1][2] Importantly, sacubitril/valsartan replaces the standalone ARB rather than being added on top of it, to avoid excessive RAAS blockade.

In the **PARAGON-HF** trial (4,822 patients with LVEF ≥45%), sacubitril/valsartan compared with valsartan alone showed a modest reduction in the composite of total HF hospitalizations and cardiovascular death (rate ratio 0.87; 95% CI 0.75–1.01), with **greater benefit in patients with LVEF at or below the median of 57%**.[3][4] Pooled analyses of PARAGLIDE-HF and PARAGON-HF confirmed significant reductions in worsening HF events and cardiovascular death (RR 0.86; 95% CI 0.75–0.98), particularly in those with LVEF ≤60%.[1] The FDA has expanded the indication for

sacubitril/valsartan to include chronic HF regardless of LVEF, with benefits most clearly evident in patients with LVEF below the normal range.[4] The 2022 AHA/ACC/HFSA guidelines give a **Class 2b recommendation** for ARNI use in HFpEF.[3]

Why the other options are incorrect:

- **Etanercept (A):** A TNF-α inhibitor that showed **no clinical benefit** in HF in the RENAISSANCE and RECOVER trials, and TNF-α inhibitors can worsen HF, particularly in older patients.[5]
- **Moxonidine (B):** A centrally acting α_2-agonist/imidazoline receptor agonist. The MOXCON trial was **terminated prematurely due to increased mortality** (5.5% vs. 3.4% with placebo) in NYHA class II–IV HF patients, likely from excessive sympathetic withdrawal.[5]
- **Aliskiren (D):** A direct renin inhibitor. The **ASTRONAUT trial** showed no benefit and increased hyperkalemia, hypotension, and renal impairment when added to standard HF therapy. The fixed combination of aliskiren + valsartan (Valturna) was **withdrawn by the FDA** due to harm in patients with diabetes or renal disease.[6][7][8]

Would you like to explore the role of SGLT2 inhibitors as foundational therapy for HFpEF?

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Question 561

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?

A. Focal segmental glomerulosclerosis
B. Membranous nephropathy
C. Minimal change disease
D. Amyloidosis

https://openevidence.com/ask/d4775c70-97b6-443c-a5d8-7b87720d2ad0

The answer is **C. Minimal change disease**.

This patient presents with classic **nephrotic syndrome** — edema, severe hypoalbuminemia (1.9 g/dL), heavy proteinuria (4+), and fatty casts (oval fat bodies) — in the setting of **Hodgkin's lymphoma**. **Minimal change disease is the most well-established paraneoplastic glomerular lesion associated with Hodgkin's lymphoma**, a relationship attributed to dysregulated T-cell function and elaboration of lymphokines (including a circulating permeability factor) by abnormal T lymphocytes that increase glomerular capillary permeability.[1][2][3]

Why the other options are less likely:

- **A. Focal segmental glomerulosclerosis (FSGS)** — Can cause nephrotic syndrome and has been reported with lymphomas, but it is not the classic paraneoplastic association with Hodgkin's disease.[4]
- **B. Membranous nephropathy** — The most common paraneoplastic glomerulopathy associated with **solid tumors** (lung, colon, prostate), not with Hodgkin's lymphoma.[2][3]

- **D. Amyloidosis** — Although AA amyloidosis can occur with Hodgkin's disease, it is far less common than MCD in this setting. Amyloidosis typically presents with Congo red–positive deposits and would show amyloid fibrils on electron microscopy rather than the podocyte foot process effacement characteristic of MCD.[5]

Key associations to remember:

- **Hodgkin's lymphoma → Minimal change disease** (T-cell–mediated mechanism)[6][7]
- **Solid tumors → Membranous nephropathy** (immune complex–mediated mechanism)[2][3]

Notably, nephrotic syndrome in this setting typically **remits with successful treatment of the lymphoma** and may relapse with disease recurrence, further supporting its paraneoplastic nature.[6][8]

Would you like to explore the management approach for paraneoplastic minimal change disease in Hodgkin lymphoma?

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Question 562

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?

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

https://openevidence.com/ask/1a2505d5-49d3-4d80-a4ff-9847ebcf79e6

The correct answer is **C. Type IV–cell-mediated (delayed) hypersensitivity reaction**.

This presentation — **red, scaly, tender plaques on the ear lobules** following exposure to new earrings — is classic for **nickel allergic contact dermatitis (ACD)**, the most common cause of jewelry-related contact dermatitis. "Silver" costume jewelry frequently contains nickel alloys, and earring posts are a leading source of nickel sensitization, particularly in children.[1][2]

Nickel ACD is a delayed-type (Type IV) hypersensitivity reaction mediated by T cells (primarily Th1 and Th17), not antibodies.[1][3] It proceeds through two phases:

- **Sensitization phase**: Nickel ions penetrate the skin and activate dendritic cells via Toll-like receptor 4 (TLR4). These cells migrate to regional lymph nodes and present nickel-modified peptides via MHC II to naive CD4+ T cells, generating allergen-specific memory T cells.[3]
- **Elicitation phase**: On re-exposure, nickel is captured by dendritic cells and presented to effector and memory T cells, triggering inflammation and the clinical eczematous reaction — typically within **48–72 hours** of contact.[1][4]

While rare reports of Type I (immediate) hypersensitivity to nickel exist, the AAP guidelines note that even rapid-onset nickel reactions are most likely delayed-type hypersensitivity, as Type IV reactions can manifest as early as 10–30 minutes in highly sensitized individuals.[1] There is no role for immune complex (Type III) mechanisms in standard contact dermatitis to metals.

Would you like to explore treatment and prevention strategies for nickel contact dermatitis in pediatric patients?

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Question 563

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?

A. Autosomal dominant
B. Autosomal recessive
C. Multifactorial
D. X-linked dominant

https://openevidence.com/ask/7b2bfe06-d42c-46fe-8edb-c28d903eaf49

The answer is **A. Autosomal dominant**.

The clinical scenario — a young woman with a **total colectomy**, **annual colonoscopies since age 10**, and a **father with a colon condition** — is classic for **familial adenomatous polyposis (FAP)**. FAP is caused by germline pathogenic variants in the **APC tumor suppressor gene** on chromosome 5q21 and is inherited in an **autosomal dominant** pattern.[1][2][3]

Key features supporting the diagnosis of FAP:

- **Onset of surveillance at age 10:** NCCN and ASGE guidelines recommend initiating colonoscopy screening at **age 10–15** in individuals at risk for classic FAP, consistent with this patient's history.[4][5]
- **Total colectomy:** Prophylactic colectomy is the standard treatment once polyp burden becomes unmanageable, as untreated classic FAP carries a **near-100% lifetime risk of colorectal cancer**.[1][4]
- **Affected father:** FAP follows autosomal dominant inheritance with close to 100% penetrance, so an affected parent confers a 50% risk to each child. Approximately 25–30% of FAP cases arise from de novo APC mutations, but in this case a clear paternal history is present.[2][3][6]

The autosomal recessive polyposis syndrome to differentiate is **MUTYH-associated polyposis (MAP)**, caused by biallelic MUTYH variants. MAP typically presents with fewer adenomas (10–

100), later onset, and would not follow a dominant pedigree pattern (affected parent-to-child transmission).[5][7][8]

Would you like to explore post-colectomy surveillance strategies for FAP, including upper GI and extracolonic cancer screening?

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Question 564

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?

A. Rationalization
B. Fantasy
C. Distortion
D. Intellectualization

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The answer is **A. Rationalization**.

This patient's response is a classic example of **rationalization** — he is providing a seemingly logical justification ("being overweight runs in my family") for his unhealthy eating behavior to avoid confronting the uncomfortable reality that his significant weight gain (BMI 27 → 32 kg/m² in one year) is likely attributable to his own dietary choices.[1] Rationalization involves offering a plausible but self-serving explanation to justify behavior that is otherwise difficult to accept. The hallmark of rationalization is that the rationale offered, while potentially containing a kernel of truth, serves primarily to **hide a more salient motive** and allows the individual to avoid experiencing deeper feelings about the problem.[1]

Why the other options are incorrect:

- **Fantasy (B):** Involves retreating into an imaginary world or daydreaming to escape reality. The patient is not engaging in wishful daydreaming; he is offering a concrete excuse.
- **Distortion (C):** Involves grossly reshaping external reality to meet internal needs, often at a psychotic level (e.g., unrealistic grandiosity or delusions). The patient is not distorting reality — he acknowledges he is overweight.
- **Intellectualization (D):** Involves using abstract, generalized thinking to distance oneself from the emotional aspects of a situation (e.g., discussing a diagnosis in purely academic or scientific terms). The patient is not abstracting or generalizing; he is making a specific

excuse. The distinction is that intellectualization removes **affect** from the idea, while rationalization provides a **false but plausible reason** to justify behavior.[1]

Rationalization is classified as a **disavowal-level (immature) defense mechanism**, along with denial and projection, reflecting the individual's refusal to acknowledge their own role in a problem.[1]

Would you like to explore the clinical significance and hierarchy of mature versus immature defense mechanisms?

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Question 565

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?

A. CAGE questions
B. Uretheral swab and culture
C. Viral core antibody
D. Viral surface antibody

https://openevidence.com/ask/10f84a5b-454f-4aa8-9d9a-e03ed24b2c1c

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C. Viral core antibody (IgM anti-HBc).

This is acute hepatitis B: unprotected sex with multiple partners, several weeks of fatigue, nausea/vomiting, low-grade fever, hepatocellular transaminase elevation (ALT 92 > AST 85), conjugated hyperbilirubinemia with amber/brown (bilirubinuric) urine. Serologic testing for HBsAg and IgM anti-HBc is what establishes acute HBV infection, since symptoms and enzyme elevations cannot distinguish hepatitis B from other causes of acute hepatitis.[1] IgM anti-HBc is the marker that specifically identifies **acute or recently acquired** infection, whereas HBsAg alone cannot separate acute from chronic disease.[2] It is also **the only positive marker during the serologic window**, when HBsAg has cleared but anti-HBs has not yet appeared — a gap that can last 1–6 months.[1][3][4] Of the choices offered, core antibody is the only test that captures the diagnosis regardless of where in the serologic course the patient falls.

Why the other options fail

- **D. Viral surface antibody (anti-HBs)** — indicates recovery/immunity from resolved infection or vaccination, not active disease. It would be negative in acute infection and during the window period, and a positive result in a vaccinated student would be uninformative.[3][5][6]
- **B. Urethral swab and culture** — the patient has already refused genital examination, and urethritis does not explain transaminitis or hyperbilirubinemia. NAAT on a urine specimen (not culture) would be the appropriate STI test if pursued, and gonorrhea/chlamydia screening remains indicated alongside HIV and syphilis testing given his risk profile.
- **A. CAGE questions** — alcohol use is a legitimate concern, but alcoholic hepatitis characteristically produces an **AST:ALT ratio >2:1**, and here ALT exceeds AST, arguing against alcohol as the primary driver. CAGE is also a screening instrument for use disorder, not a diagnostic test for the hepatitis.

Practical note: in real practice the order is HBsAg + IgM anti-HBc + anti-HBs together, plus HAV IgM, HCV antibody with reflex RNA, and HIV testing. Cocaine and amphetamine positivity also raises the possibility of injection exposure, strengthening the case for full viral hepatitis and HIV panels.[2]

Would you like to explore management and antiviral treatment thresholds for acute hepatitis B?

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Question 566

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?

A. Localized lymphatic obstruction
B. Thrombus formation in a deep vein
C. Increased capillary hydrostatic pressure
D. Decreased plasma oncotic pressure

https://openevidence.com/ask/5bd5b37f-96d3-437d-b7e7-64d508581242

The answer is **C. Increased capillary hydrostatic pressure**.[1][2][3]

This patient's presentation — **sleep apnea, exertional dyspnea, fatigue, bilateral pitting edema, widely split S2, and RBBB** — is consistent with **right heart failure secondary to cor pulmonale**. The pathophysiologic chain proceeds as follows: obstructive sleep apnea causes chronic intermittent hypoxia, which induces **hypoxic pulmonary arteriolar vasoconstriction** and, over time, pulmonary vascular remodeling leading to **pulmonary hypertension**.[4][5] The chronically elevated RV afterload eventually results in **right ventricular dysfunction and failure**.[1]

In right heart failure, the failing RV produces elevated right atrial and central venous pressures, which transmit retrograde into the systemic venous circulation. This raises **capillary hydrostatic pressure**, driving fluid from the intravascular space into the interstitium and producing the characteristic bilateral dependent pitting edema.[1][2][3] As described by the AHA, peripheral edema is often the most prominent clinical feature of chronic right heart failure, driven by increased central venous pressure.[1]

The **RBBB** accounts for the widely split S2 (delayed right ventricular depolarization causes delayed pulmonic valve closure), and bilateral symmetric pitting edema localizes the problem to systemic venous congestion rather than a localized process.

Why not the other options:

- **A (Lymphatic obstruction):** Typically causes non-pitting, often asymmetric edema without the associated cardiac findings seen here.
- **B (DVT):** Usually presents with unilateral leg swelling; bilateral symmetric pitting edema with systemic cardiac signs points to a central hemodynamic cause.
- **D (Decreased oncotic pressure):** Seen in nephrotic syndrome, cirrhosis, or severe malnutrition — none of which are suggested by this presentation.

Would you like to explore the diagnostic workup and management of pulmonary hypertension in obstructive sleep apnea?

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Question 567

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?

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.

https://openevidence.com/ask/cf1d027b-e12f-44f2-a23e-270918ae9e09

The correct answer is **B. The vascular protrusion drains into the superior rectal vein.**

This patient has multiple findings consistent with **alcoholic liver cirrhosis with portal hypertension**: a history of delirium tremens (indicating significant alcohol use), **spider angiomata** (the blanching spider web-like lesions on the chest and arms), and **ascites** (distended abdomen with shifting dullness).[1][2] The anoscopy finding of a **non-tender, dilated vascular protrusion superior to the pectinate line** is consistent with an **internal hemorrhoid**, which has increased prevalence in the setting of portal hypertension.[3][4]

The critical anatomic distinction centers on the **pectinate (dentate) line**:[4][5]

- **Internal hemorrhoids** (above the pectinate line) drain via the **superior rectal vein** → inferior mesenteric vein → **portal venous system**. This is the correct answer because the lesion is explicitly located superior to the pectinate line.[6][7]
- **External hemorrhoids** (below the pectinate line) drain via the **inferior rectal vein** → internal pudendal vein → internal iliac vein → **systemic venous circulation**.[4][6]

This portal-systemic venous communication at the anorectal junction is one of the recognized **portocaval anastomotic sites**, explaining why portal hypertension exacerbates hemorrhoidal congestion.[3][7]

Why the other options are incorrect:

- **A (Peptic ulcer disease):** The source of bleeding is directly visualized on anoscopy as an anorectal vascular protrusion, not an upper GI lesion.
- **C (Inferior rectal vein):** This would apply to external hemorrhoids below the pectinate line; the lesion here is superior to it.
- **D (Fecal leukocytes and stool culture):** These are diagnostic tools for infectious or inflammatory diarrhea, not for hemorrhoidal bleeding identified on anoscopy.[8]

It is worth noting that in cirrhotic patients, **anorectal varices** (distinct portosystemic collaterals) can coexist with hemorrhoids and should be differentiated clinically — varices appear as tortuous, bluish nonprolapsing veins, whereas hemorrhoids are soft, reddish-purple swollen veins.[4]

Would you like to explore how anorectal varices are differentiated from hemorrhoids in portal hypertension and how their management differs?

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Question 568

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?

A. Adenoma
B. Carcinoma
C. Decreased calcitriol concentration
D. Phosphate retention

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A. Adenoma.

This is classic **primary hyperparathyroidism**: hypercalcemia (13.8 mg/dL) with an inappropriately elevated PTH (230 pg/mL), polyuria from hypercalcemia-induced nephrogenic diabetes insipidus, weakness, and skeletal involvement (subperiosteal resorption, osteoporosis).[1][2][3] A **single benign parathyroid adenoma accounts for ~80–85% of cases**, with multiglandular disease in 15–20% and carcinoma in well under 1%.[4][5][6] Sestamibi scintigraphy relies on longer retention of ^{99m}Tc-sestamibi in pathologic parathyroid tissue and is the standard preoperative localization study for a solitary adenoma, with pooled sensitivity ~79% for SPECT and ~86% for SPECT/CT.[6][7][8]

Why the other options are wrong

- **B. Carcinoma** — rare (~1% of primary hyperparathyroidism). It is suggested by markedly higher calcium (often >14–15 mg/dL), PTH elevated 3–10× normal, and a palpable neck mass; this patient's values, while symptomatic, fit an adenoma far more commonly. Prevalence alone makes adenoma the answer.[4][9]

- **C. Decreased calcitriol concentration** and **D. Phosphate retention** — these are the drivers of **secondary** hyperparathyroidism in chronic kidney disease, which produces hyperphosphatemia, low or normal calcium, and elevated creatinine. This patient's metabolic panel is otherwise normal and she is hypercalcemic, excluding a CKD-driven mechanism. Also, neither is a "pathologic condition" identifiable on scintigraphy.

Clinical corollary: she meets surgical criteria on multiple counts — symptomatic disease, calcium >1 mg/dL above the upper limit of normal, osteoporosis, and overt skeletal disease — so parathyroidectomy after localization is the definitive treatment.[1][10]

Would you like to explore the features that distinguish parathyroid carcinoma from adenoma preoperatively?

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Question 569

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?

A. Bipolar I disorder
B. Cyclothymic disorder
C. Persistent depressive disorder
D. Schizoaffective disorder

https://openevidence.com/ask/969673ce-1703-44b0-a2df-e0cf5bfc4541

The correct answer is **B. Cyclothymic disorder**.

This patient demonstrates the hallmark features of **cyclothymic disorder**: a chronic, fluctuating mood disturbance with **subthreshold depressive and hypomanic symptoms** lasting well over 2 years, without meeting full criteria for a major depressive, manic, or hypomanic episode.[1]

Depressive symptoms are subthreshold for a major depressive episode. She reports depressed mood, sleep disturbances, and poor appetite — only three symptoms, while a major depressive episode requires **≥5 symptoms nearly every day for ≥2 weeks**.[1] Critically, she is at times still able to enjoy spending time with her family, suggesting her depressive episodes do not reach the severity or pervasiveness required for a full major depressive episode.[1]

Elevated mood symptoms are subthreshold for a hypomanic (or manic) episode. During her periods of elevated mood, she is productive at work and requires less sleep. A full hypomanic

episode requires elevated/expansive/irritable mood plus **≥3 additional symptoms for ≥4 consecutive days**.[1] Her presentation describes only a couple of features without evidence of the full hypomanic syndrome. The absence of functional impairment, hospitalization, or psychotic features during elevated periods also argues strongly against mania, ruling out **Bipolar I disorder (A)**.[2][3]

Why the other choices are incorrect:

- **Persistent depressive disorder (C)** involves chronic depressed mood for ≥2 years but **does not account for the episodes of elevated mood**, which are a defining feature of this patient's presentation.[4]
- **Schizoaffective disorder (D)** requires the presence of **psychotic symptoms** (delusions or hallucinations) occurring for at least 2 weeks in the absence of a major mood episode, in addition to mood episodes present for the majority of the illness duration. No psychotic features are described.[1]

The DSM-5 specifies that cyclothymic disorder is diagnosed only when criteria for major depressive, manic, or hypomanic episodes **have never been met**, and when the mood disturbance causes clinically significant distress or impairment.[1] If a full mood episode were to develop subsequently, the diagnosis would be reclassified accordingly, with a **15–50% risk of conversion to bipolar I or II disorder** over time.[1]

Would you like to explore treatment approaches for cyclothymic disorder?

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Question 570

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?

A. Pyrimethamine, sulfadiazine, and folinic acid
B. Amphotericin B and flucytosine
C. Fluconazole
D. Vancomycin and meropenem

https://openevidence.com/ask/4fb3b151-68b4-43c1-bfa5-ff65bde8795c

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B. Amphotericin B and flucytosine.

The India ink stain showing encapsulated yeast, subacute headache and fever, lymphocyte-predominant CSF pleocytosis with mildly elevated protein and low-normal glucose, and CD4 80/mm^3 with oral thrush establish HIV-associated cryptococcal meningoencephalitis. Induction therapy in a resource-available setting is an IV amphotericin B formulation plus oral flucytosine for 2 weeks, per the Office of AIDS Research Advisory Council opportunistic infection guidelines (AII).[1]

Regimen specifics

- **Preferred:** liposomal amphotericin B 3–4 mg/kg IV daily plus flucytosine 25 mg/kg PO four times daily × 2 weeks; lipid formulations are standard in high-income settings because of lower nephrotoxicity than deoxycholate at equivalent efficacy.[1][2]
- **Alternatives:** amphotericin B lipid complex 5 mg/kg IV daily plus flucytosine (BII); if only deoxycholate is available, 1 mg/kg IV daily plus flucytosine × 1 week followed by fluconazole 1,200 mg/day for a second week (BI).[1]
- **Flucytosine adds survival benefit,** not just faster CSF sterilization — amphotericin B 1 mg/kg plus flucytosine improved survival versus amphotericin B alone. Flucytosine must never be used as monotherapy (rapid resistance).[1][2][3]
- **Monitoring:** flucytosine peak levels 2 hours post-dose after 3–5 doses, target 25–100 mg/L; frequent CBCs for marrow toxicity and close renal function monitoring with dose adjustment in renal impairment.[1]
- **Consolidation:** fluconazole 800 mg daily for ≥8 weeks after successful induction (repeat LP with CSF culture at week 2), then maintenance fluconazole 200 mg daily.[1][2]

Why the other options are wrong

- **C. Fluconazole** is fungistatic and inferior to amphotericin-based induction; monotherapy at 1,200 mg/day carried ~50% 10-week mortality and is reserved for patients who cannot tolerate or access other agents. It is appropriate only for consolidation/maintenance or mild localized non-CNS disease.[1][2][3]
- **A. Pyrimethamine/sulfadiazine/folinic acid** treats CNS toxoplasmosis, which presents with focal deficits and ring-enhancing lesions, not encapsulated yeast on India ink.
- **D. Vancomycin plus meropenem** targets bacterial meningitis; the lymphocytic pleocytosis of 25/mm^3, near-normal protein, and India ink findings do not support this.

Two additional management points

- Opening pressure is normal here (150 mm H_2O), but **serial ICP monitoring is essential** — raised ICP drives early mortality and requires therapeutic LPs.[2]
- **Defer ART**, typically until ~4–6 weeks of antifungal therapy, given the mortality excess from cryptococcal IRIS with early initiation. Corticosteroids are not adjunctive therapy for cryptococcal meningitis.

Would you like to explore the optimal timing of ART initiation and management of cryptococcal IRIS in this patient?

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Question 571

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?

A. Rheumatoid factor
B. Angiotensin converting enzyme
C. Low-density lipoprotein
D. Triglycerides

https://openevidence.com/ask/78713297-598a-449f-a508-0862e77200d6

The answer is **C. Low-density lipoprotein**.

This presentation is classic for an **Achilles tendon xanthoma** in the setting of **familial hypercholesterolemia (FH)**. The key features pointing to this diagnosis include:

- **Firm, skin-colored nodule that moves with the Achilles tendon** — tendon xanthomas are localized infiltrates of lipid-containing foam cells (which is what the biopsy photomicrograph would show) deep within the tendon, with normal-colored overlying skin and a hard consistency. The Achilles tendon is the most common site.[1][2]
- **Family history of premature cardiovascular disease** — maternal MI at age 54 supports FH, as premature coronary artery disease is a hallmark.[3][4]
- **Young age of presentation** — FH causes lifelong LDL-C elevation, and tendon xanthomas can develop in adolescence, particularly in more severe phenotypes.[4]

Tendon xanthomas are **nearly pathognomonic for FH**.[2][5] FH is characterized by **markedly elevated LDL-C** with typically **normal triglyceride levels**.[3] The underlying defect (most commonly an LDL receptor mutation) impairs LDL clearance, leading to cholesterol accumulation in tendons (xanthomas) and arterial walls (atherosclerosis).[4][6]

Why the other options are incorrect:

- **A. Rheumatoid factor** — Rheumatoid nodules can occur near tendons, but they are associated with rheumatoid arthritis and would not present as an isolated finding in an otherwise healthy 16-year-old without joint disease.
- **B. ACE** — Elevated in sarcoidosis, which can cause nodular lesions but typically not a firm nodule within a tendon in this clinical context.
- **D. Triglycerides** — Hypertriglyceridemia causes eruptive xanthomas (small, yellowish papules), not tendon xanthomas. FH patients characteristically have elevated LDL-C with normal triglycerides.[3]

Would you like to explore the management of familial hypercholesterolemia in adolescents, including statin therapy initiation and LDL-C goals?

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Question 572

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?

A. Granulomas in the submucous tissue
B. Crypt abscesses
C. Villous atrophy and crypt hypertrophy
D. Villous hyperplasia

https://openevidence.com/ask/685ef4ed-0f28-4f72-b86e-f0c5c806f378

The answer is **C. Villous atrophy and crypt hypertrophy**.

This presentation — chronic malabsorptive diarrhea with malodorous stools, failure to thrive, abdominal distension, papulovesicular rash (consistent with **dermatitis herpetiformis**), aphthous ulcers, and symptom onset after introduction of gluten-containing foods (bread/cookies at 12 months) — with **positive anti-tissue transglutaminase (tTG) and anti-endomysial (EMA) antibodies** is classic for **celiac disease**.

The hallmark histological findings of celiac disease on duodenal biopsy are **villous atrophy, crypt hyperplasia (hypertrophy), and increased intraepithelial lymphocytes**.[1][2][3] These changes are graded using the **Marsh-Oberhuber classification**, where Marsh type 3 (villous atrophy with crypt hyperplasia) with positive serology confirms the diagnosis.[2][4] The compensatory crypt

hyperplasia develops in response to accelerated enterocyte loss driven by the immune-mediated mucosal injury.[4]

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 crypt epithelium), not celiac disease.
- **D. Villous hyperplasia** — not a recognized pathological finding in celiac disease; celiac disease causes villous atrophy (blunting/flattening), not hyperplasia.

Would you like to explore the ESPGHAN biopsy-avoidance strategy for diagnosing celiac disease in pediatric patients?

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Question 573

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?

A. Schizotypal personality disorder
B. Generalized anxiety disorder
C. Avoidant personality disorder
D. Dependent personality disorder

https://openevidence.com/ask/25409ddd-2f07-4cb1-a5b3-51d11215d5b2

The answer is **C. Avoidant personality disorder**.

This presentation is a textbook case of **avoidant personality disorder (AVPD)**, defined by the DSM-5 as a pervasive pattern of **social inhibition, feelings of inadequacy, and hypersensitivity to negative evaluation**.[1] The patient demonstrates each hallmark feature:

- **Low self-esteem and self-appraisal as socially inept or unappealing** — she calls herself "lame and ugly" and believes she is "untalented"[1]
- **Hypersensitivity to criticism**, even from family[1][2]
- **Avoidance of interpersonal situations due to fear of rejection** — she declined the cashier position (which involves more social interaction) and has not joined extracurriculars despite genuine interest[1]

- **Conviction that others will reject her** — "Nobody wants to be friends with me... I just know I'll end up getting rejected"[1]

Why not the other choices:

- **Schizotypal personality disorder (A):** Characterized by **cognitive/perceptual distortions, eccentric behavior, and magical thinking**, with social withdrawal driven by a lack of desire for relationships rather than fear of rejection. This patient has no odd beliefs or perceptual disturbances.[1][3][4]
- **Generalized anxiety disorder (B):** GAD involves **excessive worry across multiple domains** (health, finances, work, etc.), not a pattern centered on social inadequacy and rejection sensitivity. The patient's anxiety is specifically interpersonal and tied to a deeply ingrained negative self-concept.[1]
- **Dependent personality disorder (D):** While both AVPD and dependent PD share feelings of inadequacy and sensitivity to criticism, the key distinction is behavioral: dependent PD features **proximity-seeking and clinging behavior** driven by a need to be taken care of, whereas AVPD features **avoidance and withdrawal** driven by fear of humiliation and rejection. This patient clearly withdraws from relationships rather than clinging to them.[1]

Would you like to explore evidence-based treatment options for avoidant personality disorder in this age group?

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Question 574

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?

A. Condoms
B. Anti-HIV prophylaxis
C. Spermicidal foam
D. Vaccination

https://openevidence.com/ask/749974df-5498-462e-b315-4675c1f46ab5

The answer is **D. Vaccination**.

The clinical presentation — **hyperkeratotic exophytic papules** on the vulva that turn **acetowhite** with 3% acetic acid — is classic for **condylomata acuminata (genital warts)**, caused by human papillomavirus (HPV), most commonly **types 6 and 11** (responsible for >90% of genital warts).[1][2]

Why vaccination is the best answer:

- **HPV vaccination is the primary recommended modality for prevention** of genital warts. The 9-valent HPV vaccine (Gardasil 9) targets HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58, and clinical trials demonstrated **100% efficacy for prevention of anogenital warts** in per-protocol populations. ACIP recommends routine vaccination at age **11–12 years**, ideally before sexual debut.[2][3][4]
- Since this patient is 15 years old, she would have been in the recommended age window for routine vaccination several years prior.

Why the other options are inferior:

- **A. Condoms** — While consistent condom use can reduce the risk of HPV transmission, condoms **do not fully protect against HPV** because the virus can infect skin areas not covered by a condom. Evidence for condom effectiveness against genital warts specifically is conflicting.[2][5][6]

- **B. Anti-HIV prophylaxis** — Pre-exposure prophylaxis (e.g., tenofovir/emtricitabine) prevents HIV, not HPV.
- **C. Spermicidal foam** — Spermicides have no demonstrated role in preventing HPV transmission.

Would you like to explore the recommended treatment options for genital warts in this patient?

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Question 575

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?

A. Calcium phosphate
B. Calcium oxalate
C. Monosodium urate
D. Copper

https://openevidence.com/ask/d73a4896-5411-4b1c-8279-c77f8f659bcb

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The answer is **C. Monosodium urate**.

This presentation — **acute, excruciating monoarticular pain at the first metatarsophalangeal joint (podagra)** with erythema and swelling reaching peak intensity within hours — is the classic presentation of **acute gout**.[1][2] The patient's risk factors (male sex, obesity, diabetes, and chronic kidney disease) further support this diagnosis.[2]

Gout is caused by the **deposition of monosodium urate (MSU) crystals** in articular and periarticular tissues when serum urate exceeds the solubility threshold (~6.8 mg/dL).[3] These crystals activate the **NLRP3 inflammasome** in macrophages, triggering IL-1β release and an intense neutrophilic inflammatory response.[1][4] The first MTP joint is the most commonly affected site, and CKD is a major predisposing factor due to impaired renal urate excretion.[1][3]

Regarding the other choices:

- **Calcium phosphate** (basic calcium phosphate crystals) — associated with calcific tendinitis and Milwaukee shoulder syndrome, not podagra
- **Calcium oxalate** — crystal arthropathy seen in primary hyperoxaluria or dialysis-dependent patients, rare
- **Copper** — deposits in Wilson disease (hepatolenticular degeneration), which causes hepatic and neuropsychiatric disease, not acute monoarticular arthritis

Would you like to explore acute gout management in patients with chronic kidney disease?

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Question 576

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?

A. Stress fracture of proximal tibia
B. Medial meniscus tear
C. Medical collateral ligament (MCL) sprain
D. Pes anserine bursitis

https://openevidence.com/ask/c91eb103-7efb-4bc3-97fa-3c469992b8d5

The correct answer is **D. Pes anserine bursitis**.

The clinical presentation is classic for this diagnosis. The **pes anserine bursa** lies at the conjoined insertion of the **sartorius, gracilis, and semitendinosus** muscles on the proximal anteromedial tibia, approximately **5–6 cm distal to the medial joint line** — precisely matching the location of this patient's tenderness.[1][2] Pain that worsens with **stair climbing and rising from a chair** is a hallmark of this condition, first described by Moschcowitz in 1937.[2]

Multiple risk factors are present: **obesity, female sex, and coexisting osteoarthritis** are all well-established associations with pes anserine bursitis/tendinobursitis.[2][3] The condition results from repetitive friction of the hamstring tendons over the medial tibial condyle, which is exacerbated by increased body weight and valgus knee alignment.[4]

The other diagnoses can be excluded based on the clinical findings:

- **A. Stress fracture of proximal tibia** — Radiographs show no fracture or bony lesion. While early stress fractures can be radiographically occult, the symptom pattern and anatomic localization are far more consistent with bursitis.

- **B. Medial meniscus tear** — Meniscal tears present with **joint line tenderness**, often with effusion and mechanical symptoms (clicking, catching, locking). This patient's tenderness is 6 cm below the joint line with no effusion — inconsistent with meniscal pathology. Notably, pes anserine bursitis is known to **mimic medial meniscal tears**, and accurate diagnosis can prevent unnecessary arthroscopy.[5][6][7]
- **C. MCL sprain** — **Valgus stress testing is negative** for pain or instability, making an MCL injury unlikely. MCL sprains also typically follow a traumatic valgus force, which is absent here.[8]

Would you like to explore treatment options for pes anserine bursitis, including injection technique?

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Question 577

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?

A. Tamoxifen
B. Terbutaline
C. Mifepristone
D. Copper intrauterine device

https://openevidence.com/ask/0d7d1d4b-e8b7-4a57-b15e-12cc063d47b8

The correct answer is **C. Mifepristone**.

Mifepristone is a **selective progesterone receptor antagonist** (antiprogestin) that is FDA-approved for medical termination of intrauterine pregnancy through **70 days' (10 weeks') gestation**.[1] It competitively binds the progesterone receptor with an affinity five times greater than progesterone itself, resulting in **decidual necrosis, cervical softening, and increased myometrial sensitivity to prostaglandins**.[2][3] The FDA-approved regimen is **mifepristone 200 mg orally**, followed 24–48 hours later by **misoprostol 800 mcg buccally**.[1] This combined regimen achieves complete abortion in **95–97%** of cases with a serious adverse event rate of less than 0.5%.[4]

At 6 weeks' gestation, this patient is well within the approved window and is an appropriate candidate for this regimen.

Why the other options are incorrect:

- **Tamoxifen** — A selective estrogen receptor modulator used in breast cancer treatment and chemoprevention; it has no role in pregnancy termination.
- **Terbutaline** — A beta-2 adrenergic agonist used as a **tocolytic** to suppress preterm uterine contractions — the opposite of what is desired here.

- **Copper intrauterine device** — Effective as **emergency contraception** when placed within 5 days of unprotected intercourse by preventing fertilization/implantation, but it cannot terminate an established 6-week pregnancy.[2]

Would you like to explore the expected side effects and complication profile of the mifepristone-misoprostol regimen?

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Question 578

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?

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

https://openevidence.com/ask/8f30377e-6100-4d77-bfd0-0ef1604346c1

The answer is **A. Demyelination of the medial longitudinal fasciculus**.

This patient demonstrates **bilateral internuclear ophthalmoplegia (INO)**: adduction deficit in the ipsilateral eye with abducting nystagmus in the contralateral eye, present in both directions of lateral gaze. This is the hallmark of a lesion in 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 (multiple sclerosis)?

- **Bilateral INO in a young patient (<45 years) is most commonly caused by MS**. MS accounts for approximately one-third of all INO cases overall, but is the predominant etiology in younger patients, where most cases are bilateral.[3][4][5]
- The brainstem tegmentum adjacent to the fourth ventricle has a high concentration of periventricular post-capillary venules, making it particularly susceptible to inflammatory demyelination.[2][3]

- **Bilateral disc hyperemia with decreased visual acuity** (20/40 bilaterally) suggests concurrent optic nerve involvement, further supporting a multifocal demyelinating process.
- The episode of **imbalance preceding the current symptoms** may represent an earlier demyelinating event (e.g., cerebellar involvement), and a **normal head CT does not exclude MS** — MRI is the modality required to detect demyelinating plaques.[6]

Why not the other options?

- **B (Compressive tumor of the pons):** While pontine tumors can rarely cause bilateral INO, this would typically present with additional brainstem signs and a more progressive course rather than an acute, isolated presentation in a young woman.[7]
- **C (Thiamine deficiency — Wernicke encephalopathy):** Wernicke can cause ophthalmoplegia, but it typically involves lateral gaze palsy and nystagmus rather than a specific bilateral INO pattern, and this patient lacks risk factors (malnutrition, alcohol use).
- **D (Brainstem infarction):** Ischemic stroke is the most common cause of INO in **older patients** (>45 years) but is very unlikely in a 25-year-old without vascular risk factors.[4][5]

Would you like to explore the recommended workup and diagnostic criteria for MS presenting with bilateral INO?

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Question 579

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?

A. Cilostazol
B. Femoral embolectomy
C. Femoral-to-popliteal bypass graft
D. Interventional endovascular treatment

https://openevidence.com/ask/07e009a6-e93c-4075-abdb-ebf315de357d

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The answer is **A. Cilostazol**.

This patient presents with classic **intermittent claudication** — reproducible left calf pain provoked by walking >200 meters that resolves with rest — in the setting of extensive atherosclerotic risk factors (80 pack-year smoking history, diabetes, prior PCI, family history of CAD, and hypertension). This presentation is consistent with **Fontaine stage II peripheral arterial disease (PAD)**.

Cilostazol, a phosphodiesterase III inhibitor, is a **Class I, Level of Evidence A recommendation** per the 2024 ACC/AHA guidelines for improving leg symptoms and increasing walking distance in patients with claudication.[1] A Cochrane review of 15 double-blind RCTs (3,718 participants) demonstrated that cilostazol improved claudication symptoms compared with placebo, and a network meta-analysis showed an increase in maximum walking distance of approximately 63 meters over placebo.[1][2] The typical dose is **50 mg twice daily, titrated up to 100 mg twice daily**.[3] Cilostazol is **contraindicated in heart failure** of any severity; this patient has normal cardiac auscultation with no evidence of heart failure.[1]

Why the other options are incorrect:

- **Femoral embolectomy (B):** This is an emergent surgical procedure for **acute arterial embolism** causing acute limb ischemia — not appropriate for chronic, stable intermittent claudication.
- **Femoral-to-popliteal bypass graft (C) and endovascular intervention (D):** Per ACC/AHA guidelines, revascularization (whether surgical or endovascular) is a Class 2a recommendation reserved for patients with **functionally limiting claudication and an inadequate response to guideline-directed medical therapy including structured exercise**. This patient has not yet undergone a trial of medical therapy, making revascularization premature. Additionally, revascularization is not recommended in patients who have had an adequate clinical response to GDMT.[1]

Beyond cilostazol, this patient's comprehensive management should include **supervised exercise therapy** (also a first-line intervention), **smoking cessation**, **high-intensity statin therapy**, and **blood pressure optimization** to <130/80 mmHg.[4] Antiplatelet therapy should also be optimized, with clopidogrel preferred over aspirin for symptomatic PAD.[4]

Would you like to explore the comparative evidence between supervised exercise therapy and endovascular revascularization for claudication?

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Question 580

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?

A. Pulmonary hypertension
B. Lower extremity gangrene
C. Palpable purpura
D. Thoracic aortic aneurysm

https://openevidence.com/ask/a3c836fa-02c0-44f2-86ac-d891d29df288

The correct answer is **D. Thoracic aortic aneurysm**.

This vignette describes classic **giant cell arteritis (GCA)**: a patient over 50 with headaches, diplopia (cranial nerve VI palsy causing inward deviation), elevated ESR, and temporal artery biopsy showing **transmural granulomatous inflammation with internal elastic lamina fragmentation**. GCA is a large-vessel vasculitis affecting the aorta and its branches, and the most important long-term complication is **thoracic aortic aneurysm**.[1][2]

Why thoracic aortic aneurysm?

GCA patients have a **markedly increased risk of thoracic aortic aneurysm**, with a 15-year relative risk of **11.2** compared to the general population in a Danish nationwide cohort study.[3] Thoracic aortic aneurysms may develop years after diagnosis (median ~7.5 years), even after disease activity has apparently resolved, and long-term monitoring is recommended even after therapy discontinuation.[1][3] Prospective data show that up to **33% of GCA patients** develop aortic structural damage (predominantly thoracic) over long-term follow-up.[4] Notably, the risk is specifically for **thoracic** (not abdominal) aortic aneurysm, reflecting the predilection of GCA-related inflammation for the thoracic aorta.[3][5]

Why not the other options?

- **A. Pulmonary hypertension** — Not a recognized complication of GCA.

- **B. Lower extremity gangrene** — While large-artery stenosis can occur, frank gangrene is characteristic of other vasculitides (e.g., polyarteritis nodosa or thromboangiitis obliterans), not a typical GCA complication.
- **C. Palpable purpura** — Associated with small-vessel vasculitis (e.g., IgA vasculitis, ANCA-associated vasculitis), not large-vessel vasculitis like GCA.

Would you like to explore recommended screening protocols for aortic aneurysm surveillance in GCA patients?

References

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Question 581

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?

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

https://openevidence.com/ask/72a09548-d62b-4b3c-af56-f43a0957c6e1

The correct answer is **A. Brownish inclusions in the pulmonary macrophages on H&E staining**.

This patient had **chronic heart failure** (history of two MIs, chronic HF) presenting with **acute decompensated heart failure and cardiogenic shock** (hypotension, tachycardia, pink frothy sputum, bilateral rales, S3, loud P2, apical systolic murmur consistent with mitral regurgitation). The expected autopsy finding is **hemosiderin-laden alveolar macrophages**, classically termed **"heart failure cells."**

In chronic left-sided heart failure, sustained elevation of pulmonary venous pressure causes capillary engorgement and stress failure, leading to **focal capillary rupture and alveolar hemorrhage**.[1] Alveolar macrophages phagocytose the extravasated red blood cells and degrade hemoglobin, accumulating **hemosiderin** — an iron-storage complex that appears as **coarse, golden-brown granular pigment** on H&E staining.[1][2] Heart failure cells were found in **83% of autopsy lungs** from patients with chronic left-sided cardiac failure in one series.[1]

The other options are incorrect:

- **B. Prussian-blue staining of kidney tissue** — While Prussian blue does stain hemosiderin (iron), this finding in the kidneys is not the hallmark of chronic heart failure. Renal hemosiderosis is classically associated with chronic intravascular hemolysis (e.g., paroxysmal nocturnal hemoglobinuria), not heart failure.
- **C. Ground-glass hepatocytes** — This is the characteristic finding in **chronic hepatitis B**, where hepatocytes accumulate hepatitis B surface antigen (HBsAg) in the endoplasmic reticulum, producing a ground-glass cytoplasmic appearance on H&E. Not relevant here.
- **D. Congo-red staining of cardiac tissue** — Positive Congo-red staining with apple-green birefringence under polarized light identifies **amyloid deposits**, seen in cardiac amyloidosis. Although amyloidosis can cause heart failure, this patient's heart failure is clearly attributable to ischemic cardiomyopathy from prior MIs.

Would you like to explore the histopathologic changes seen in myocardial infarction at different stages?

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Question 582

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?

A. Propranolol
B. Digoxin
C. Amiodarone
D. Warfarin

https://openevidence.com/ask/21a0b9a7-edf2-4bd9-be87-3f0471ec8748

The answer is **A. Propranolol**.

This patient presents with **hyperthyroidism (most likely Graves disease) complicated by atrial fibrillation**. Key findings pointing to thyrotoxicosis include the fine bilateral hand tremor, eyelid retraction, digital swelling (acropachy), warm extremities, tachycardia, and an irregularly irregular pulse consistent with AF. The systolic ejection murmur along the right upper sternal border reflects a hyperdynamic, high-output state.

Beta-blockers are the Class I recommended first-line pharmacotherapy for rate control in AF complicating thyrotoxicosis.[1][2] Among beta-blockers, **propranolol** is particularly favored because, as a nonselective agent, it provides broader symptom relief and also **inhibits peripheral conversion of T4 to T3**.[1][3][4] Typical starting doses range from 40–160 mg/day.[4]

Why the other options are incorrect:

- **Digoxin (B):** Less effective for rate control in thyrotoxicosis due to increased drug clearance and catecholamine hypersensitivity; not first-line therapy.

- **Amiodarone (C):** Antiarrhythmic drugs generally fail to achieve sustained sinus rhythm while thyrotoxicosis persists. Moreover, amiodarone itself can cause thyrotoxicosis, making it a poor choice in this setting.[2][5]
- **Warfarin (D):** Anticoagulation in thyrotoxic AF is guided by the **CHA_2DS_2-VASc score**. This 35-year-old woman with no heart failure, hypertension requiring treatment, diabetes, vascular disease, or prior stroke has a score of 0 (female sex alone does not add a point unless another risk factor is present), so anticoagulation is not indicated. Additionally, warfarin addresses thromboembolic risk, not the acute symptomatic management that is being asked about.[2][3]

Would you like to explore the definitive treatment options for Graves disease beyond symptomatic beta-blockade?

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Question 583

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?

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

https://openevidence.com/ask/781d46cd-c30f-4416-8d75-b6845257d3f5

The answer is **D. Dilation of the intracerebral arterioles**.

This patient's headache is best explained as an **adverse effect of isosorbide mononitrate**, which was likely initiated 3 weeks ago when she was diagnosed with stable angina — precisely coinciding with headache onset. The critical temporal clue is that the headache **worsens approximately one hour after taking her morning medications**, aligning with the pharmacokinetic onset of the drug.

Mechanism of nitrate-induced headache

Isosorbide mononitrate is a nitric oxide (NO) donor. NO activates guanylyl cyclase in vascular smooth muscle, increasing cyclic GMP and causing **relaxation and dilation of intracerebral arterioles**.[1][2][3] Two types of nitrate-induced headache have been described:[1]

- **Immediate headache** (within the first hour): mild-to-moderate severity, non-migrainous, caused by **NO-mediated vasodilation** — matching this patient's presentation
- **Delayed headache** (3–6 hours): migraine-type with nausea, photophobia, and phonophobia, driven by CGRP release, glutamate, and ion channel modulation

This patient's headache profile — **bilateral, mild (4/10), without nausea, vomiting, photophobia, or phonophobia** — is consistent with the immediate vasodilatory type. Headache is the most common adverse effect of isosorbide mononitrate, occurring in **38–57% of patients** depending on dose.[4]

Why not the other options

- **A (Chronic subdural hematoma):** No history of trauma or fall, no focal neurologic deficits, and the headache timing correlates directly with medication initiation rather than a progressive space-occupying process.
- **B (Intracerebral vessel dissection):** Dissection typically presents with sudden severe headache, often unilateral with neck pain and focal neurologic signs — none of which are present here.
- **C (Intracranial neoplasm):** The absence of focal neurologic findings and the precise temporal link to a new vasodilatory medication make this far less likely than a drug side effect.

The worsening with cough and Valsalva maneuvers is notable but can occur with any headache exacerbated by transient increases in intracranial venous pressure, including nitrate-related vasodilation. That said, in clinical practice (outside this exam context), a new persistent headache in a 68-year-old warrants consideration of neuroimaging to rule out secondary causes.

Would you like to explore strategies for managing nitrate-induced headaches without compromising antianginal therapy?

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Question 584

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?

A. Pneumococcal vaccine
B. Tetanus, diphtheria, and acellular pertussis booster (Tdap) vaccine
C. Haemophilus influenza B (HIB) vaccine
D. Human papillomavirus (HPV) vaccine

https://openevidence.com/ask/4f1f4592-6b8c-4ee9-b518-1eff5f7a9bb7

The answer is **B. Tetanus, diphtheria, and acellular pertussis booster (Tdap) vaccine**.

This patient received all recommended vaccines before college (approximately age 18), which would have included Tdap. Now at age 31, **13 years have elapsed — exceeding the 10-year booster interval**. Per ACIP recommendations, after completing a primary series and receiving at least one dose of Tdap at age ≥10, a **Td or Tdap booster should be administered every 10 years**.[1][2] This makes a tetanus-containing booster the most clearly indicated vaccine at this visit.

Why not the other options:

- **A. Pneumococcal vaccine** — ACIP does list "asthma" among chronic lung diseases that qualify as a risk-based indication for pneumococcal vaccination in adults aged 19–64. However, this patient's asthma is specifically described as **intermittent and exercise-induced**, a mild phenotype. Notably, GINA 2026 guidelines state that "asthma alone is not a specific indication for pneumococcal vaccination". In exam contexts, exercise-induced bronchospasm is typically distinguished from chronic persistent asthma as a disease state conferring significant pneumococcal risk.[3][4][5]
- **C. HIB vaccine** — Not routinely recommended for immunocompetent adults.
- **D. HPV vaccine** — Routine catch-up HPV vaccination is recommended **through age 26**. At age 31, ACIP recommends only **shared clinical decision-making** (ages 27–45), not routine

administration. Despite his history of multiple sexual partners, this would not make HPV a vaccine that "should be administered" at this visit.[6][7]

Would you like to explore the shared clinical decision-making framework for HPV vaccination in adults aged 27–45?

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Question 585

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?

A. Gram-negative bacilli
B. Gram-negative diplococci
C. Gram-positive cocci in chains
D. Gram-positive cocci in clusters

https://openevidence.com/ask/a80b4b17-92b9-4621-a0f3-8c2778651ae5

The answer is **A. Gram-negative bacilli**.

This presentation is classic for **Pseudomonas aeruginosa osteomyelitis** complicating a nail puncture wound sustained while wearing tennis shoes. The key clinical features pointing to this diagnosis include:

- **Puncture wound through a sneaker** — *P. aeruginosa* colonizes the warm, moist foam inner sole of athletic shoes and is inoculated deep into the foot during a nail puncture. The IDSA identifies *P. aeruginosa* as **the most common bacterial cause of calcaneal osteomyelitis** in individuals who sustain nail puncture wounds while wearing sneakers.[1]
- **Fruity odor** — *Pseudomonas* classically produces a **grape-like or fruity smell** due to the production of 2-aminoacetophenone, which is a distinguishing microbiologic feature.
- **Probe-to-bone positive** — probing to bone through an ulcer is highly suggestive of underlying osteomyelitis.[1]

Pseudomonas aeruginosa is an **aerobic, gram-negative bacillus (rod)**, making option A correct.

Why the other options are incorrect:

- **B. Gram-negative diplococci** — describes *Neisseria* species (e.g., gonorrhea, meningitidis), not typical in this scenario.

- **C. Gram-positive cocci in chains** — describes *Streptococcus* species, which can cause superficial wound infections but are not the classic pathogen associated with sneaker puncture wound osteomyelitis.[2]
- **D. Gram-positive cocci in clusters** — describes *Staphylococcus aureus*, which is the most common cause of osteomyelitis overall but is not the classic organism associated with this specific mechanism of injury (nail through a tennis shoe).[3]

Would you like to explore the recommended antibiotic therapy and surgical management for Pseudomonas osteomyelitis following puncture wounds?

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Question 586

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?

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

https://openevidence.com/ask/0aa3e5eb-b33c-4b06-b3a8-2904ec34cca8

D. Increased breakdown of intracellular RNA.

The molecule responsible is **type I interferon (IFN-α/β)**, released by hepatocytes infected with hepatitis A virus. Type I IFN transcriptionally upregulates MHC class I genes through the interferon consensus sequence in the class I promoter, increasing surface class I density and rendering infected cells better targets for CD8+ cytotoxic T lymphocytes.[1][2][3] This mechanism has been demonstrated directly for virus-infected cells: IFN-β produced by measles virus– and RSV-infected cells accounts for essentially all of the observed HLA class I upregulation.[4][5]

The same IFN-α/β signal induces the **2′-5′-oligoadenylate synthetase (OAS) family**. Upon binding cytosolic viral double-stranded RNA, OAS polymerizes ATP into 2′-5′-linked oligoadenylates (2-5A), which dimerize and activate **latent RNase L**, an endoribonuclease that cleaves viral and cellular single-stranded RNA — degrading rRNA, tRNA, and mRNA to halt viral replication.[6][7][8] OAS3 is the dominant isoform driving RNase L activation across diverse human viruses.[9]

Why the other options are wrong

- **A. Upregulated expression of exogenously synthesized antigens** — Exogenous (extracellular) antigens are presented on **MHC class II**, not class I. IFN-γ, not type I IFN, is

the principal inducer of MHC class II; type I IFN inducers such as poly I:C raise class I markedly with little effect on class II.[3]

- **B. Enhanced macrophage phagocytic function** — This is the signature action of **IFN-γ**, the classic macrophage-activating cytokine. Although IFN-γ also upregulates MHC class I, the upregulation occurring within the **infected cell itself** as a direct consequence of viral replication is mediated by autocrine/paracrine IFN-α/β.[4][5]
- **C. Activation of eukaryotic initiation factor 2** — Directionally reversed. Type I IFN induces **PKR**, which phosphorylates eIF2α at Ser51; phosphorylated eIF2 sequesters eIF2B and blocks GDP-GTP exchange, **inhibiting** translation initiation rather than activating it.[10][11][12]

Clinical correlate: the immunopathology of acute hepatitis A — transaminase elevation, tender hepatomegaly, jaundice — reflects CD8+ T-cell and NK-cell killing of hepatocytes displaying viral peptide on IFN-upregulated MHC class I, not direct cytopathic effect of the virus.

Would you like to explore how hepatitis A virus antagonizes type I interferon signaling?

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Question 587

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?

A. Amitriptyline
B. Octreotide
C. Gluten-free diet
D. Methysergide maleate

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The correct answer is **C. Gluten-free diet**.

This presentation is classic for **celiac disease with dermatitis herpetiformis (DH)**. The key findings include:

- **Malabsorptive symptoms**: foul-smelling diarrhea with floating, bulky stools (steatorrhea), weight loss, and macrocytic anemia (from folate/B12 malabsorption)
- **Grouped erythematous papulovesicular lesions**: characteristic of DH, the cutaneous manifestation of celiac disease, which typically presents as an intensely pruritic, symmetrically distributed blistering rash on extensor surfaces, elbows, knees, buttocks, and trunk[1][2][3]

DH is currently considered a cutaneous manifestation of celiac disease; both conditions share the same genetic background (HLA-DQ2/DQ8), gluten-dependent enteropathy, and autoimmune response against tissue transglutaminase.[1][4] Nearly all DH patients have celiac-type small bowel changes, with three-fourths having villous atrophy.[4]

A gluten-free diet is the only effective therapy for both celiac disease and its dermatitis herpetiformis manifestation.[1][5][6] Per the ACG and AGA guidelines, strict lifelong adherence to a gluten-free diet resolves symptoms (diarrhea improves in ~80% within 60 days), heals the intestinal mucosa, normalizes serologic markers, and clears the skin rash over time.[5][6][7]

Dapsone can be added initially for rapid control of the skin lesions but is not among the answer choices.[4]

Why the other options are incorrect:

- **A. Amitriptyline** — Used for functional GI disorders (e.g., IBS) as a visceral analgesic; does not address the underlying autoimmune/malabsorptive pathology.
- **B. Octreotide** — A somatostatin analog used for secretory diarrheas (e.g., carcinoid syndrome, VIPoma); not indicated here.
- **D. Methysergide maleate** — A serotonin antagonist historically used for carcinoid syndrome or migraine prophylaxis; no role in celiac disease management.

Would you like to explore the diagnostic workup for celiac disease, including serology and biopsy criteria?

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Question 588

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?

A. Degranulation of presensitized mast cells
B. Formation of drug-induced autoantibodies
C. Accumulation of porphobilinogen
D. Cell injury due to drug metabolites

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The answer is **D. Cell injury due to drug metabolites**.[1][2][3]

This patient is experiencing a **demeclocycline-induced phototoxic reaction**. Demeclocycline is among the most phototoxic of the tetracyclines, and the FDA label specifically warns that phototoxic reactions "are characterized by severe burns of exposed surfaces resulting from direct exposure of patients to sunlight".[1] The presentation — an exaggerated sunburn with erythema and papules confined to sun-exposed areas (face, neck, dorsal hands) after brief UV exposure that would normally be tolerated — is classic.

Mechanism of phototoxicity: The drug (or its metabolite) acts as a chromophore that **absorbs UVA radiation** and transitions to an excited state. Upon returning to the ground state, it generates **reactive oxygen species (ROS) and free radicals** that cause direct, non-immunological cellular damage to keratinocytes, lipids, proteins, and DNA.[2][3][4] This is a dose-dependent, non-immune reaction — it does not require prior sensitization and can theoretically occur in anyone given sufficient drug and UV exposure.[3][5]

Why the other choices are incorrect:

- **A (Mast cell degranulation)** — This describes a type I (IgE-mediated) hypersensitivity reaction such as solar urticaria, not a phototoxic drug reaction.
- **B (Drug-induced autoantibodies)** — This describes drug-induced lupus erythematosus, which involves a different clinical picture (e.g., arthralgias, serositis, anti-histone antibodies) and is not the mechanism here.
- **C (Porphobilinogen accumulation)** — This would suggest porphyria (e.g., acute intermittent porphyria or porphyria cutanea tarda). While tetracyclines can rarely cause pseudoporphyria, this patient's acute phototoxic presentation is better explained by the direct ROS-mediated mechanism of phototoxicity.

Would you like to explore the management of drug-induced phototoxic reactions and guidance on restarting the offending medication?

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Question 589

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?

A. Pelvic inflammatory disease
B. Diminished ovarian reserve
C. Hypogonadotropic hypogonadism
D. Premature ovarian failure

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The most likely cause is **B. Diminished ovarian reserve (DOR)**.

DOR is defined as a condition in women of reproductive age with **regular menses whose response to ovarian stimulation is reduced** relative to women of comparable age.[1] This patient fits the classic profile:

- **Age 35** — female age is the **single most important predictor of fecundity**, and fecundity declines meaningfully after age 30–35 due to progressive loss of follicles and deterioration of oocyte quality. DOR is observed in approximately **26% of patients presenting to IVF centers**.[2][3]
- **Regular 28-day menstrual cycles** — a key distinguishing feature of DOR is the **preservation of regular menses** despite reduced ovarian reserve. Women with critically diminished ovarian reserve may continue to menstruate regularly.[1][4][5]
- **Failed IVF** — poor response to ovarian hyperstimulation is a hallmark of DOR and reflects a reduced follicular pool.[1][6]

- **Secondary infertility** with a previously uncomplicated pregnancy 6 years earlier, consistent with interval decline in oocyte quantity/quality.

Why the other options are less likely:

- **A. Pelvic inflammatory disease** — No history of sexually transmitted infections, pelvic pain, or risk factors for tubal disease. While tubal factor is a common cause of infertility, there is nothing in this vignette to suggest it.
- **C. Hypogonadotropic hypogonadism** — Typically presents with **irregular cycles, oligomenorrhea, or amenorrhea**. While excessive exercise can cause functional hypothalamic amenorrhea, one hour daily at the gym is not sufficient to suppress the hypothalamic-pituitary-gonadal axis. Her regular cycles effectively exclude this.[3]
- **D. Premature ovarian failure (primary ovarian insufficiency)** — Characterized by **amenorrhea or oligomenorrhea** for ≥4 months with FSH >25 mIU/mL, reflecting near-complete loss of ovarian function. This patient's regular menses rule out POF. DOR can be conceptualized as an earlier stage on the same spectrum, but with preserved menstrual cyclicity and some residual ovarian function.[5][7][8][9][10]

Would you like to explore the recommended ovarian reserve testing and interpretation for evaluating DOR?

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Question 590

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?

A. N-acetylcysteine
B. Charcoal
C. IV fluids
D. Syrup of ipecac

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The answer is **A. N-acetylcysteine (NAC)**.

This patient presents with a **suspected intentional overdose** — found somnolent with scattered pill bottles and admitting to acetaminophen ingestion while minimizing the amount ("only a few pills"). In this setting, the history is considered **unreliable**, which is the key determinant of management.

The 2023 US/Canada consensus statement on acetaminophen poisoning management defines an unreliable history as one that "lacks sufficient detail to establish dose and time of ingestion, that contains conflicting statements, or when the patient has symptoms, signs, or laboratory values inconsistent with the history," and explicitly recommends that **if there is any doubt about the history, the patient should receive acetylcysteine**.[1] The ACG/AGA Acute Liver Failure guidelines concur: "**Administration of NAC should begin as soon as toxicity is suspected, especially if time of ingestion is unknown,**" and state that "**it is reasonable to proceed with treatment while awaiting diagnostic test results**".[2] NAC administered early — particularly within 8 hours — is associated with very low rates of hepatotoxicity (~5–7%), whereas delay beyond 8–10 hours significantly increases risk.[3]

Why not the other options:

- **B. Activated charcoal** — While charcoal is effective for acetaminophen within the first 4 hours, it is an adjunctive measure that reduces absorption rather than a definitive antidote. NAC takes priority in an unreliable-history scenario. Additionally, this patient was recently somnolent, raising aspiration risk concerns.[2][4]
- **C. IV fluids** — Appropriate supportive care but does not address the potential for life-threatening hepatotoxicity.
- **D. Syrup of ipecac** — **No longer recommended** for poisoning management. No clinical data support its use, and it may increase adverse events without improving outcomes.[5][6]

The somnolence and mildly depressed respiratory rate (11/min) are notable — acetaminophen alone does not typically cause early sedation, raising concern for **co-ingestants** (e.g., opioids, benzodiazepines). A complete evaluation including serum acetaminophen and salicylate levels, LFTs, INR, BMP, ECG, and consideration of naloxone would also be part of the initial workup, though NAC initiation should not be delayed.

Would you like to explore NAC dosing protocols and stopping criteria for acetaminophen overdose?

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Question 591

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?

A. High T4 and T3
B. Low T4 and T3
C. High TSH
D. Hypercholesterolemia

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The answer is **C. High TSH**.

This clinical vignette describes classic **primary hypothyroidism**: weight gain, exercise intolerance, cognitive slowing, and thickened, dry skin in a middle-aged woman. The finding most helpful in confirming this diagnosis is an **elevated TSH (thyrotropin)**.

Why high TSH is the best answer:

- **TSH is the single best biomarker** for diagnosing primary thyroid disease, with approximately **98% sensitivity and 92% specificity** for identifying overt thyroid dysfunction. It is recommended as the initial diagnostic test because of the **log-linear TSH–FT4 relationship**: modest decreases in thyroid hormone levels produce proportionally larger increases in TSH, making TSH the earliest and most sensitive indicator of thyroid failure.[1][2][3][4]
- **Low T4 and T3 (choice B)** are also present in overt hypothyroidism, but TSH is more diagnostically useful for two reasons: (1) T3 typically remains within the reference range until **profound hypothyroidism** develops, and (2) in subclinical hypothyroidism, TSH is elevated while T4 is still normal — TSH catches the disease earlier.[4][5]
- **High T4 and T3 (choice A)** would indicate hyperthyroidism, which is the opposite diagnosis.

- **Hypercholesterolemia (choice D)** is an associated finding in hypothyroidism but is nonspecific and has many other causes; it may prompt evaluation for thyroid dysfunction but is not diagnostic on its own.[1]

Would you like to explore the initial levothyroxine dosing and monitoring approach for a newly diagnosed hypothyroid patient like this one?

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Question 592

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?

A. Fibroadenoma
B. Normal pregnancy-related changes
C. Fat necrosis
D. Phyllodes tumor

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The answer is **A. Fibroadenoma**.

Fibroadenoma is the most common benign breast tumor in women of reproductive age (median presentation age ~25 years) and the **most frequent breast lesion found during pregnancy**.[1][2][3] The clinical and histological features in this case are classic:

- **Clinical presentation**: A **2.5-cm, rubbery, mobile, painless mass** is the hallmark description of fibroadenoma — often referred to as a "marble" or "breast mouse." The typical size is 1–3 cm. Fibroadenomas are **estrogen-sensitive** and may enlarge or become palpable during pregnancy.[1][2][3][4]
- **Biopsy findings**: The description of a **rounded contour with overgrowth of fibrous and glandular tissue** corresponds to the well-circumscribed **biphasic proliferation** of both stromal and epithelial components that defines fibroadenoma histologically.[4][5]

Why not the other options:

- **Phyllodes tumor (D)**: Although also a biphasic fibroepithelial lesion, phyllodes tumors present at a **median age of ~40 years**, are typically **>3 cm with rapid growth**, and histologically exhibit a characteristic **leaf-like (phyllodes) architecture with stromal hypercellularity, stromal overgrowth, atypia, and increased mitotic activity** — none of which are described here. The biopsy description of balanced fibrous and glandular proliferation with rounded contour is inconsistent with phyllodes.[2][6]

- **Normal pregnancy-related changes (B)**: Pregnancy causes diffuse lobular and alveolar proliferation and increased breast density, but these are diffuse physiologic changes — not a **discrete, well-circumscribed mass** with the described biopsy features.[7]
- **Fat necrosis (C)**: This typically follows trauma and shows **necrotic fat cells, lipid-laden macrophages (foamy histiocytes), and fibrosis** on biopsy — an entirely different histologic picture than what is described.

Would you like to explore the management approach for fibroadenomas during pregnancy?

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Question 593

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?

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

https://openevidence.com/ask/002daa3c-5fd8-4cb1-b3b9-3637dfa8c6c2

The answer is **C — respect the patient's written instructions and do not administer a blood transfusion**.

This scenario tests the principle of **patient autonomy**, which generally outweighs beneficence when an adult patient has refused a specific treatment. The key elements here are:

- The patient has a **documented annotation in the medical chart** refusing blood transfusions for religious reasons, representing a prior autonomous decision.
- The **wife corroborates** this refusal, providing additional confirmation of the patient's wishes.
- The WSES-AAST consensus guidelines state that **"when a patient has an advance directive clearly refusing allogeneic blood transfusion, that directive must be followed,"** and that when an incapacitated patient's wishes can be confirmed through an advance directive or surrogate decision-maker, those wishes take precedence over presumed consent.[1]
- The American Academy of Family Physicians similarly notes that **"in almost all instances, a physician is liable for violating the religious belief of a Jehovah's Witness patient"** if a transfusion is administered against documented wishes.[2]
- Respecting a patient's **autonomy generally outweighs** the other principles of medical ethics (beneficence, nonmaleficence, justice) when treatment is refused.[2]

Why the other options are incorrect:

- **A (administer a transfusion)** — This would violate the patient's documented wishes. Presumed consent applies only when there is **no** advance directive and **no** surrogate available, which is not the case here.[1]
- **B (call the ethics board)** — While ethics consultation is valuable in ambiguous situations, the patient's written refusal combined with surrogate corroboration provides clear direction. In an emergency, the documented directive should be followed without delay.[1] [2]
- **D (convince the wife)** — The wife is reinforcing the patient's own documented wishes, not imposing her own. Attempting to persuade family members constitutes a form of coercion and is discouraged.[2]

Clinically, the care team should pursue **alternative blood conservation strategies** acceptable to the patient, which may include tranexamic acid, volume expanders, cell salvage, or blood fractions — though each must be individually discussed for acceptability, as significant heterogeneity exists among patients who refuse blood products.[2]

Would you like to explore the specific bloodless medicine strategies available for managing hemorrhagic shock in patients who refuse transfusion?

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Question 594

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?

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.

https://openevidence.com/ask/187090dd-03d8-43c0-b9c7-fdfb22dcdcf8

The answer is **A. Increase the frequency of blood glucose checks**.

Sick day management in type 1 diabetes centers on more frequent glucose monitoring, continued insulin administration, and ketone testing — not withholding or reducing insulin. Intercurrent illness (even a mild URI) triggers counter-regulatory hormone release (cortisol, catecholamines, glucagon), which typically raises blood glucose and increases insulin requirements.[1][2]

Key principles supporting this answer:

- **Never hold insulin in type 1 diabetes.** The ADA Standards of Care (2026) explicitly state that individuals treated with intensive insulin therapy **should not stop or hold basal insulin**, even if not eating, as doing so will precipitate DKA. This eliminates option D.[3]
- **Reducing insulin is generally inappropriate during illness.** Illness more commonly causes hyperglycemia, not hypoglycemia, due to stress hormone release. Sick day guidelines advise giving **extra insulin** (10–20% increase in basal and bolus doses) when glucose is elevated. Reducing insulin would increase the risk of hyperglycemia and ketosis, eliminating option B.[1][4]
- **Continuing the exact same regimen without increased monitoring is insufficient.** A consensus panel on sick day management recommended **frequent glucose monitoring** and ketone checking as cornerstones of self-management during illness. Simply maintaining

the baseline regimen (option C) without additional surveillance misses the opportunity to detect and respond to glycemic excursions early.[1][5]

- **More frequent blood glucose checks** allow timely detection of hyperglycemia or hypoglycemia (e.g., from reduced oral intake) and guide insulin dose adjustments. Sick day education universally advises checking glucose at least every 3–4 hours and testing for ketones when levels exceed 250 mg/dL.[1][5]

Additionally, the parents should be counseled to **check for ketones** if blood glucose rises above 250 mg/dL, ensure adequate hydration, and contact the diabetes care team if glucose or ketones remain persistently elevated.[3][5]

Would you like to explore the specific sick day insulin adjustment protocols and ketone management thresholds for pediatric type 1 diabetes?

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Question 595

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?

A. Hyperplasia
B. Hypertrophy
C. Atrophy
D. Metaplasia

https://openevidence.com/ask/6b61baea-ef0a-437f-9104-0ae41ad584a8

The correct answer is **A. Hyperplasia**.

The question describes an **increased number of acinar glands with epithelial proliferation**, which is the defining feature of **hyperplasia** — an increase in the number of cells. This is distinct from hypertrophy, which refers to an increase in individual cell size without an increase in cell number.

During pregnancy, the breast undergoes **progressive ductal and lobular hyperplasia** driven by rising levels of estrogen, progesterone, and prolactin.[1] Specifically:

- During the first and second trimesters, **lobules, alveoli, and lactiferous ducts proliferate and differentiate**.[2]
- Estrogen stimulates **ductal proliferation and elongation**, while progesterone promotes side-branching and **lobuloalveolar development**.[3][4]
- This culminates in a **massive increase in the number of epithelial cells** and the formation of thousands of alveoli (acini) — saccular outpouchings from the ductal system.[5][6]

The other options are incorrect:

- **Hypertrophy (B)** would involve enlargement of existing cells without an increase in cell number. While individual epithelial cells do undergo some functional changes, the question specifically highlights an increased number of glands and epithelial proliferation, pointing to hyperplasia.

- **Atrophy (C)** refers to a decrease in cell size or number, which is the opposite of what is described.
- **Metaplasia (D)** refers to the replacement of one differentiated cell type with another, which is not what occurs here — the proliferating cells remain mammary epithelial cells.

Would you like to explore the specific hormonal mechanisms driving lobuloalveolar development during pregnancy?

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Question 596

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?

A. Vitamin D supplementation
B. Reassurance and follow-up
C. X-ray of the lower extremities
D. Bracing of the lower extremities

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

This child presents with **bilateral genu varum (bowlegs)**, which is a **normal physiologic finding in children under 2 years of age**. The description of the knees not staying together when feet and ankles are placed together is the classic examination finding of genu varum.[1]

Key features supporting physiologic genu varum:

- **Age under 2 years** — physiologic bowing is most commonly seen in walking children under age 2 and has a well-documented favorable natural history, with spontaneous correction typically occurring between **18–24 months** and resolution by **30–36 months**[2][3]
- **Normal growth percentiles** (40th for height, 50th for weight) — argues against rickets or skeletal dysplasias, which characteristically cause **short stature**[3]
- **Normal developmental milestones** — kicking a ball, 2-word phrases, and social play are all age-appropriate

- **Unremarkable gait** — absence of a lateral thrust gait, which would raise concern for **Blount disease** (infantile tibia vara), the most common pathologic cause of bowlegs[1]

Why not the other options:

- **Vitamin D supplementation (A)** — There are no clinical features suggesting rickets (no short stature, widened wrists, or rachitic rosary), so empiric supplementation is not indicated as the next step
- **X-ray of the lower extremities (C)** — Radiologic studies are **not routinely required** for physiologic bowing; imaging is reserved for suspected pathologic conditions such as progressive bowing after age 2, asymmetric deformity, short stature, or lateral thrust gait[4]
- **Bracing (D)** — Not indicated for physiologic genu varum, which resolves spontaneously; orthotics have **not been shown to be beneficial** for normal angular variants[4]

The family history of developmental dysplasia of the hip in the sister is a distractor and does not alter management of physiologic bowlegs. Appropriate management is parental reassurance that this is a normal variant with expected spontaneous resolution, combined with routine follow-up to confirm progressive correction.

Would you like to explore the clinical red flags that warrant further workup for pathologic genu varum versus physiologic bowing?

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Question 597

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?

A. Ventricular septal defect
B. Ebstein's anomaly
C. Pheochromocytoma
D. Holoprosencephaly

https://openevidence.com/ask/f0137e21-37da-4609-9719-68e17fa4757f

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The answer is **A. Ventricular septal defect**.

This vignette describes the classic presentation of **Trisomy 18 (Edwards syndrome)**: IUGR, polyhydramnios, prominent occiput, low-set ears, micrognathia, clenched fists with overlapping fingers, rocker-bottom feet, and omphalocele.[1][2] Congenital heart disease occurs in **80–90% of affected infants**, and **VSD is the most common cardiac defect**, reported in 31–94% of cases across multiple series.[3][4] A landmark autopsy study of 41 karyotyped trisomy 18 cases found a VSD in **100%**.[5]

Why the other options are incorrect:

- **B. Ebstein's anomaly** — classically associated with in-utero lithium exposure, not trisomy 18.
- **C. Pheochromocytoma** — a tumor of chromaffin cells with no association with trisomy 18.
- **D. Holoprosencephaly** — a hallmark of **Trisomy 13 (Patau syndrome)**, which presents with midline defects (cleft lip/palate, hypotelorism, microphthalmia, polydactyly) rather than the overlapping fingers and rocker-bottom feet seen here.[1]

Would you like to explore the current surveillance and management guidelines for neonates with trisomy 18?

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Question 598

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?

A. Overflow proteinuria
B. Transient (functional) proteinuria

C. Orthostatic proteinuria
D. Isolated proteinuria

https://openevidence.com/ask/3398dba7-a884-42ec-90b6-d3630d6c02c1

A. Overflow proteinuria. The constellation of anemia, hypercalcemia (12.1 mg/dL), renal insufficiency (creatinine 2.7 mg/dL), and progressive midline lumbar back pain in a 68-year-old identifies multiple myeloma — all four CRAB myeloma-defining events are present.[1] The proteinuria reflects glomerular filtration of overproduced monoclonal free light chains (Bence Jones protein) in quantities that exceed proximal tubular reabsorptive capacity, the definition of overflow (overproduction) proteinuria.[2] The bland sediment — protein without RBCs or pyuria — fits this mechanism rather than a nephritic or infectious process.

Why the alternatives do not fit

- **Transient (functional) proteinuria** follows fever, exercise, stress, or cold exposure and resolves once the trigger is removed. This patient has a year of progressive symptoms with established end-organ damage.[3]
- **Orthostatic proteinuria** is a benign postural phenomenon predominantly of adolescents and young adults, excluded by a first-morning void. It does not cause anemia, hypercalcemia, or an elevated creatinine.[3][4]
- **Isolated proteinuria** implies proteinuria as the sole abnormality in an otherwise well patient with normal renal function; the systemic findings here exclude that label.

Testing caveat worth noting: routine dipstick is most sensitive to albumin and can miss low-molecular-weight light chains, so a negative or only trace dipstick does not exclude Bence Jones proteinuria.[2][5] A protein-to-creatinine ratio disproportionate to the albumin-to-creatinine ratio should prompt specific testing. Conversely, if significant albuminuria is present, concurrent AL amyloidosis, light-chain deposition disease, or another glomerular lesion should be considered, since myeloma also causes light-chain proximal tubulopathy and glomerulopathies.[1][6][7]

Confirmatory workup: SPEP with immunofixation, serum free light chain assay, 24-hour urine for total protein with UPEP/UIFE, whole-body low-dose CT or FDG-PET/CT, and bone marrow aspirate and biopsy.[1][8] Renal biopsy is indicated if albuminuria or unexplained renal dysfunction persists.[1] Supportive management includes hydration targeting urine output of 100–150 cc/h to dilute tubular light chains, correction of hypercalcemia and hyperuricemia, and discontinuation of nephrotoxins with renal dosing of all medications; zoledronic acid is not

recommended in severe renal impairment, and denosumab carries a risk of severe hypocalcemia when creatinine clearance is <30 mL/min.[1]

One internal inconsistency in the data: a hematocrit of 41% does not correspond to a hemoglobin of 9.8 g/dL (expected roughly 29–30%). This does not alter the answer.

Would you like to explore how to manage hypercalcemia of malignancy in myeloma when renal function is already impaired?

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Question 599

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?

A. T-score of 1.2
B. T-score of -0.8
C. Z-score of -2.0
D. T-score of -1.6

https://openevidence.com/ask/ac95986d-8d9b-45a5-9932-ecb6f2eca131

The correct answer is **D. T-score of -1.6**.

The WHO defines **osteopenia as a T-score between -1.0 and -2.5**.[1][2][3] A T-score of **-1.6** falls squarely within this range, consistent with the physician's diagnosis of osteopenia in this postmenopausal woman.

The other options are incorrect for the following reasons:

- **A (T-score of 1.2)** and **B (T-score of -0.8)**: Both represent **normal bone density** (T-score ≥ -1.0).[4]
- **C (Z-score of -2.0)**: A Z-score compares BMD to an **age-, sex-, and ethnicity-matched** reference population, rather than to a young-adult reference. Z-scores are used diagnostically in **premenopausal women and men under 50**, not for postmenopausal women, where the **T-score** is the standard diagnostic metric. A Z-score of -2.0 in a postmenopausal woman would prompt evaluation for secondary causes of osteoporosis but would not itself define osteopenia.[1][5]

Key distinctions to remember: the **T-score** compares an individual's BMD to that of a healthy young adult, while the **Z-score** compares it to age-matched peers.[6] Because BMD naturally declines with age, T-scores are consistently lower than Z-scores after approximately age 40.[6]

Would you like to explore when pharmacologic treatment is indicated for osteopenia, including FRAX-based thresholds?

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Question 600

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?

A. Legionella pneumophila
B. Haemophilus influenzae
C. Bordetella pertussis
D. Corynebacterium diphtheriae

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The answer is **D. Corynebacterium diphtheriae**.

The culture medium described — containing **sheep blood, cystine, and potassium tellurite** — is **cystine-tellurite blood agar (CTBA)**, also known as Tinsdale medium, the classic selective and differential medium for isolating *C. diphtheriae*.[1][2] The organism reduces tellurite to metallic tellurium, producing characteristic **black colonies** with a glistening surface.[2] On modified Tinsdale medium, *C. diphtheriae* also produces **black halos** around colonies due to cystinase activity in the presence of tellurite, cystine, and thiosulfate.[2][3]

The clinical scenario — a **respiratory disease outbreak in children in rural Venezuela** — is consistent with diphtheria, which remains a significant cause of outbreaks in under-vaccinated populations, particularly in children.[4]

Why the other options are incorrect:

- **A. Legionella pneumophila** — Requires **buffered charcoal yeast extract (BCYE) agar** supplemented with L-cysteine and iron; does not grow on blood agar or tellurite-containing media.
- **B. Haemophilus influenzae** — Requires factors **X (hemin)** and **V (NAD)** for growth; grows on chocolate agar, not on tellurite-containing media.

- **C. Bordetella pertussis** — Grows on **Bordet-Gengou agar** (potato-glycerol-blood agar) or **Regan-Lowe medium** (charcoal agar with horse blood and cephalexin); does not produce black colonies on tellurite media.

Would you like to explore the recommended treatment protocol for diphtheria, including antitoxin and antibiotic therapy?

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Question 601

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?

A. Transforming growth factor-β
B. Erythropoietin
C. Interleukin-5
D. Granulocyte-macrophage colony-stimulating factor

https://openevidence.com/ask/47920856-0cf6-41e8-af5e-15a5d586636f

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The answer is **D. Granulocyte-macrophage colony-stimulating factor (GM-CSF)**.

This patient has **febrile neutropenia** following myeloablative conditioning for allogeneic bone marrow transplantation. The absolute neutrophil count (ANC) is **280/mm³** (1,400 × 20%), indicating severe neutropenia (ANC <500), and fever of 38.5°C meets the definition of febrile neutropenia.[1]

Why GM-CSF is correct:

GM-CSF (sargramostim) is **FDA-approved for neutropenia associated with stem cell transplantation**.[2] It stimulates the proliferation and differentiation of myeloid progenitors, resulting in a dose-dependent increase in circulating neutrophils, monocytes, macrophages, and eosinophils.[3][4] Randomized controlled trials have demonstrated that GM-CSF **accelerates neutrophil recovery after allogeneic BMT**, reducing the time to achieve an ANC ≥500/mm³ and decreasing the incidence of pneumonia and duration of hospitalization.[5][6] The NCCN Hematopoietic Growth Factors guidelines list sargramostim (GM-CSF) as a therapeutic option in febrile neutropenia, particularly when risk factors for infection-associated complications are

present, such as ANC <100, expected prolonged neutropenia >10 days, or hospitalization at the time of fever.[1]

Why the other choices are incorrect:

- **A. TGF-β** — An immunoregulatory cytokine involved in fibrosis, immune suppression, and cell differentiation. It has no role in stimulating neutrophil production and would be counterproductive in neutropenia.
- **B. Erythropoietin** — Stimulates red blood cell production. While the hemoglobin is low (8 g/dL), the immediate life-threatening concern is neutropenia with fever, not anemia. Erythropoietin does not address the neutropenia.
- **C. Interleukin-5** — A cytokine primarily responsible for eosinophil differentiation and activation. It has no therapeutic role in neutropenia and would not address the granulocyte deficit.

Would you like to explore the clinical differences between G-CSF and GM-CSF in the post-transplant setting?

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Question 602

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?

A. Gout
B. Reactive arthritis
C. Psoriatic arthritis
D. Dermatomyositis

https://openevidence.com/ask/5aaef20f-08cf-4c18-9e72-8a9ca0777f15

The answer is **C. Psoriatic arthritis**.

This presentation is classic for **psoriatic arthritis (PsA)**, with multiple hallmark features converging in a single patient:

- **DIP joint involvement**: Swollen, warm, and painful distal interphalangeal joints are characteristic of PsA and occur in over 50% of patients, distinguishing it from rheumatoid arthritis, which typically spares the DIP joints.[1]
- **Nail dystrophy**: Pitting and cracking of the nails occur in approximately **80–90%** of PsA patients and are a key feature in the CASPAR classification criteria.[1][2]
- **Psoriatic skin lesions**: The rough, erythematous plaques over the elbows are typical psoriasis, which precedes arthritis onset in the majority of PsA cases.[2]
- **Large joint involvement**: The chronic knee stiffness and swelling is consistent with the oligoarticular pattern frequently seen in PsA.[1]

- **Family history**: A positive family history of psoriasis (the father's similar condition treated with emollients and topical steroids) further supports this diagnosis and contributes a point in the CASPAR criteria.[3][4]

Why the other options are incorrect:

- **A. Gout** — typically presents as acute monoarticular attacks (classically the first MTP joint), not with DIP inflammation, nail pitting, or psoriatic plaques. While PsA can be misdiagnosed as gout when the toes are involved, the constellation here is far more consistent with PsA.[1]
- **B. Reactive arthritis** — presents as an asymmetric oligoarthritis following genitourinary or gastrointestinal infection. Although skin lesions (keratoderma blennorrhagicum) can occur, the chronic psoriatic plaques, nail pitting, and family history point away from this diagnosis.[1]
- **D. Dermatomyositis** — presents with proximal muscle weakness and characteristic skin findings (heliotrope rash, Gottron papules), not with inflammatory DIP arthritis, nail pitting, or psoriatic plaques.

Would you like to explore the recommended initial treatment approach for psoriatic arthritis?

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Question 603

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?

A. Required for collagen hydroxylation
B. Required for dehydrogenase enzymes
C. Required for methionine processing
D. Required for methylmalonyl-CoA processing

https://openevidence.com/ask/9579eb7b-cc3d-48a0-893a-599bdda6e9d3

The answer is **B. Required for dehydrogenase enzymes**.

This question describes a classic presentation of **tuberculosis** (fever, chest pain, cough with hemoptysis in a returned traveler, confirmed by acid-fast stain) treated with the standard **RIPE regimen** (Rifampin, Isoniazid, Pyrazinamide, Ethambutol). The subsequent triad of **skin rash, diarrhea, and confusion** corresponds to the **3 D's of pellagra** (dermatitis, diarrhea, dementia), caused by **niacin (vitamin B3) deficiency**.[1]

Isoniazid is the culprit: it inhibits the conversion of tryptophan to niacin and also impairs intestinal niacin absorption, thereby depleting body niacin stores and precipitating pellagra.[1][2] The "factor" prescribed is **niacin (vitamin B3)**.

Niacin is the precursor to **NAD+/NADH and NADP+/NADPH**, which serve as essential coenzymes for **dehydrogenase enzymes** — hydride-transfer (redox) reactions central to glycolysis, β-oxidation, oxidative phosphorylation, and hundreds of other metabolic pathways.[3][4] NAD+ or NADH participates in approximately 400 redox reactions.[5]

Why not the other options:

- **A. Collagen hydroxylation** — This describes **vitamin C**, required as a cofactor for prolyl and lysyl hydroxylase in collagen synthesis.
- **C. Methionine processing** — This describes **vitamin B12** (and folate), required for methionine synthase (homocysteine → methionine conversion).
- **D. Methylmalonyl-CoA processing** — This also describes **vitamin B12**, specifically adenosylcobalamin as a cofactor for methylmalonyl-CoA mutase.

Would you like to explore the vitamin deficiencies and nutritional complications associated with anti-tuberculosis therapy?

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Question 604

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?

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

https://openevidence.com/ask/4d0093eb-601c-47d2-a1ec-0a5c532d6fe7

The correct answer is **D: Sentinel node → right lumbar trunk → cisterna chyli → thoracic duct → left subclavian vein → systemic circulation**.

Two anatomical principles determine the answer:

Right ovary → right lumbar trunk. Ovarian lymphatic drainage follows the ovarian (gonadal) vessels and is predominantly ipsilateral. The right lower quadrant localization points to a right ovarian primary. Cadaveric injection studies confirm that right ovarian lymphatics drain preferentially to the **lateral-caval (right para-aortic) nodes**, while the left ovary drains to the lateral-aortic territory.[1] The right lumbar nodes feed into the **right lumbar trunk**, eliminating choices A and B (which specify the left lumbar trunk).

Cisterna chyli → thoracic duct → left subclavian vein. The right and left lumbar trunks converge at the **cisterna chyli**, which gives rise to the **thoracic duct** — the largest lymphatic trunk, responsible for draining the entire body below the diaphragm plus the left upper quadrant.[2] The thoracic duct empties into the venous system at the **left venous angle** (junction of the left internal jugular and left subclavian veins).[2][3][4] This eliminates choice C, which incorrectly routes abdominal lymph through the right bronchomediastinal trunk. The **right lymphatic duct**

drains only the right arm, right side of the head, and right lung — it plays no role in abdominal lymphatic drainage.[2][3]

Once tumor cells enter the left subclavian vein, they access the systemic venous circulation → right heart → pulmonary vasculature (explaining lung metastases) → left heart → systemic arterial circulation → brain (explaining brain metastases). Though the final spread to the brain is hematogenous, the question traces the lymphatic pathway that first delivers ovarian cancer cells into the bloodstream.

Would you like to explore the different patterns of lymphatic versus hematogenous metastasis in ovarian cancer?

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Question 605

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?

A. Clomipramine
B. Phenelzine
C. Fluoxetine
D. Propranolol

https://openevidence.com/ask/4e562bb8-ac54-4737-bd5d-e314296a27d3

The answer is **C. Fluoxetine**.

This patient presents with **social anxiety disorder (SAD)** — characterized by persistent fear of negative evaluation by peers, avoidance of social interactions (eating alone, avoiding speaking in class), physical symptoms during social performance (tachycardia, flushing), and significant functional impairment (declining grades, social isolation), all lasting well over 6 months.

SSRIs are the first-line pharmacotherapy for social anxiety disorder in children and adolescents. The AACAP clinical practice guideline recommends SSRIs for patients aged 6–18 with social anxiety disorder.[1] Fluoxetine has demonstrated efficacy in reducing anxiety symptoms in youth with SAD specifically — in a 12-week RCT, 61% of anxious youth treated with fluoxetine showed much to very much improvement versus 35% on placebo, with social phobia moderating the clinical and functional response.[2] SSRIs are preferred over other pharmacologic classes due to their **favorable risk-benefit ratio**, particularly in pediatric populations.[3][4]

Why the other options are incorrect:

- **A. Clomipramine** — A serotonergic tricyclic antidepressant primarily indicated for **OCD**, not first-line for social anxiety disorder. It carries greater risks of anticholinergic side effects, cardiac toxicity, and lethality in overdose compared to SSRIs.
- **B. Phenelzine** — An MAOI with demonstrated efficacy for SAD in adults, but its **dietary restrictions** (tyramine-containing foods) and risk of hypertensive crisis make it inappropriate as first-line therapy, especially in an adolescent.
- **D. Propranolol** — A beta-blocker useful for **isolated performance anxiety** (e.g., a single public-speaking event), as it attenuates autonomic symptoms like tachycardia. However, this patient has **generalized social anxiety disorder** affecting multiple domains of functioning, not merely performance anxiety, and propranolol does not address the pervasive avoidance, cognitive distortions, and social withdrawal seen here.[5]

Would you like to explore the dosing and titration of fluoxetine for social anxiety in adolescents?

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Question 606

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?

A. Tumor necrosis factor-α
B. Interleukin-5
C. Interleukin-12
D. Interleukin-4

https://openevidence.com/ask/908f5cfc-4d6a-4501-a2df-b9a84bed81a2

The answer is **A. Tumor necrosis factor-α (TNF-α)**.

TNF-α is a pivotal and well-established mediator of septic shock pathogenesis. It is the first cytokine to appear in the circulation following exposure to bacterial endotoxin (e.g., from *Neisseria meningitidis*), with release from activated macrophages beginning within 30 minutes and peak plasma levels at approximately 60–90 minutes.[1] Injection of TNF-α into experimental animals produces a syndrome **largely indistinguishable from septic shock**, and neutralization of TNF-α prevents endotoxic shock even in the presence of circulating endotoxins.[2][3]

TNF-α drives septic shock through several mechanisms:[1][4]

- **Vasodilation and increased vascular permeability**, leading to hypotension, systemic edema, and decreased blood volume
- **Upregulation of endothelial adhesion molecules** (ICAM-1, VCAM-1) and neutrophil integrin adhesiveness, promoting leukocyte extravasation and tissue injury
- **Procoagulant activation**, contributing to disseminated intravascular coagulation (DIC) — relevant to the petechiae and purpura seen in meningococcal sepsis
- **Synergistic action with IL-1**, amplifying pulmonary edema, hemorrhage, and shock

The other cytokines listed do not play a central role in septic shock pathogenesis. **IL-4** and **IL-5** are Th2 cytokines primarily involved in allergic responses and eosinophilic inflammation,

respectively. **IL-12** promotes Th1 differentiation and NK cell activation but is not a direct mediator of the hemodynamic collapse and organ failure characteristic of septic shock.

Would you like to explore the pathophysiology of Waterhouse-Friderichsen syndrome in meningococcal septicemia?

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Question 607

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?

A. Achalasia
B. Diffuse esophageal spasm
C. Eosinophilic esophagitis
D. Esophageal reflux disease

https://openevidence.com/ask/2f813edd-1743-4778-9396-236e0335c845

The answer is **C. Eosinophilic esophagitis (EoE)**.

This presentation is classic for EoE: a young adult with **dysphagia to solids only**, **PPI-refractory heartburn**, and a strong **atopic history** (asthma and eczema). More than 90% of patients with EoE have concomitant atopic conditions such as asthma, atopic dermatitis, or allergic rhinitis, and the more atopic comorbidities present, the higher the likelihood of EoE.[1][2] In adults, **dysphagia and food impaction** are the most common presenting symptoms, with over 70% reporting dysphagia.[3] Heartburn and chest pain can also occur and may not respond to acid suppression.[2][4]

Why the other options are less likely:

- **Achalasia** — Causes progressive dysphagia to **both solids and liquids** due to impaired lower esophageal sphincter relaxation and absent peristalsis. Weight loss and regurgitation of undigested food are typical. This patient's solid-only dysphagia and lack of liquid dysphagia argue strongly against achalasia.[5]
- **Diffuse esophageal spasm** — Also causes dysphagia to **both solids and liquids**, with intermittent, nonprogressive chest pain often triggered by hot or cold foods. The pattern here does not fit.

- **Esophageal reflux disease (GERD)** — GERD-related dysphagia typically results from peptic strictures, which would be unusual in a 35-year-old and would be expected to respond to high-dose PPI. This patient's **failure to respond to high-dose omeprazole** and the absence of red-flag features for stricture make GERD unlikely as the primary explanation.[6][7]

The key distinguishing clues are the **solid-food-only dysphagia** (suggesting a mechanical or inflammatory esophageal process rather than a motility disorder), **PPI-refractory symptoms**, and the **atopic diathesis** — together these point definitively to EoE.

Would you like to explore current first-line treatment options for eosinophilic esophagitis?

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Question 608

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?

A. Exertional heat stroke
B. Malignant hyperthermia
C. Neuroleptic malignant syndrome
D. Thyroid storm

https://openevidence.com/ask/9f7062ca-ee25-45c8-bf83-695ece5e4ed2

The most likely diagnosis is **A. Exertional heat stroke**.

Heat stroke is characterized by the triad of **hyperthermia (core temperature >40°C), CNS dysfunction, and recent physical exertion or hot weather exposure**.[1] This patient — a construction worker found down at a work site with a temperature of 106°F (41.1°C), altered mental status (GCS 10), tachycardia, and hypotension — fits this presentation precisely. Notably, **sweating is typical of exertional heat stroke**, distinguishing it from classic heat stroke, in which the skin is often hot and dry.[1] The ACSM consensus statement lists **flaccid muscles** among the clinical features of exertional heat stroke, consistent with the minimal muscle tone seen here.[2]

Why the other options are less likely:

- **B. Malignant hyperthermia** — This occurs **during anesthesia or within hours** of exposure to triggering agents (volatile anesthetics, succinylcholine), not months later. The appendectomy was several months ago, making this diagnosis essentially impossible in the current timeframe. Additionally, MH characteristically presents with **severe muscular rigidity**, which is absent here.[3][4][5][6]

- **C. Neuroleptic malignant syndrome (NMS)** — Although the patient takes haloperidol (a first-generation antipsychotic and common NMS trigger), a **cardinal feature of NMS is "lead-pipe" muscular rigidity**, which is described as the hallmark extrapyramidal sign. This patient has **minimal muscle tone**, which argues strongly against NMS. Per DSM-5 criteria, NMS requires exposure to a dopamine antagonist within 72 hours plus severe rigidity, fever, and additional features.[7][8][9]

- **D. Thyroid storm** — While the patient has hyperthyroidism and thyroid storm can cause fever and altered mental status, temperatures as extreme as 106°F would be unusual. More importantly, the **exertional context** (construction worker found down at the work site) and the absence of classic thyroid storm features such as atrial fibrillation, heart failure, or GI/hepatic dysfunction make this far less likely than heat stroke.[10]

The question is designed with several distractors — haloperidol for NMS, recent anesthesia for MH, and hyperthyroidism for thyroid storm — but the **occupational exertional context and absence of rigidity** are the key clinical features that point to exertional heat stroke.

Would you like to explore the recommended cooling strategies and acute management of exertional heat stroke?

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Question 609

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?

A. Synovial fluid analysis
B. Anti-cyclic citrullinated peptide (anti-CCP) antibody
C. Rheumatoid factor
D. X-ray of cervical spine

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The answer is **B. Anti-cyclic citrullinated peptide (anti-CCP) antibody**.

This presentation — a young woman with **symmetric MCP joint involvement**, **morning stiffness improving with activity**, and **symptom duration >6 weeks** — is classic for **rheumatoid arthritis (RA)**. Among the options listed, anti-CCP antibody is the most helpful diagnostic test due to its **superior specificity** for RA compared to rheumatoid factor.

Why anti-CCP over the other choices:

- **Anti-CCP antibody (B):** Meta-analyses demonstrate a **specificity of 95–97%** for RA, with a sensitivity of ~57–67% and a positive likelihood ratio of ~12.5. Anti-CCP is also included in the **2010 ACR/EULAR classification criteria**, where high-positive serology (RF or ACPA >3× upper limit of normal) contributes 3 points toward the ≥6-point threshold for RA classification. Importantly, anti-CCP can be positive in ~35% of RF-negative RA patients, making it valuable in seronegative cases.[1][2][3][4][5]
- **Rheumatoid factor (C):** While RF has comparable sensitivity (~69%), its **specificity is only ~85%**. RF can be elevated in numerous other conditions (hepatitis C, Sjögren syndrome, endocarditis, advanced age), making it less discriminatory. As noted in a Lancet review,

anti-CCP antibodies have shown the **highest specificity** among RA-related autoantibodies. [1][6]

- **Synovial fluid analysis (A):** Primarily useful for ruling out crystal arthropathy or septic arthritis, not for confirming RA.
- **X-ray of cervical spine (D):** Cervical spine changes (e.g., atlantoaxial subluxation) are findings of **late/established RA** and would not be expected with only 2 months of symptoms.[6]

"Since early diagnosis and treatment prevents progression of joint damage in 90% of patients with early RA, it is important to identify patients with RA as soon as possible. Specific symptoms that may indicate possible RA include articular pain and swelling in metacarpophalangeal joints, metatarsophalangeal joints, or both, morning stiffness of finger joints lasting 30 minutes or longer, and autoantibody positivity."

—Daniel Aletaha, MD et al., Division of Rheumatology, Department of Medicine 3, Medical University of Vienna, Vienna, Austria. Diagnosis and Management of Rheumatoid Arthritis. JAMA. October 02, 2018.

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Would you like to explore the recommended initial treatment approach for newly diagnosed rheumatoid arthritis?

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Question 610

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?

A. Adverse effect of ibuprofen
B. Decreased cardiac ejection fraction
C. Renal deposition of AL amyloid
D. Increased serum amyloid A production

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The answer is **D. Increased serum amyloid A production**.

This patient with **longstanding, severe rheumatoid arthritis** (swan-neck deformities, rheumatoid nodules) presents with **nephrotic syndrome** — periorbital edema, pedal edema, ascites, frothy urine, 3+ proteinuria, and hypoalbuminemia (albumin 2.8 g/dL). The most likely etiology is **AA (secondary) amyloidosis** from chronic inflammation.

Pathogenesis of AA amyloidosis in RA

Serum amyloid A (SAA) is an acute-phase reactant synthesized by hepatocytes under the transcriptional regulation of proinflammatory cytokines.[1][2] In chronic inflammatory conditions such as RA, **sustained overproduction of SAA** leads to misfolding and extracellular deposition of AA amyloid fibrils in target organs.[3][4] RA is the most common underlying disease complicated by AA amyloidosis in Western countries.[5][6] The **kidney is involved in >90% of cases**, with proteinuria, nephrotic syndrome, and progressive renal dysfunction dominating the clinical picture.[3][7]

> "Sustained overproduction of SAA is a prerequisite for the development of AA amyloidosis, although for reasons that are not known, amyloidosis occurs only in a small proportion of patients with chronic inflammatory disorders."
>
> —Helen J. Lachmann, M.D. et al., Royal Free and University College Medical School. Natural History and Outcome in Systemic AA Amyloidosis. N Engl J Med. June 07, 2007.
>
> Used under license from The New England Journal of Medicine.

Why not the other options?

- **A (Ibuprofen adverse effect):** NSAIDs can cause minimal change disease or membranous nephropathy, but the presence of severe, longstanding RA with deformities makes AA amyloidosis far more likely.
- **B (Decreased cardiac ejection fraction):** Heart failure causes edema and ascites but does not explain heavy proteinuria and hypoalbuminemia from urinary protein loss.
- **C (AL amyloid):** This is the key distinction. **AL amyloidosis** results from immunoglobulin **light chain** deposition in plasma cell dyscrasias (e.g., multiple myeloma), not from chronic inflammatory conditions. RA causes **AA** amyloidosis (from SAA), not AL amyloidosis. The question correctly separates the two pathogenetic mechanisms.[8][9]

Would you like to explore treatment strategies for AA amyloidosis secondary to rheumatoid arthritis?

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Question 611

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?

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

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The correct answer is **B. Gram-positive bacteria producing exotoxin that acts via ADP ribosylation**.

This presentation — a **febrile, unvaccinated child** from a region with suboptimal vaccine coverage presenting with **dyspnea**, a **grayish-white pharyngeal pseudomembrane**, **soft palate involvement**, and **marked cervical lymphadenopathy** ("bull neck") — is classic **pharyngeal diphtheria**, caused by **Corynebacterium diphtheriae**.[1][2]

Why B is correct

C. diphtheriae is an aerobic, non-motile, non-encapsulated, club-shaped **gram-positive bacillus**.[2][3] Toxigenic strains produce **diphtheria toxin**, a potent AB exotoxin whose A subunit catalyzes the **ADP-ribosylation of elongation factor 2 (EF-2)**, using NAD^+ as the ADP-ribose donor.[4][5] This inactivates EF-2 and **blocks protein synthesis**, leading to cell death.[6][7] The toxin is responsible for systemic complications including **myocarditis and polyneuropathy**, as well as the local tissue necrosis forming the pseudomembrane.[8][9]

The uneven soft palate elevation in this patient reflects **early palatal nerve paralysis**, a well-recognized neurologic complication of diphtheria toxin.

Why the other choices are incorrect

- **A (Yeast with pseudohyphae):** Describes *Candida* species, which cause oral thrush (white, scrapable plaques) but not adherent pseudomembranes with bull neck or systemic toxicity.

- **C (Gram-positive cocci with hyaluronic acid capsule):** Describes *Streptococcus pyogenes* (Group A Strep), which causes exudative pharyngitis but not a true pseudomembrane or this degree of cervical edema.
- **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 management of pharyngeal diphtheria, including antitoxin and antibiotic therapy?

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Question 612

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?

A. Increased creatine kinase concentration
B. Decreased glucose concentration
C. Increased triglyceride concentration
D. Increased bradykinin concentration

https://openevidence.com/ask/d3202318-7c64-4e92-ba9e-9978b2e770c8

The answer is **A. Increased creatine kinase concentration**.

The medication that **decreases the production of mevalonate** is a **statin (HMG-CoA reductase inhibitor)**. HMG-CoA reductase catalyzes the rate-limiting step in cholesterol biosynthesis — the conversion of HMG-CoA to mevalonate.[1][2][3] This patient has multiple ASCVD risk factors (hypertension, diabetes, smoking), making statin therapy appropriate.

Myopathy with elevated creatine kinase (CK) is the hallmark serious adverse effect of statins, defined as unexplained muscle pain or weakness with CK elevation >10 times the upper limit of normal.[4][5] While rare (<0.1% at maximal recommended doses), this is the most recognized adverse effect and can progress to rhabdomyolysis with acute renal failure in severe cases.[6][7]

The other options are incorrect:

- **B. Decreased glucose** — Statins actually **increase** glucose levels and raise the risk of new-onset type 2 diabetes by approximately 10–20% depending on intensity.[5]
- **C. Increased triglycerides** — Statins modestly **lower** triglycerides rather than raising them.
- **D. Increased bradykinin** — This is characteristic of **ACE inhibitors**, which block bradykinin degradation and can cause angioedema and cough. Statins do not affect bradykinin metabolism.

Would you like to explore the risk factors and management approach for statin-associated muscle symptoms?

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Question 613

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?

A. Hyperproliferation of theca interna cells
B. Exogenous anabolic steroid use
C. Ovarian fibrosis and multiple cystic follicles
D. Hyperplasia of the adrenal cortex

https://openevidence.com/ask/5db9da38-6afe-480d-8e88-3f53f29037b9

The answer is **D. Hyperplasia of the adrenal cortex**.

This presentation — **hirsutism, acne, oligomenorrhea, elevated 17-hydroxyprogesterone (390 ng/dL), and elevated testosterone** in a young woman with normal BMI — is consistent with **non-classic congenital adrenal hyperplasia (NCAH)** due to 21-hydroxylase deficiency.

Why NCAH and not PCOS?

While the clinical features (hirsutism, acne, menstrual irregularity) overlap substantially with PCOS, the **elevated 17-OHP above the normal range** is the distinguishing finding. A baseline 17-OHP >200 ng/dL should raise suspicion for NCAH, and values above the upper limit of normal (here, >300 ng/dL) warrant confirmatory testing with an ACTH stimulation test.[1][2][3] In PCOS, 17-OHP is typically normal. NCAH accounts for up to 10% of women presenting with hyperandrogenism.[4]

Pathophysiology and adrenal hyperplasia

In 21-hydroxylase deficiency, impaired cortisol synthesis leads to **loss of negative feedback on the pituitary**, resulting in increased ACTH secretion. Chronically elevated ACTH drives **bilateral hyperplasia of the adrenal cortex**.[4] Steroidogenic precursors proximal to the enzymatic block (including 17-OHP) accumulate and are shunted into the androgen synthesis pathway, producing the hyperandrogenic phenotype.[3][4]

Why not the other options?

- **A (Hyperproliferation of theca interna cells)** and **C (Ovarian fibrosis and multiple cystic follicles)** — both describe features of PCOS, which would not account for the elevated 17-OHP above normal.
- **B (Exogenous anabolic steroid use)** — no history suggests this, and exogenous androgens would suppress gonadotropins rather than elevate 17-OHP.

Would you like to explore the role of ACTH stimulation testing in confirming non-classic CAH?

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Question 614

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?

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

https://openevidence.com/ask/c5ae7dec-7618-4abf-889f-ad53da832f06

The answer is **A. Hyperplasia of juxtaglomerular cells**.

This patient has **renovascular hypertension** due to atherosclerotic renal artery stenosis (90% occlusion), presenting with resistant hypertension despite three antihypertensive agents. The pathophysiology centers on the **renin-angiotensin-aldosterone system (RAAS)**: decreased renal perfusion pressure distal to the stenosis causes hypoperfusion of the juxtaglomerular apparatus, which chronically stimulates renin release and leads to **striking hyperplasia of the juxtaglomerular (JG) cells**.[1][2] The juxtaglomerular index and renal renin content are elevated in the ischemic kidney in experimental models.[3]

Why the other options are incorrect:

- **B. Dilation of efferent arteriole** — Angiotensin II, produced in excess in this setting, causes **constriction** (not dilation) of the efferent arteriole to maintain glomerular filtration pressure.[2]
- **C. Decreased prostaglandin synthesis by macula densa** — Intrarenal prostaglandin synthesis actually **increases** in renovascular hypertension as a compensatory vasodilatory response to ischemia.[4]

- **D. Decreased reabsorption of bicarbonate at proximal tubule** — Angiotensin II stimulates **increased** sodium and bicarbonate reabsorption in the proximal tubule, not decreased.[2] [5]

Would you like to explore the current evidence on revascularization versus medical therapy for atherosclerotic renal artery stenosis?

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Question 615

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?

A. Dantrolene
B. Bromocriptine
C. Cyproheptadine
D. Surgical embolectomy

https://openevidence.com/ask/dc151b75-94ee-436f-bc50-fa1482756b49

The answer is **A. Dantrolene**.

This patient is experiencing **malignant hyperthermia (MH)** during general anesthesia, a life-threatening hypermetabolic crisis triggered by volatile inhalational anesthetics (and/or succinylcholine) in genetically susceptible individuals. The hallmark findings here are:

- **Markedly elevated end-tidal CO_2 (85 mmHg)** — the earliest and most sensitive sign of MH, reflecting uncontrolled skeletal muscle hypermetabolism[1][2]
- **Muscle rigidity** — almost pathognomonic when it occurs despite neuromuscular blockade[2]
- **Rapid-onset hyperthermia** (37.3°C → 39.1°C)
- **Tachycardia, hypertension, and profuse diaphoresis**

Why dantrolene: Dantrolene is the **only FDA-approved specific treatment** for MH. It inhibits calcium release from the sarcoplasmic reticulum via the ryanodine receptor, directly halting the hypermetabolic cascade.[3][4] The initial dose is **2.5 mg/kg IV push**, continued until symptoms subside or a maximum cumulative dose of 10 mg/kg is reached.[3][5] Early administration is critical — mortality increases 1.6-fold for every 30-minute delay.[6] Since dantrolene became available, MH mortality has dropped from >80% to <5%.[1]

Why not the other options:

- **Bromocriptine** — a dopamine agonist used for **neuroleptic malignant syndrome (NMS)**. Although this patient takes haloperidol (a dopamine antagonist), NMS develops over **hours to days** after drug exposure, not acutely intraoperatively, and does not cause a markedly elevated end-tidal CO_2.[7]
- **Cyproheptadine** — a serotonin antagonist used for **serotonin syndrome**. Although the patient takes sertraline, serotonin syndrome features **hyperreflexia, clonus, and myoclonus** rather than lead-pipe rigidity and massively elevated $ETCO_2$.[7]
- **Surgical embolectomy** — treatment for massive pulmonary embolism, which would present with hemodynamic collapse and hypoxia, not rigidity and hypercarbia of this magnitude.

The intraoperative setting, explosive hypercarbia, and muscle rigidity make MH the unequivocal diagnosis, and **dantrolene** is the definitive therapy.

Would you like to explore the post-crisis genetic testing and family screening protocol for malignant hyperthermia susceptibility?

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Question 616

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?

A. Pre-T cell
B. Double-positive T cell
C. Single-positive CD4+ T cell
D. Single-positive CD8+ T cell

https://openevidence.com/ask/cae69818-18f1-4f0a-8456-548d86b10f41

The answer is **B. Double-positive T cell**.

Positive selection occurs at the $CD4^+$ $CD8^+$ double-positive (DP) stage in the thymic cortex.[1][2][3] At this stage, DP thymocytes express newly rearranged αβ TCRs that are tested for their ability to recognize self-peptide–MHC complexes displayed by cortical thymic epithelial cells (cTECs). The outcomes are as follows:

- **Moderate-affinity TCR–MHC interaction** → the DP thymocyte is rescued from apoptosis and undergoes positive selection, subsequently differentiating into a single-positive $CD4^+$ or $CD8^+$ T cell depending on whether the TCR engaged MHC class II or class I, respectively.[1][3]
- **No or insufficient TCR–MHC interaction** (~90% of DP thymocytes) → "death by neglect" via apoptosis within ~3 days.[2][3]
- **Excessively high-affinity TCR–MHC interaction** → negative selection (clonal deletion) or, in some cases, agonist selection into regulatory T cells.[1][2]

The logic for positive selection occurring at the DP stage is straightforward: both CD4 and CD8 coreceptors are expressed simultaneously, allowing the thymocyte to be tested against both MHC class I and class II molecules before committing to one lineage.[4][5] Only after passing positive selection does the cell downregulate one coreceptor and become a single-positive (SP) thymocyte, which then migrates to the medulla for further maturation and additional rounds of negative selection.[6]

Would you like to explore how CD4 versus CD8 lineage commitment is determined after positive selection?

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Question 617

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?

A. Acute stress disorder
B. Performance anxiety
C. Posttraumatic stress disorder
D. Panic attack

https://openevidence.com/ask/c9029ddd-4741-4fb2-a9b9-07d1f922c862

The answer is **C. Posttraumatic stress disorder (PTSD)**.

This patient meets **DSM-5 diagnostic criteria for PTSD** based on all key elements of the presentation:[1][2][3]

- **Criterion A (traumatic exposure):** Direct exposure to bombing attacks during combat in Iraq.
- **Criterion B (intrusion):** Disturbing flashbacks to bombing attacks and upsetting dreams.
- **Criterion C (avoidance):** Refusing to leave his house and inability to tolerate shooting ranges and explosions during training.
- **Criterion E (alterations in arousal/reactivity):** Intense fear of loud noises (hyperarousal/exaggerated startle).
- **Criterion F (duration ≥1 month):** Symptoms have persisted for **7 weeks**, well exceeding the 1-month minimum.

Why not the other choices?

- **A. Acute stress disorder** is the closest mimic but is distinguished from PTSD solely by duration — ASD can only be diagnosed when symptoms persist between **3 days and 1 month** after the trauma. Once symptoms exceed 1 month, the diagnosis is reclassified as PTSD.[2]
- **B. Performance anxiety** does not account for the flashbacks, nightmares, avoidance behavior, and hyperarousal linked to a specific traumatic event.
- **D. Panic attack** describes an acute episode of intense fear with somatic symptoms (palpitations, dyspnea, chest pain); it does not explain the sustained trauma-related re-experiencing, avoidance, and arousal pattern seen here.

The **critical differentiator** in this question is the **7-week symptom duration**, which places the presentation beyond the ASD window and firmly into PTSD.[2][4]

Would you like to explore first-line treatment options for combat-related PTSD?

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Question 618

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?

A. Major Basic Protein
B. Mucus
C. Surfactant
D. Elastase

https://openevidence.com/ask/a6c1a940-7466-4e20-bd4f-af5666b08c64

The answer is **D. Elastase**.

Elastase, specifically **neutrophil elastase**, is the key protease responsible for alveolar destruction in alpha-1 antitrypsin (AAT) deficiency. AAT is a serine protease inhibitor whose primary role is to neutralize neutrophil elastase in the lung. When AAT is deficient, unopposed elastase cleaves structural proteins of the lung — particularly elastin — leading to emphysema.[1]

Both **neutrophils and alveolar macrophages** contribute to elastase burden in the lower respiratory tract. Alveolar macrophages in AAT-deficient individuals also amplify neutrophil recruitment by releasing leukotriene B4 in response to uninhibited elastase, creating a destructive feedback loop.[2]

Cigarette smoking compounds the problem through two mechanisms:[1][3]

- Oxidants in cigarette smoke inactivate the already-insufficient Z-form AAT by oxidizing its active-site methionine residues, reducing its inhibitory capacity approximately 2,000-fold.
- Smoking increases polymerization of Z AAT, which further impairs its function and acts as a neutrophil chemoattractant.

The other choices are incorrect:

- **Major basic protein** is released by eosinophils (not neutrophils/macrophages) and is relevant to parasitic infections and asthma.
- **Mucus** is produced by goblet cells and submucosal glands, not neutrophils/macrophages.

- **Surfactant** is produced by type II alveolar epithelial cells and reduces surface tension; it is unrelated to the protease-antiprotease mechanism of emphysema.

Would you like to explore the evidence for AAT augmentation therapy in slowing disease progression?

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Question 619

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?

A. Can form an endospore
B. Has no cell wall
C. Is more common in parrot owners
D. Is transmitted by air conditioning

https://openevidence.com/ask/07729ace-49c1-48af-a5f7-47aff5060559

The answer is **D. Transmitted by air conditioning**.[1][2][3]

This presentation is classic for **Legionnaires' disease** caused by **Legionella pneumophila**. The constellation of **atypical pneumonia** (bilateral patchy infiltrates, fine crackles), **gastrointestinal symptoms** (diarrhea), **hyponatremia**, and **elevated hepatic transaminases** in a patient with recent water-aerosol exposure (spas, kayaking) is highly characteristic.[1][4][5] The incubation period of 2–14 days aligns with the timeline of symptom onset after travel.[1][3]

Why the other options are incorrect:

- **A. Endospore formation** — Legionella does not form endospores. This feature is associated with *Bacillus* and *Clostridium* species.
- **B. No cell wall** — This describes *Mycoplasma*. Legionella is a **gram-negative rod** (though it stains poorly on Gram stain and is typically visualized with silver staining or direct fluorescent antibody).

- **C. More common in parrot owners** — This describes *Chlamydia psittaci* (psittacosis). While psittacosis can cause atypical pneumonia, the hyponatremia, diarrhea, hepatic enzyme elevation, and water-source exposure strongly favor Legionella.

Legionella and air conditioning: *L. pneumophila* colonizes freshwater environments and thrives in anthropogenic water systems, particularly **cooling towers** associated with large air conditioning systems, as well as hot tubs, thermal spas, and plumbing systems.[1][2][6] Transmission occurs via **inhalation of contaminated water aerosols** generated by these systems.[3][7] This patient's spa visits during travel represent a well-recognized exposure source.[1][3]

Would you like to explore the diagnostic workup and empiric treatment for Legionnaires' disease?

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Question 620

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?

A. Radiograph of the wrist
B. MRI of the wrist
C. Thumb spica cast
D. Radial gutter cast

https://openevidence.com/ask/0405aebc-dbdd-4364-9ab7-035fa44b4ed2

The answer is **A. Radiograph of the wrist**.

This patient presents with a classic mechanism for **scaphoid fracture** — a fall on an outstretched hand (FOOSH) — with tenderness in the **anatomical snuffbox** (the region between the extensor pollicis longus and extensor pollicis brevis). **Plain radiographs are the initial imaging modality of choice** for suspected scaphoid fractures.[1][2] A standard series includes anteroposterior, lateral, oblique, and scaphoid (ulnar deviation) views.[3][4]

Why the other choices are incorrect:

- **B. MRI of the wrist** — MRI is indicated when radiographs are negative but clinical suspicion for an occult scaphoid fracture remains high. Up to 16% of scaphoid fractures are missed on initial radiographs, and in that scenario MRI is the most accurate second-line test. However, it is not the first-line study — radiographs must be obtained first.[1][3][5]
- **C. Thumb spica cast** — A thumb spica cast (or splint) is the appropriate immobilization for a confirmed or highly suspected scaphoid fracture, but applying one without any imaging

would be premature. Imaging is needed to confirm the diagnosis, assess fracture displacement, and guide management (nondisplaced fractures are treated conservatively; displaced fractures require surgical referral).[4][6]

- **D. Radial gutter cast** — This is used for **4th and 5th metacarpal fractures** (e.g., boxer's fracture), not scaphoid fractures. The clinical presentation here localizes to the radial side of the wrist, not the ulnar metacarpals.

Would you like to explore the management of suspected scaphoid fracture with negative initial radiographs?

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Question 621

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?

A. In vitro fertilization with patient's egg
B. Progesterone therapy
C. Clomiphene therapy
D. Leuprolide therapy

https://openevidence.com/ask/c4972fea-0e73-4170-99d8-814244bf1e5e

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The correct answer is **C. Clomiphene therapy**.

This patient presents with classic **polycystic ovary syndrome (PCOS)**: oligomenorrhea since menarche (45–90 day cycles), two years of infertility, elevated BMI, oily skin, severe acne, and hirsutism — satisfying the Rotterdam criteria (oligo-anovulation + clinical hyperandrogenism). Given her desire for fertility, the question is which pharmacologic therapy to initiate alongside lifestyle modifications.

Clomiphene citrate is a selective estrogen receptor modulator that blocks estradiol-mediated negative feedback at the hypothalamus, increasing GnRH pulse frequency and subsequent FSH/LH release to promote follicular growth and ovulation.[1] It has long been the standard first-line oral ovulation induction agent for anovulatory infertility in PCOS.[2][3]

Of note, current evidence and the 2023 International Evidence-Based Guideline for PCOS now recommend **letrozole** over clomiphene as the preferred first-line agent, given higher live birth rates (27.5% vs. 19.1%; RR 1.44) and ovulation rates demonstrated in the landmark PPCOS II trial.

[4] However, letrozole is not among the answer choices, making clomiphene the best available option.

Why the other choices are incorrect:

- **A. In vitro fertilization** — Reserved for cases refractory to ovulation induction and simpler interventions; not a first-line approach.[5]
- **B. Progesterone therapy** — Produces a withdrawal bleed and protects the endometrium from unopposed estrogen, but does **not** induce ovulation or address infertility.
- **D. Leuprolide therapy** — A GnRH agonist that, after initial stimulation, downregulates the hypothalamic-pituitary-gonadal axis and **suppresses** ovulation — counterproductive for a patient trying to conceive.

Would you like to explore the evidence comparing letrozole to clomiphene for ovulation induction in PCOS, including dosing protocols?

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Question 622

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?

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

https://openevidence.com/ask/bf2beb0c-332b-463b-ad6b-e4d0ef87e78a

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The correct answer is **B. Request further information about which drugs he has taken recently and in the past**.

In a patient with a known substance use history presenting with pain complaints disproportionate to examination findings and demanding opioid refills, the **most appropriate initial step is a thorough, nonjudgmental substance use history**. The CDC 2022 Clinical Practice Guideline for Prescribing Opioids specifically recommends that clinicians **ask patients about their drug and alcohol use** before making prescribing decisions, particularly in those with substance use disorders.[1] This history — including current and past substance use, opioid exposure, adherence to the prescribed regimen, and any concurrent use of other substances — is the foundational assessment that guides all subsequent management.

Why not the other options:

- **A (Long-acting opioid with pain contract):** Escalating to a long-acting opioid is inappropriate here. The physical exam shows a healing surgical site with no effusion, erythema, or gait abnormality — findings inconsistent with severe pain requiring opioid escalation. Prescribing a long-acting opioid to a patient with a substance abuse history and pain out of proportion to findings carries significant risk for misuse and overdose.[1]

- **C (Urine drug test):** While toxicology screening has a role in opioid risk assessment per CDC guidelines, it is a **supplementary tool**, not the first response. Ordering a urine test before taking a history bypasses the clinical foundation needed to interpret results and can damage the therapeutic relationship. History should precede and contextualize any testing. [1]
- **D (Substance use counselor referral):** Referral to addiction counseling may ultimately be appropriate, but it is premature without first gathering the information needed to determine whether the patient has an active substance use disorder, is experiencing undertreated pain, or both. Assessment precedes referral.

Notably, pain disproportionate to findings in a postoperative patient should also prompt consideration of other causes (e.g., neuropathic pain, complex regional pain syndrome, or surgical complications), but the question specifically asks about responding to the opioid refill request. The substance use history is the essential clinical step that informs whether opioids can be safely continued with risk mitigation, whether alternative analgesic strategies are needed, or whether referral is warranted.[2]

Would you like to explore multimodal analgesic strategies for managing postoperative pain in patients with substance use disorders?

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Question 623

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?

A. Transesophageal echocardiography
B. Intravenous vancomycin therapy
C. X-ray of the chest
D. CT pulmonary angiogram

https://openevidence.com/ask/02d45840-0cdc-42a8-9bc5-e31eee3f7b46

The answer is **B. Intravenous vancomycin therapy**.

This patient presents with classic **right-sided infective endocarditis (IE) in the setting of IV drug use** — fever, Roth spots, a new holosystolic murmur at the lower left sternal border (tricuspid regurgitation), and TTE-confirmed tricuspid valve vegetations. Blood cultures have already been obtained, making **empiric antibiotic therapy the most appropriate next step**.

Vancomycin is the cornerstone of empiric therapy because **Staphylococcus aureus — particularly MRSA — is the predominant pathogen** in injection drug use–associated IE.[1] The AHA guidelines and multiple consensus statements recommend that empiric coverage include anti-MRSA agents such as vancomycin once blood cultures have been drawn.[2][3][4] Antibiotics should be started promptly in patients with an acute presentation (as in this case with fever, tachycardia, and leukocytosis).[5][6]

Why the other options are incorrect:

- **A. TEE** — Transesophageal echocardiography is indicated when TTE is nondiagnostic or when there is concern for left-sided involvement, perivalvular abscess, or prosthetic valve IE. Here, TTE has already demonstrated vegetations and confirmed the diagnosis; TEE would not change immediate management.
- **C. Chest X-ray** — While septic pulmonary emboli are common with right-sided IE, imaging is secondary to initiating antibiotics. A chest X-ray may be obtained as part of the workup but is not the most urgent next step.
- **D. CT pulmonary angiogram** — There is no clinical suspicion for pulmonary embolism as the primary diagnosis; the presentation is explained by IE with possible septic emboli, which does not require CTPA for management.

Would you like to explore the indications for surgical intervention in right-sided infective endocarditis?

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Question 624

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?

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.

https://openevidence.com/ask/4ff06b06-c00e-4981-ae0b-78952b3c2c19

The correct answer is **C. Bupropion lowers the seizure threshold and it should not be taken by patients with a history of seizure disorder.**

Bupropion is FDA-approved for both depression and smoking cessation, and the medication the patient's friend described — an antidepressant that helps with smoking cessation — fits bupropion. However, **seizure disorder is a labeled contraindication**. The FDA prescribing information explicitly states that bupropion "can cause seizure" and is "contraindicated in patients with a seizure disorder or conditions that increase the risk of seizure (e.g., severe head injury...)".[1][2][3] This patient has a history of head trauma with two seizure episodes, making bupropion contraindicated.

Among individual antidepressants, bupropion carries the highest disproportionality signal for seizures (ROR 8.57) in a large pharmacovigilance analysis.[4]

Why the other options are incorrect:

- **A** — Omeprazole primarily inhibits **CYP2C19 and CYP3A4**, while bupropion is metabolized by **CYP2B6**. There is no clinically significant interaction, and no timing-based dosing strategy is needed.[5][6][7]
- **B** — Bupropion is **effective as monotherapy** for smoking cessation and does not require co-administration with NRT, though combination with nicotine patch can enhance efficacy.[8]
- **D** — No cardiac workup is required before prescribing bupropion. Clinical trials have not shown increased cardiovascular events with bupropion compared to placebo.[8][9]

Would you like to explore alternative smoking cessation pharmacotherapy options for patients with seizure disorders?

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Question 625

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?

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.”

https://openevidence.com/ask/f39a04d4-b814-4d6c-b7f7-b8ed093fbde4

The correct answer is **A: "I'm sorry for your loss. This must be a difficult situation for you."**

This response exemplifies the principles of **empathetic, patient-centered bereavement communication** after perinatal loss. It acknowledges the loss directly, validates the patient's emotional experience, and uses open-ended language that invites further expression of her feelings without imposing assumptions about how she should grieve.

Why the other options are inappropriate:

- **B ("next time it'll work out")** — Offers **premature and false reassurance**, minimizing the current loss by redirecting to a hypothetical future pregnancy. This invalidates the patient's grief and is particularly problematic given her history (G2P0, suggesting a prior pregnancy loss as well).
- **C ("I see this every day")** — **Trivializes the loss** by normalizing it through the physician's experience. The focus should be on the patient's feelings, not the clinician's familiarity with perinatal death.

- **D (offering a prescription)** — While the opening is appropriate, **immediately medicalizing a normal grief response** bypasses the essential step of emotional support. Grief after perinatal loss is expected and should not be treated pharmacologically as an initial intervention.[1]

The ACOG/SMFM Obstetric Care Consensus on Management of Stillbirth emphasizes that **bereavement care should be individualized**, communication should be **clear and honest**, and clinicians should **acknowledge that grief is individual** — all principles reflected in option A.[2][3] The initial physician response should provide emotional support before any other interventions are considered.[1][4]

Would you like to explore the full ACOG/SMFM framework for bereavement care and follow-up after stillbirth?

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Question 626

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?

A. Metabolic inhibitor
B. Cell wall inhibitor
C. Neutrophil migration inhibitor
D. Prostaglandin inhibitor

https://openevidence.com/ask/3aa8f85f-2e52-4ab6-9871-cc8a0919e861

The answer is **B. Cell wall inhibitor**.

This clinical scenario — a **23-year-old sexually active male** with multiple sexual partners and **acute monoarticular knee swelling** with a synovial fluid WBC of **90,000 cells/mm³** — is classic for **gonococcal septic arthritis** (disseminated gonococcal infection). *Neisseria gonorrhoeae* is the most common cause of septic arthritis in adolescents and young, sexually active adults.[1] A synovial fluid WBC count >50,000 cells/mm³ strongly suggests septic arthritis, with a likelihood ratio of 7.7.[2]

Treatment: Ceftriaxone, a third-generation cephalosporin, is the recommended first-line agent. Per CDC STI Treatment Guidelines, the regimen for gonococcal arthritis is **ceftriaxone 1 g IM or IV every 24 hours**, with transition to an oral agent guided by susceptibility testing after 24–48 hours of clinical improvement, for a total course of at least 7 days.[3][4]

Mechanism of action: Ceftriaxone is a **bactericidal agent that acts by inhibition of bacterial cell wall synthesis** — specifically, it binds penicillin-binding proteins (PBPs) and disrupts peptidoglycan cross-linking.[5] This makes it a **cell wall inhibitor** (answer B).

Why the other options are incorrect:

- **A. Metabolic inhibitor** — refers to drugs like sulfonamides or trimethoprim (folate synthesis inhibitors), not used for gonococcal arthritis.

- **C. Neutrophil migration inhibitor** — refers to colchicine, used for gout/crystal arthropathy, not septic arthritis.
- **D. Prostaglandin inhibitor** — refers to NSAIDs (COX inhibitors), which are anti-inflammatory but not definitive treatment for septic arthritis.

Would you like to explore the empiric antibiotic approach for non-gonococcal septic arthritis?

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Question 627

Which of the following patient presentations seen in a pediatric immunology clinic is most consistent with a diagnosis of Bruton's agammaglobulinemia?

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

https://openevidence.com/ask/8426793d-fa8b-4ea8-a084-fc56e8bc3511

The answer is **D: a 9-month-old boy with recurrent otitis media and pneumococcal pneumonia in the past three months**. This presentation is the classic phenotype of Bruton's (X-linked) agammaglobulinemia (XLA).

XLA is an **X-linked recessive** disorder caused by mutations in the **BTK gene**, resulting in a near-complete absence of mature B cells and all immunoglobulin isotypes.[1][2] Because the gene is on the X chromosome, it occurs **almost exclusively in males**.[3] Affected boys are typically well for the first 6–12 months of life, protected by transplacentally acquired maternal IgG; symptoms emerge once maternal antibodies wane.[4][5] The hallmark infections are **recurrent pyogenic bacterial infections** — particularly **otitis media** (the most common infection prior to diagnosis), **sinusitis**, and **pneumonia** — caused predominantly by **S. pneumoniae** and **H. influenzae**.[1][6]

Option D fits every cardinal feature: male sex, onset after ~6 months when maternal antibodies decline, and recurrent bacterial infections with encapsulated organisms (pneumococcal pneumonia, otitis media).

Why the other choices are incorrect:

- **A (15-month-old girl, otitis media, pneumonia, progressive clumsiness):** The female sex essentially excludes XLA. The combination of recurrent sinopulmonary infections with **progressive ataxia** is instead classic for **ataxia-telangiectasia**, an autosomal recessive combined immunodeficiency.

- **B (10-month-old boy, recurrent viral infections, neonatal hypocalcemia):** Recurrent **viral** infections point to a **T-cell defect**, not a B-cell/antibody deficiency. Neonatal hypocalcemia from hypoparathyroidism is characteristic of **DiGeorge syndrome** (22q11.2 deletion), which causes thymic hypoplasia and impaired T-cell immunity.
- **C (4-year-old girl, recurrent oral candidiasis):** Mucocutaneous candidiasis reflects defective **T-cell or innate immunity**, not antibody deficiency. This presentation is more consistent with **chronic mucocutaneous candidiasis** or another T-cell disorder. The female sex also argues against XLA.

Would you like to explore the diagnostic workup and management of X-linked agammaglobulinemia?

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Question 628

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?

A. Affective symptoms
B. Being single
C. Male sex
D. Negative symptoms

https://openevidence.com/ask/8a7c8ebf-b7b8-4d67-ada2-d20b832f7dd3

The answer is **A. Affective symptoms**.

This patient presents with features of a psychotic disorder — **auditory hallucinations, flat affect, and disheveled appearance** — alongside prominent **affective (manic-like) symptoms** including grandiosity, increased talkativeness, heightened sociability, and agitation. The presence of affective symptoms in the context of a schizophrenia spectrum disorder is a classically taught **predictor of favorable prognosis**.

The other options are all associated with **poor prognosis**:

- **Being single (B):** Lack of stable interpersonal relationships is a well-recognized poor prognostic indicator; married status is favorable.
- **Male sex (C):** Males with schizophrenia have more prominent **negative symptoms, cognitive impairment, and generally worse functional outcomes** than females. Female sex and higher education at first admission predict favorable outcome.[1][2]

- **Negative symptoms (D):** Consistently among the strongest predictors of poor outcome. Fewer negative symptoms at first presentation significantly predicted better outcome at follow-up, and baseline PANSS negative symptom scores are inversely associated with remission.[2][3][4]

The rationale for affective symptoms predicting better outcomes is that their presence may indicate a greater mood-disorder component to the illness, which is generally more treatment-responsive. Multiple studies have noted that schizophrenia patients with prominent affective features tend toward a more favorable course, though some authors have challenged the universality of this association, particularly regarding depressive symptoms and suicide risk.[5][6][7][8]

Would you like to explore the diagnostic distinctions between schizophrenia, schizoaffective disorder, and brief psychotic disorder?

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Question 629

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?

A. Deep brain stimulation
B. Thalamotomy
C. Levodopa and carbidopa therapy
D. Propranolol therapy

https://openevidence.com/ask/15b7e303-27d4-4f26-b543-ff578f71e259

D. Propranolol therapy.

This is essential tremor: a bilateral, symmetric action tremor of the upper limbs — postural (present immediately on arm extension) with a kinetic/intention component worsening on target approach — progressive over months, interfering with activities of daily living, with an autosomal dominant family history and no other neurologic signs (normal tone, strength, reflexes, no bradykinesia or hypophonia).[1][2][3] Propranolol is the only FDA-approved treatment for essential tremor and, with primidone, constitutes first-line therapy (AAN Level A).[1][4]

Dosing and monitoring

- Effective in randomized trials at **120–240 mg/day**, with mean accelerometric tremor amplitude reduction of ~55%; titrate gradually to the lowest effective dose.[3]
- Long-acting propranolol has efficacy similar to the immediate-release formulation.[3]
- Screen for contraindications before starting: **asthma/bronchospastic disease, symptomatic bradycardia or heart block, decompensated heart failure, hypotension**; adverse effects include bradycardia and bronchospasm. Avoid abrupt discontinuation.[3]

- Roughly **30–50% of patients do not respond** to propranolol or primidone. Second-line is switching to the other first-line agent, then combination therapy.[1][3][4]
- Reasonable baseline workup to exclude enhanced physiologic tremor: **TSH**, electrolytes, liver and renal function, plus a review of tremorogenic drugs (SSRIs, valproate, lithium, β-agonists, stimulants).[1][3]

Why the other options are wrong

- **Deep brain stimulation (A)** and **thalamotomy (B)** are reserved for **medication-refractory, disabling tremor**; this patient has had no pharmacologic trial. Where they are compared, VIM DBS yields fewer adverse events and greater functional improvement than radiofrequency thalamotomy, and bilateral thalamotomy is avoided because of the risk of irreversible dysarthria and ataxia — relevant here given bilateral symptoms.[1][3]
- **Levodopa–carbidopa (C)** treats Parkinson disease, which is excluded by the absence of rest tremor, bradykinesia, rigidity, and asymmetry; Parkinson postural tremor characteristically re-emerges after a latency rather than appearing immediately on arm extension.[1][2][5]

Would you like to explore how to choose between propranolol and primidone as the initial agent?

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Question 630

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?

A. Recipient T-cells in the graft
B. Drug-induced nephrotoxicity
C. Fibrosis of the glomerular vessels
D. Newly formed anti-HLA antibodies

https://openevidence.com/ask/799d1f49-dd54-46e1-b9cd-159b469c94a1

The answer is **A. Recipient T-cells in the graft**.

This presentation — acute graft dysfunction at **10 days post-transplant** with rising creatinine, graft tenderness, low-grade fever, and biopsy showing **tubulitis with negative C4d staining** — is the classic picture of **acute T-cell mediated (cellular) rejection**.

Why tubulitis and C4d negativity are key:

- **Tubulitis** (mononuclear cell invasion across the tubular basement membrane into renal tubules) is the hallmark histologic lesion of T-cell mediated rejection per the Banff classification. In this process, **recipient T-cells recognize donor alloantigens**, undergo clonal expansion, infiltrate the graft, and cause tissue injury.[1][2][3]
- **Negative C4d staining** effectively rules out antibody-mediated rejection. C4d deposition in peritubular capillaries reflects complement activation via the classical pathway and is a

specific marker of antibody-mediated rejection. Its absence here confirms the rejection is cellular, not humoral.[1][3][4]

Why the other options are incorrect:

- **B. Drug-induced nephrotoxicity** — Cyclosporine toxicity can cause graft dysfunction, but biopsy typically shows arteriolar hyalinosis ("striped fibrosis"), not tubulitis. The biopsy findings here point definitively to rejection.[5]
- **C. Fibrosis of glomerular vessels** — This describes **chronic rejection**, which develops over months to years with progressive vascular obliteration and interstitial fibrosis, not at 10 days post-transplant.[5][6]
- **D. Newly formed anti-HLA antibodies** — This would cause **antibody-mediated rejection**, which requires positive C4d staining in peritubular capillaries along with circulating donor-specific antibodies. The C4d-negative biopsy here excludes this diagnosis.[1][2]

The clinical timeline is also characteristic: the graft functioned initially (5 L urine output on POD 2, creatinine 2.1), then deteriorated — consistent with the days-to-weeks timeframe of acute cellular rejection in the first year post-transplant.[1]

Would you like to explore the treatment of acute T-cell mediated rejection in kidney transplant recipients?

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Question 631

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?

A. Proton-pump inhibitors
B. Thiazide diuretics
C. Lithium
D. Estrogen

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The answer is **A. Proton-pump inhibitors**.

PPIs are the only medication class listed that is associated with decreased bone density and increased fracture risk, making them the appropriate class to discontinue in a patient with osteopenia concerned about progressive bone loss.[1][2][3] A meta-analysis found PPI use was associated with increased risk of hip fracture (HR 1.22), spine fracture (HR 1.49), and osteoporosis (HR 1.23).[3] Proposed mechanisms include hypochlorhydria-associated calcium malabsorption, PPI-induced hypomagnesemia with secondary hypocalcemia, and gastrin-induced parathyroid hyperplasia.[4] Importantly, this patient is already being treated with an **H2RA** for GERD, providing an alternative acid-suppression strategy that allows PPI discontinuation without leaving her reflux untreated.

The other three medications are **bone-protective** and should be continued:

- **Thiazide diuretics (B)** increase bone mineral density through enhanced renal calcium reabsorption and direct stimulation of osteoblast differentiation. Thiazide users demonstrate slower BMD decline compared to nonusers.[5][6][7]

- **Lithium (C)** is associated with a **38% decreased risk of osteoporosis** (HRR 0.62; 95% CI 0.53–0.72) in a dose-response manner, likely mediated by activation of Wnt/β-catenin signaling via GSK-3β inhibition.[8]
- **Estrogen/HRT (D)** is well established as bone-protective and is FDA-approved for prevention of postmenopausal osteoporosis.

Would you like to explore how to use FRAX to determine fracture risk and treatment thresholds in postmenopausal women with osteopenia?

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Question 632

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?

A. Bronchoalveolar wash
B. Pulmonary function studies
C. Echocardiography
D. Chest CT

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The correct answer is **C. Echocardiography**.

This patient presents with progressive dyspnea, exercise intolerance, fatigue, bilateral lower extremity edema, elevated JVP, decreased breath sounds at the lung bases, and an **enlarged cardiac silhouette on chest X-ray** — findings highly suggestive of heart failure with both left- and right-sided congestion. However, this constellation also raises the possibility of **pericardial effusion**, which could account for the enlarged silhouette.

Transthoracic echocardiography (TTE) is the recommended initial imaging study (Class I, AHA/ACC/HFSA 2022) in patients with suspected or new-onset heart failure to assess cardiac structure and function.[1] It provides comprehensive evaluation of LVEF, diastolic function, chamber dimensions, wall thickness, valvular abnormalities, and hemodynamic parameters, and critically, can also identify pericardial effusion.[1][2] Both ACC/AHA and ESC guidelines assign this a Class I recommendation.[3]

Why not the other options:

- **Bronchoalveolar wash (A):** Indicated for infectious or inflammatory lung disease workup; not appropriate when signs of cardiac pathology (elevated JVP, cardiomegaly) predominate.

- **Pulmonary function studies (B):** Would evaluate primary pulmonary disease, but elevated JVP, peripheral edema, and enlarged cardiac silhouette point to a cardiac etiology.
- **Chest CT (D):** Can provide anatomic information but does not offer the real-time functional assessment (EF, diastolic function, valvular dynamics, filling pressures) that echocardiography provides and that is essential for classifying and managing heart failure. [2][4]

Would you like to explore guideline-directed medical therapy for heart failure once an echocardiographic diagnosis is established?

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Question 633

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?

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

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The answer is **C. Nasal congestion due to a viral infection**.

Phenylephrine, the prototypical **selective alpha-1 adrenergic agonist**, acts directly on alpha-1 receptors on vascular smooth muscle in the nasal mucosa, causing **vasoconstriction** that reduces mucosal edema and secretions, thereby relieving nasal congestion.[1][2] Nasal decongestion occurs within 15–20 minutes of oral administration and may persist for up to 4 hours.[2] It is widely available over-the-counter for symptomatic relief of the common cold.[3]

Why the other options are incorrect:

- **A. Bronchospasm due to bronchial asthma** — Treated with **beta-2 agonists** (e.g., albuterol), which relax bronchial smooth muscle. Alpha-1 agonists do not address bronchospasm.
- **B. Urinary hesitancy due to BPH** — Treated with alpha-1 **antagonists** (e.g., tamsulosin, alfuzosin), which relax prostatic smooth muscle to improve urinary flow. An alpha-1 agonist would worsen obstruction.[4]
- **D. Blood pressure management prior to pheochromocytoma excision** — Requires preoperative alpha **blockade** (e.g., phenoxybenzamine or doxazosin), the opposite of alpha-1 agonism.

Would you like to explore the current evidence on oral phenylephrine's efficacy as a decongestant?

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Question 634

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?

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

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The correct answer is **A: Hepatocytes with shrunken, eosinophilic cytoplasm and pyknotic nuclei**.

This description corresponds to **Councilman bodies (acidophil bodies)**, which are **apoptotic hepatocytes** and a characteristic histopathological finding of acute viral hepatitis, including hepatitis A.[1][2][3] Apoptosis is morphologically defined by **cellular shrinkage, cytoplasmic eosinophilia, chromatin condensation, and nuclear pyknosis/fragmentation (karyorrhexis)** — features driven by caspase-mediated proteolysis.[1][2]

In acute hepatitis A specifically, liver biopsy shows **portal and lobular inflammatory infiltration, focal hepatocyte necrosis, and acidophil body formation**.[4][5] The portal inflammation tends to be prominent and plasma cell–rich, with periportal hepatocyte dropout.[6][7] Immune-mediated killing of infected hepatocytes occurs primarily through **CD8+ T cells and NK cells** via the Fas/FasL pathway and, to a lesser extent, granzyme B/perforin.[1]

Why the other options are incorrect:

- **B (Cystic spaces with cellular debris)** — Describes **liquefactive necrosis**, typical of abscess formation (e.g., brain infarcts, bacterial abscesses), not viral hepatitis.
- **C (Basophilic adipocyte remnants with calcifications)** — Describes **fat necrosis with dystrophic calcification (saponification)**, characteristic of enzymatic fat necrosis in acute pancreatitis.

- **D (Engorged hepatocytes with RBC infiltration)** — Describes findings of **passive hepatic congestion**, as seen in right heart failure or Budd-Chiari syndrome, with blood-filled sinusoids and centrilobular congestion.

Would you like to explore when liver biopsy is actually indicated in acute viral hepatitis and how histological findings guide clinical decisions?

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Question 635

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?

A. Iron supplementation only
B. Proper diet and iron supplementation
C. Multivitamins
D. Proper diet only

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The answer is **B. Proper diet and iron supplementation**.

This infant has **iron deficiency anemia (IDA)** caused by **premature introduction of cow's milk** at 3 months of age. The lab findings are classic for iron deficiency: **microcytic anemia** (Hb 9.1 g/dL, MCV 65 fL), **elevated TIBC** (550 µg/dL), and **low serum iron** (45 µg/dL), with a normal lead level excluding lead poisoning.[1]

Why cow's milk is the culprit:

The AAP explicitly recommends that **cow's milk should not be offered before 12 months of age**.[2] Cow's milk contributes to IDA through multiple mechanisms: its **low iron content and poor iron bioavailability** (~10% absorption vs. ~50% from breast milk), **occult intestinal blood loss**

during infancy, and **inhibition of non-heme iron absorption** by its high calcium and casein content.[3][4]

Why both diet correction AND iron supplementation are needed:

- **Dietary correction** addresses the root cause: cow's milk must be replaced with **iron-fortified formula** (appropriate for a 9-month-old), and **iron-rich complementary foods** (iron-fortified cereals, meats) should be emphasized — the current fruits and vegetables alone are insufficient sources of bioavailable iron.[2]
- **Iron supplementation** is necessary to treat the established anemia. The AAP recommends **oral elemental iron at 3 mg/kg/day once daily as ferrous sulfate** for young children with IDA, continued for a minimum of 3 months. Hemoglobin should be rechecked in 2–4 weeks to confirm response.[1][2]

Why the other options are incorrect:

- **A (Iron supplementation only)** fails to correct the underlying dietary cause — continuing cow's milk would perpetuate iron losses and poor absorption.
- **C (Multivitamins)** do not provide sufficient elemental iron to treat IDA.
- **D (Proper diet only)** would not correct the existing moderate anemia rapidly enough; established IDA requires therapeutic iron dosing.

Would you like to explore recommended iron-rich complementary foods and feeding strategies for infants to prevent iron deficiency?

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Question 636

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?

A. Staphylococcal coagulase
B. Lipoteichoic acid
C. Interleukin-3
D. Lysosomal enzymes

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The answer is **D. Lysosomal enzymes**.

This clinical scenario describes **complicated diverticulitis with pelvic abscess formation** (Hinchey stage II) — the CT findings of segmental descending colon wall thickening with diverticula, combined with a 5-cm low-attenuation pelvic lesion containing air-fluid levels, are classic.[1][2] The yellow-greenish fluid drained is **pus**, composed of dead and dying neutrophils, bacteria, and liquefied tissue.

Abscess cavity formation results from liquefactive necrosis caused by the extracellular release of **lysosomal (granular) enzymes** — including proteases, elastase, collagenase, and acid hydrolases — from neutrophils during phagocytosis and degranulation.[3][4] As neutrophils are recruited to the site of contained diverticular perforation, they release these enzymes from azurophilic (primary) granules both into phagosomes and into the extracellular space, destroying surrounding tissue and creating the abscess cavity.[5][6]

Why the other options are incorrect:

- **A. Staphylococcal coagulase** — Diverticular abscesses are typically polymicrobial (gram-negative enterics and anaerobes), not staphylococcal. Coagulase converts fibrinogen to

fibrin and helps wall off staphylococcal infections; it does not produce the tissue destruction that forms pus.

- **B. Lipoteichoic acid** — A gram-positive cell wall component that activates innate immunity via TLR2 signaling. It contributes to inflammatory signaling but is not the direct mediator of the tissue liquefaction that creates an abscess cavity.

- **C. Interleukin-3** — A hematopoietic growth factor that stimulates granulocyte and mast cell production in bone marrow. It does not directly cause the tissue destruction underlying abscess formation.

Would you like to explore the current management guidelines for diverticular abscess, including drainage indications?

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Question 637

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?

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.

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The correct answer is **A**.

A **Type I error (α error)** occurs when the **null hypothesis is true but is rejected in error** — a false-positive conclusion.[1][2][3] In the context of this mepolizumab trial, a Type I error would mean that the drug truly has no effect on asthma exacerbations, but the trial erroneously concluded that it does ($p<0.001$). Conventionally, the Type I error rate is set at $\alpha = 0.05$, meaning investigators accept a less than 5% chance of this false-positive conclusion.[4][5]

The other options are incorrect:

- **B** describes a **Type II (β) error** — failing to reject the null hypothesis when it is actually false (a false-negative conclusion).[3][5]
- **C** misattributes the beta (β) designation and its conventional values (0.1–0.2) to a Type I error. Type I error is designated by **α** (conventionally 0.05), while **β** (conventionally 0.10–0.20) denotes Type II error.[5][6]
- **D** reverses the relationship. The confidence interval is derived from the chosen α level (e.g., a 95% CI corresponds to $\alpha = 0.05$), but the Type I error rate is a pre-specified threshold set by the investigator, not something dependent on the confidence interval.[2][4]

Would you like to explore how multiple comparisons in clinical trials inflate Type I error and the correction methods available?

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Question 638

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?

A. Myocardial infarction
B. Tongue infarction
C. Palpable purpura
D. Polyneuropathy

https://openevidence.com/ask/048d8682-851d-41b9-b16f-8df959ad5dc9

The answer is **A. Myocardial infarction**.

This presentation is classic for **Takayasu arteritis** — a large-vessel granulomatous vasculitis affecting the aorta and its major branches. Key features include a **young Asian woman** with constitutional symptoms (fatigue, arthralgias over 4 months), **absent right radial pulse** with diminished left radial pulse ("pulseless disease"), low measured blood pressure, elevated ESR (56 mm/h), and microcytic anemia.[1]

Coronary artery involvement is a well-recognized complication of Takayasu arteritis, typically manifesting as **ostial and proximal coronary stenosis** due to extension of aortic wall inflammation. A meta-analysis of 3,262 patients found a pooled MI prevalence of **3.4%** during the disease course.[2] In a cohort with confirmed coronary lesions, **myocardial ischemia was the**

major cause of long-term death, with 7 of 9 deaths attributable to MI.[3] The JACC review explicitly lists angina, heart failure, and myocardial infarction among clinical manifestations of coronary involvement.[1]

Why the other options are incorrect:

- **B. Tongue infarction** — classically associated with **giant cell arteritis** (temporal arteritis), which involves external carotid branches including the lingual artery. Takayasu arteritis affects larger, more proximal vessels.
- **C. Palpable purpura** — a hallmark of **small-vessel vasculitides** (e.g., IgA vasculitis, cryoglobulinemic vasculitis, ANCA-associated vasculitis), not large-vessel vasculitis.
- **D. Polyneuropathy** — characteristic of **small- and medium-vessel vasculitides** such as polyarteritis nodosa or eosinophilic granulomatosis with polyangiitis (Churg-Strauss), not Takayasu arteritis.

Notably, measured arm blood pressures in Takayasu arteritis may be **spuriously low** due to subclavian or brachiocephalic stenosis (pseudohypotension), and leg blood pressures should also be assessed.[4]

Would you like to explore the recommended diagnostic workup and imaging approach for Takayasu arteritis?

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Question 639

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?

A. Von Hippel-Lindau syndrome
B. Multiple endocrine neoplasia (MEN) 2A
C. Multiple endocrine neoplasia (MEN) 2B
D. Neurofibromatosis

https://openevidence.com/ask/07ccd72f-dfcc-4007-ae9d-544e15b4bdeb

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The answer is **B. Multiple endocrine neoplasia (MEN) 2A**. This patient presents with the **classic triad of MEN 2A**: **medullary thyroid carcinoma (MTC)**, **pheochromocytoma**, and **primary hyperparathyroidism**.[1][2]

Mapping the clinical features to the triad:

- **Pheochromocytoma**: Headache, palpitations, episodic diaphoresis, refractory hypertension (196/102 mm Hg despite amlodipine), tachycardia, and hyperglycemia (catecholamine-induced), confirmed by **elevated 24-hour urinary VMA and metanephrines** and **elevated serum epinephrine**.[1][3]
- **Medullary thyroid carcinoma**: Diffuse, firm thyromegaly with **elevated serum calcitonin** — calcitonin is secreted by the parafollicular C cells from which MTC arises.[2]

- **Primary hyperparathyroidism**: **Elevated parathormone and hypercalcemia**, with bone pain in the long bones consistent with PTH-mediated bone resorption. Hyperparathyroidism occurs in 20–30% of MEN 2A patients.[1][4]

Why not the other options:

- **MEN 2B (C)** shares MTC and pheochromocytoma with MEN 2A but is characterized by **mucosal neuromas, marfanoid habitus, and ganglioneuromatosis** — none of which are present here. Critically, **parathyroid disease is rare in MEN 2B**. This patient's prominent hyperparathyroidism strongly favors MEN 2A.[1][2]
- **Von Hippel-Lindau syndrome (A)** involves pheochromocytoma, renal cell carcinoma, CNS hemangioblastomas, and retinal angiomas — not MTC or hyperparathyroidism.[3]
- **Neurofibromatosis (D)** may include pheochromocytoma but does not account for MTC, elevated calcitonin, or hyperparathyroidism.

MEN 2A (also known as Sipple syndrome) is the most common MEN 2 subtype, accounting for over 90% of MEN 2 cases, and is caused by germline gain-of-function mutations in the **RET proto-oncogene**.[2]

Would you like to explore the recommended workup and surgical management sequencing in MEN 2A?

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Question 640

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?

A. Distal peripheral microembolism
B. Necrotizing fasciitis
C. Protein S deficiency
D. Waldenström macroglobulinemia

https://openevidence.com/ask/87bf746a-5e14-4616-adf6-e8420f9d33b8

The answer is **C. Protein S deficiency**.

The question asks about the underlying **etiology** of this patient's DVT and pulmonary embolism. The key features pointing to an inherited thrombophilia are:

- **VTE at age 45** (age <50 is a recognized indicator for thrombophilia testing)[1][2]
- **Strong family history**: sister died at age 35 from PE — VTE in a first-degree relative, especially at a young age, significantly raises suspicion for a heritable prothrombotic state[2]

Among the answer choices, **protein S deficiency** is the only inherited thrombophilia. Protein S is a **vitamin K-dependent natural anticoagulant** that serves as a cofactor for activated protein C, and hereditary deficiency is associated with a significantly increased risk of VTE (OR ~2.5 for protein S antigen <60%).[3][4]

The detail that anticoagulation was started with a **vitamin K inhibitor (warfarin) alone** is also clinically significant. Warfarin inhibits not only procoagulant factors II, VII, IX, and X, but also the natural anticoagulant proteins C and S. Because proteins C and S have relatively **short half-lives**, they are depleted early, creating a **transient prothrombotic state** before the procoagulant factors are fully suppressed.[5][6] This effect is particularly dangerous in patients with baseline protein S deficiency, where warfarin can paradoxically worsen the hypercoagulable state.[7][8] Parenteral anticoagulation (heparin) must be maintained for at least 5 days and until the INR is therapeutic to prevent this complication.[6]

Why the other options are incorrect:

- **A. Distal peripheral microembolism** — Does not explain the familial pattern or her massive PE presentation (S3 gallop, hemodynamic compromise).
- **B. Necrotizing fasciitis** — The erythema and swelling over varicose veins represent **superficial thrombophlebitis**, not soft tissue infection. Necrotizing fasciitis would present with rapidly progressive pain, crepitus, and systemic toxicity disproportionate to skin findings.
- **D. Waldenström macroglobulinemia** — A lymphoplasmacytic lymphoma causing hyperviscosity syndrome; does not explain the strong family history of VTE or the clinical presentation.

Would you like to explore the recommended approach to thrombophilia testing in patients with suspected inherited hypercoagulable states?

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Question 641

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?

A. X-linked recessive
B. X-linked dominant
C. Autosomal dominant
D. Maternally inherited mitochondrial defect

https://openevidence.com/ask/fdc0a559-e57d-4932-a296-8338742a0930

The answer is **A. X-linked recessive**.

This presentation is classic **Lesch-Nyhan syndrome (LNS)**, caused by deficiency of **hypoxanthine-guanine phosphoribosyltransferase (HPRT)** encoded by the *HPRT1* gene on the X chromosome. The syndrome is inherited in an **X-linked recessive** pattern.[1][2][3]

Several features in this vignette are characteristic:

- **Self-injurious behavior** — biting of the lips, tongue, and fingers is the hallmark behavioral manifestation of LNS, typically emerging between ages 2 and 4 years. Finger biting is the most common initial form (37%), followed by lip biting (25%) and tongue biting (18%).[4][5]
- **Hyperuricemia/hyperuricosuria** — uric acid overproduction is present in all HPRT-deficient patients and reflects the underlying defect in purine salvage metabolism.[3][6]
- **Family history of affected males on the maternal side** — consistent with X-linked recessive inheritance, where carrier mothers transmit the mutation to affected sons. Fathers cannot pass X-linked traits to sons.[2]

The other options are incorrect: X-linked dominant conditions typically affect both sexes (often more severely or lethally in males); autosomal dominant would show father-to-son transmission; and mitochondrial inheritance would show maternal transmission to all offspring regardless of sex.

Would you like to explore the current treatment and management strategies for Lesch-Nyhan syndrome?

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Question 642

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?

A. Skin infections
B. Osteosarcoma
C. Hypercholesterolemia
D. Deep vein thrombosis

https://openevidence.com/ask/9eaa94a1-c99b-4b90-8a67-507535891b43

The answer is **D. Deep vein thrombosis**.

The drug described is **raloxifene**, a selective estrogen receptor modulator (SERM) that acts as an **estrogen agonist on bone** (inhibiting bone resorption) and an **estrogen antagonist on breast and uterine tissue** (reducing breast cancer risk).[1][2] It is the ideal choice in this patient for several reasons:

- **Osteoporosis** (T-score −2.6) requiring antiresorptive therapy
- **Esophageal stricture** from severe GERD, which **contraindicates oral bisphosphonates**
- **Family history of breast cancer** (mother at age 45), making the dual benefit of raloxifene particularly valuable

Why DVT is the correct adverse effect

Raloxifene carries an **FDA boxed warning for increased risk of venous thromboembolism**, including deep vein thrombosis and pulmonary embolism.[3] In the MORE trial, raloxifene

increased VTE risk with an RR of 3.1 (95% CI 1.5–6.2).[4] The RUTH trial similarly showed increased VTE (HR 1.44; 95% CI 1.06–1.95).[5] ACOG guidelines state that **venous thromboembolism** is among the principal adverse effects and that raloxifene is **contraindicated in patients with current or past VTE**.[1]

Why the other options are incorrect:

- **A. Skin infections** — associated with **denosumab**, not raloxifene
- **B. Osteosarcoma** — a boxed warning concern with **teriparatide** and PTH analogs (based on preclinical rodent data), not SERMs
- **C. Hypercholesterolemia** — raloxifene actually has **estrogenic effects on lipid metabolism** and tends to lower LDL cholesterol, not raise it[4]

Would you like to explore alternative osteoporosis treatments for patients with esophageal pathology who cannot tolerate oral bisphosphonates?

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Question 643

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?

A. Gastroesophageal reflux disease
B. Gastric adenocarcinoma, intestinal type
C. VIPoma
D. MEN1

https://openevidence.com/ask/c578095b-b14c-44c9-a382-f9ae2b886aee

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The correct answer is **D. MEN1** (Multiple Endocrine Neoplasia type 1). This young patient presents with two hallmark MEN1 manifestations — **multiple duodenal ulcers** (consistent with Zollinger-Ellison syndrome from a gastrinoma) and **hypercalcemia** (calcium 13.2 mg/dL, consistent with primary hyperparathyroidism) — along with a **family history** suggesting autosomal dominant inheritance.[1][2][3]

MEN1 is characterized by the **"3 P's"**: **Parathyroid** adenomas (>95% penetrance, often the earliest manifestation with onset around age 20–25), duodeno**Pancreatic** neuroendocrine tumors (20–80%, with gastrinoma being the most common functioning type at 20–61%), and **Pituitary** adenomas (30–40%).[1][3][4] Gastrinomas in MEN1 are invariably duodenal, typically multiple, and cause gastric acid hypersecretion leading to peptic ulceration (Zollinger-Ellison syndrome).[5][6] Notably, the hypercalcemia from concurrent hyperparathyroidism can itself exacerbate gastrin secretion and worsen peptic disease — a recognized parathyroid-gut axis.[7][8]

Why the other options are incorrect:

- **A. GERD** — Does not explain hypercalcemia or multiple duodenal ulcers. The presentation of postprandial epigastric pain with duodenal ulceration points to peptic ulcer disease, not reflux.
- **B. Gastric adenocarcinoma, intestinal type** — Extremely unlikely at age 26, does not account for hypercalcemia, and endoscopy showed duodenal ulcers rather than a gastric mass.
- **C. VIPoma** — Presents with the WDHA syndrome (watery diarrhea, hypokalemia, achlorhydria), not epigastric pain and duodenal ulcers. While VIPomas can rarely occur in MEN1, this clinical picture does not fit.[3]

Would you like to explore the recommended diagnostic workup and screening protocols for suspected MEN1?

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Question 644

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?

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.

https://openevidence.com/ask/8bab3980-561f-440a-9364-0a7a594bcc8d

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The answer is **A: Insulin production by the pancreas is insufficient for exenatide to be effective**.

Exenatide is a **GLP-1 receptor agonist** whose principal glucose-lowering mechanism is **stimulating glucose-dependent insulin secretion from pancreatic beta cells**.[1] In **type 1 diabetes**, autoimmune beta-cell destruction leaves insufficient residual beta-cell function for this mechanism to work. A review of GLP-1 RA trials in T1DM confirmed that these agents are **unable to increase insulin secretion in C-peptide-negative patients** and produce only clinically insignificant HbA1c reductions (~0.2%).[2] The MAG1C trial similarly found that exenatide added to insulin in T1DM **did not significantly reduce HbA1c**.[3]

This patient's clinical picture — **polyphagia with failure to gain weight** (BMI 19 kg/m²) and poor glycemic control — reflects significant insulin deficiency, further underscoring why a drug dependent on endogenous beta-cell function cannot substitute for insulin.

Why the other options are less correct:

- **B (Glucagon suppression causing hypoglycemia):** Exenatide does suppress glucagon, but this effect is **glucose-dependent** and is actually modest in T1DM. This is not the primary reason to avoid it.[2]

- **C (Appetite suppression):** Exenatide does reduce appetite and promote weight loss, which is a relevant concern in this underweight patient, but it is **not the fundamental reason** the drug cannot serve as glucose-lowering therapy in T1DM.[1][4]
- **D (Contraindicated under 18):** This is incorrect. Exenatide extended-release (once-weekly, 2 mg) is **FDA-approved for children aged 10–17 years** with type 2 diabetes.[5][6][7]

Would you like to explore strategies for improving insulin adherence in adolescents with type 1 diabetes?

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Question 645

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?

A. Cisplatin
B. Lamivudine
C. Isoniazid
D. Prednisone

https://openevidence.com/ask/72cf61e1-de68-4cfd-98ea-9c384ad8d4c5

The answer is **D. Prednisone**.

The clinical presentation — fatigue, fever, weight loss, non-productive cough, bilateral lymphadenopathy, and a biopsy demonstrating **non-caseating granulomas** (organized epithelioid histiocytes and multinucleated giant cells without focal necrosis) — is classic for **sarcoidosis**. Non-necrotizing granulomas are the histological hallmark of sarcoidosis, composed of epithelioid histiocytes and multinucleated giant cells surrounded by lymphocytes.[1][2] The **absence of necrosis** is a critical distinguishing feature from tuberculosis, where caseating granulomas would be expected.[3][4]

Oral glucocorticoids are the first-line treatment for symptomatic pulmonary sarcoidosis. A typical initial dose of **prednisone 20–40 mg/day for 2–6 weeks**, followed by a gradual taper over 6–18 months, is recommended for patients with symptomatic stage II–III disease.[1] Treatment improves radiographic infiltrates and lung function within 4–12 weeks.[1]

Why the other options are incorrect:

- **A. Cisplatin** — A platinum-based chemotherapy agent used for malignancies, not granulomatous disease.
- **B. Lamivudine** — A nucleoside reverse transcriptase inhibitor for HIV/hepatitis B; not relevant here.

- **C. Isoniazid** — First-line anti-tuberculosis therapy. TB characteristically produces **caseating** (necrotizing) granulomas, which are explicitly absent in this biopsy.[3]

Would you like to explore when to add steroid-sparing agents in sarcoidosis and how they compare?

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Question 646

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?

A. Efavirenz
B. Ritonavir
C. Raltegravir
D. Lamivudine

https://openevidence.com/ask/5a3a3142-7092-4882-bffb-b19d92488db9

The answer is **A. Efavirenz**.

Efavirenz is a non-nucleoside reverse transcriptase inhibitor (NNRTI) that prevents viral DNA synthesis by noncompetitively inhibiting HIV-1 reverse transcriptase through binding to an allosteric hydrophobic pocket, thereby altering the enzyme's active site conformation and blocking polymerization.[1][2] Critically, unlike NRTIs (nucleoside reverse transcriptase inhibitors), **NNRTIs do not require sequential intracellular phosphorylation** to exert their antiretroviral activity.[3]

This distinguishes efavirenz from the other choices:

- **Lamivudine (D)** is an NRTI that prevents viral DNA synthesis but **requires** intracellular phosphorylation to its active triphosphate form — so it does not match the stem.
- **Ritonavir (B)** is a protease inhibitor that blocks Gag-Pol polyprotein processing, not viral DNA synthesis.
- **Raltegravir (C)** is an integrase inhibitor that prevents integration of proviral DNA into host chromosomal DNA, not DNA synthesis itself. Additionally, the patient's failing regimen already includes dolutegravir (also an integrase inhibitor), making cross-resistance likely and raltegravir an unlikely switch choice.

Would you like to explore key NNRTI resistance mutations and their impact on treatment selection?

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Question 647

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?

A. Ixodes scapularis
B. Tsetse fly
C. Culicidae
D. Anopheles

https://openevidence.com/ask/39b30d85-a724-4c2d-b7e6-cd0f5f1aaeb3

The answer is **A. Ixodes scapularis**.

This presentation is classic for **disseminated Lyme disease** caused by *Borrelia burgdorferi*. The key features include:

- **Erythema migrans** — the circular red rash with central clearing ("bull's-eye" appearance), present in 70–80% of infected patients[1][2]
- **Facial nerve (CN VII) palsy** — the most common cranial neuropathy in Lyme neuroborreliosis, manifesting here as right-sided facial droop, inability to whistle or close the eye, drooling, and excessive tearing[1][2][3]
- **Decreased taste sensation** — consistent with facial nerve involvement (chorda tympani branch)
- **Epidemiologic exposure** — outdoor activity in northern Maine, a highly endemic area for Lyme disease[3][4]

Ixodes scapularis (the black-legged or deer tick) is the vector responsible for **>95% of Lyme disease cases in North America**, particularly in the northeastern and upper midwestern United States.[3][4] Nymphs are the primary stage responsible for human transmission due to their small size and seasonal activity coinciding with outdoor recreation.[4][5]

The other options are incorrect:

- **Tsetse fly** — transmits *Trypanosoma brucei* (African trypanosomiasis/sleeping sickness)
- **Culicidae** — the mosquito family; vectors for dengue, Zika, West Nile virus, among others
- **Anopheles** — a mosquito genus that transmits *Plasmodium* species (malaria)

Would you like to explore the recommended antibiotic treatment for Lyme neuroborreliosis with facial palsy in this age group?

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Question 648

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?

A. Metformin
B. Simvastatin
C. Glyburide
D. Lisinopril

https://openevidence.com/ask/1eaecae3-9662-4fd8-8ab2-239f57a1b2c3

The answer is **B. Simvastatin**.

Simvastatin is the medication among the choices most likely to cause transaminitis. The FDA label for simvastatin warns that **increases in serum transaminases** have been reported, with **persistent elevations >3x the upper limit of normal (ULN) occurring in approximately 1%** of patients in clinical studies.[1] Both acute cholestatic and hepatocellular patterns of injury have been observed.[2] Transaminase elevations with statins are typically **dose-related**, with ALT elevations exceeding AST, and usually occur **within the first 3 months** of initiation, resolving in ~70% of patients with continued use.[3][4]

A pharmacovigilance study of the FAERS database identified **simvastatin as the third most commonly reported statin associated with drug-induced liver injury** (19.46% of statin-related DILI cases), with a significant reporting odds ratio of 2.96 (95% CI 2.81–3.12).[5]

Regarding the other answer choices:

- **Metformin (A):** A large DILIN study found that metformin had **fewer than 5 bona fide DILI cases** despite >5 million new prescriptions, indicating a very low DILI incidence.[6]
- **Glyburide (C):** Sulfonylureas are rare causes of hepatotoxicity and are not prominently listed among common DILI-causing agents.

- **Lisinopril (D):** Similarly, ACE inhibitors had **fewer than 5 DILIN cases** despite >5 million new prescriptions. Though lisinopril is listed as an idiosyncratic DILI cause, the incidence is exceedingly low compared to statins.[6][7]

Notably, **fenofibrate** (also on this patient's medication list but not among the answer choices) can also cause DILI, though such instances are exceedingly rare.[7][8]

Would you like to explore the recommended monitoring and management approach for statin-induced transaminase elevations?

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Question 649

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?

A. Scarlet fever
B. Scalded skin syndrome
C. Impetigo
D. Pyoderma

https://openevidence.com/ask/539ac680-bd1f-4645-b799-9498539754c3

The answer is **B. Scalded skin syndrome (staphylococcal scalded skin syndrome, SSSS)**.

This presentation is a textbook case of SSSS. Every cardinal feature is present:

- **Neonatal age**: SSSS predominantly affects **neonates and children under 5 years**, owing to immunological immaturity (low anti-exfoliative toxin antibody titers) and immature renal clearance of the causative exotoxins.[1][2]
- **Prodrome of fever and irritability**, followed by diffuse tender erythema progressing to **flaccid blisters** — the classic disease course of SSSS.[3][4]
- **Positive Nikolsky sign** — gentle lateral pressure causes the upper epidermis to shear off, a hallmark finding.[3][5]
- **Mucosal sparing** (ears, nose, and oral mucosa preserved) — this is a critical differentiating feature. The staphylococcal exfoliative toxin is a serine protease that specifically cleaves **desmoglein 1**, which predominates in superficial epidermis but not in mucous membranes (where desmoglein 3 predominates). This explains why mucosa is spared in SSSS, unlike in toxic epidermal necrolysis.[4][6]

Why the other options are incorrect:

- **A. Scarlet fever**: Caused by Group A Streptococcus; presents with a sandpaper-like erythematous rash, strawberry tongue, and pharyngitis — typically in school-age children, not neonates. It does not produce flaccid bullae or a positive Nikolsky sign.
- **C. Impetigo**: A localized superficial infection. Bullous impetigo (also toxin-mediated) produces localized blisters but does **not** cause diffuse erythroderma or a positive Nikolsky sign. It represents the localized end of the same exfoliative toxin spectrum, whereas SSSS represents the generalized, hematogenously disseminated end.[7]
- **D. Pyoderma**: A general term for purulent skin infections (e.g., folliculitis, ecthyma); these are localized and do not produce generalized erythema, widespread blistering, or Nikolsky sign.

Would you like to explore the recommended antibiotic therapy and management approach for neonatal SSSS?

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Question 650

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?

A. Squamous cell hyperplasia
B. Lichen sclerosus
C. Squamous cell carcinoma of the vulva
D. Lichen planus

https://openevidence.com/ask/68106b75-e684-4e69-bf38-ff2c87ba62a2

The answer is **B. Lichen sclerosus**.

This presentation is classic for **vulvar lichen sclerosus (VLS)**, a chronic inflammatory dermatosis with a predilection for postmenopausal women in hypoestrogenic states.[1][2] Every feature described aligns with the hallmark findings:

- **Severe pruritus** is the most common symptom of VLS.[3][4]
- **Dyspareunia** results from introital narrowing and skin fragility.[3][5]
- **White, thin, plaque-like lesions** with epithelial thinning give the characteristic "porcelain-white" or "cigarette paper" appearance.[1][4]
- **Atrophy of the labia minora** (regression) and **clitoral retraction** (phimosis of the clitoral hood) are hallmark anatomic changes of advancing disease.[1][3]
- **Pale, wrinkled perianal skin** involvement, extending from the vulva to the perianal region, creates the classic "**figure-of-eight**" distribution pathognomonic for VLS.[4][6]

Why not the other options:

- **A. Squamous cell hyperplasia** — presents with **thickened**, raised vulvar skin rather than the thin, atrophic, white plaques described here. It does not cause architectural changes such as labial regression or clitoral phimosis.
- **C. Squamous cell carcinoma** — typically presents as a focal mass, ulcer, or nodule, not as diffuse bilateral white plaques with symmetric architectural changes. VLS does carry a **2–7% risk of progression to SCC** if untreated, but the diffuse pattern here points to the inflammatory condition itself.[3][4]
- **D. Lichen planus** — the erosive form (most common vulvar variant) presents with **erythematous erosions** in the vestibule, not white atrophic plaques. Classical LP shows **Wickham striae** (lacy white reticulations), and it preferentially affects **mucosal surfaces** rather than keratinized skin. Perianal involvement in a figure-of-eight pattern is not characteristic of LP.[4][7]

The gold-standard treatment is **ultra-high-potency topical corticosteroids** (clobetasol propionate 0.05% ointment), with long-term maintenance to control symptoms, prevent further architectural damage, and reduce malignancy risk.[1][3]

Would you like to explore the treatment regimen and long-term surveillance protocol for vulvar lichen sclerosus?

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Question 651

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?

A. Bilateral miosis
B. Miosis of the right eye only
C. Miosis of the left eye only
D. Mydriasis of the left eye

https://openevidence.com/ask/c9ed2bb2-9d40-4fa7-9732-f31a11c54e42

The answer is **A. Bilateral miosis**.

This patient with SLE has developed **left optic neuritis**, a rare but serious neuro-ophthalmologic manifestation occurring in approximately 1% of SLE patients.[1] The complete left-sided vision loss and absent direct pupillary response to light confirm a **left afferent pupillary defect (RAPD)** — the afferent limb (left optic nerve, CN II) of the pupillary light reflex is non-functional.

Why bilateral miosis occurs with right eye illumination:

The pupillary light reflex arc has two limbs:[2][3]

- **Afferent:** Retinal ganglion cells → optic nerve → pretectal nucleus
- **Efferent:** Edinger-Westphal nucleus → CN III → ciliary ganglion → sphincter pupillae

Critically, each pretectal nucleus projects to **both** Edinger-Westphal nuclei, which is the anatomical basis for the consensual response.[2][3] When light is shined in the right eye:

1. The **right optic nerve is intact** (20/30 acuity), so the afferent signal is transmitted normally.

2. The signal reaches **both** Edinger-Westphal nuclei.

3. **Both CN III efferent pathways are intact** (no efferent lesion in this scenario), so both pupils constrict — the right eye via the **direct response** and the left eye via the **consensual response**.

Why the other options are incorrect:

- **B (right eye miosis only)** would imply a left efferent (CN III) lesion, which is not present here.
- **C (left eye miosis only)** is not physiologically possible — a consensual response without a direct response would require an intact afferent pathway but a damaged efferent pathway on the right, contradicting her intact right-eye acuity and normal right pupillary function.
- **D (left eye mydriasis)** would occur during the **swinging flashlight test** when the light is moved to the affected left eye, not when illuminating the right eye.[4][5]

This is the classic presentation used to demonstrate a **relative afferent pupillary defect (Marcus Gunn pupil)** on the swinging flashlight test: the pupil dilates when the light swings to the affected eye (due to loss of afferent input) but constricts consensually when the unaffected eye is illuminated.[4][5][6]

Would you like to explore the workup and treatment approach for SLE-associated optic neuritis?

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Question 652

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?

A. Laparoscopy
B. Laparotomy
C. MRI of the pelvis
D. Observation and serial abdominal exams

https://openevidence.com/ask/6a441d72-3653-43a4-8817-c51cd7636ead

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The best answer is **A. Laparoscopy**.

This presentation — **sudden-onset severe abdominal pain with nausea/vomiting, a left adnexal mass, adnexal tenderness, and ultrasound showing free fluid with ovarian edema** — is highly suspicious for **ovarian torsion**. Critically, **the presence of Doppler flow does not exclude torsion**; ACOG states that normal Doppler arterial flow is found in up to **60% of surgically confirmed torsion cases**, and "Doppler flow alone should not guide clinical decision making".[1]

Ovarian torsion is a **surgical diagnosis**. Per ACOG, when torsion is suspected, **timely diagnostic laparoscopy** is indicated to preserve ovarian function and future fertility.[1] A **minimally invasive (laparoscopic) approach with detorsion and adnexal preservation** is the standard of care, particularly in young women of reproductive age.[1] Laparoscopy also results in shorter hospitalization and fewer post-operative complications compared to laparotomy.[2]

Why not the other options:

- **B. Laparotomy** — While it achieves surgical management, **laparoscopy is the preferred approach** per ACOG guidelines. Laparotomy is reserved for situations where laparoscopy is not feasible (e.g., very large masses, hemodynamic instability).[1][3]
- **C. MRI of the pelvis** — Would **delay definitive management** in a time-sensitive condition. ACOG emphasizes that no imaging modality can sufficiently confirm or exclude torsion preoperatively; it remains a surgical diagnosis.[1]
- **D. Observation and serial abdominal exams** — Inappropriate given the **risk of irreversible ovarian ischemia and necrosis** with delayed intervention, particularly when symptoms are refractory to analgesics.[1][4]

Would you like to explore indications for oophoropexy to prevent recurrent ovarian torsion after detorsion?

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Question 653

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?

A. Vasovagal syncope
B. Orthostatic syncope
C. Cardiac arrhythmia
D. Cardiac structural abnormality

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The correct answer is **A. Vasovagal syncope**.

This presentation is classic for **vasovagal syncope (VVS)**: a clear painful stimulus (tattooing), a characteristic prodrome of **diaphoresis and pallor**, brief loss of consciousness with rapid recovery, and **immediate return to full orientation** without postictal confusion.[1][2] The 2017 ACC/AHA/HRS syncope guideline defines VVS as reflex syncope that may occur with exposure to **pain or emotional stress**, is characterized by diaphoresis, warmth, and pallor, and is the most common form of syncope overall.[1]

Brief jerking movements do not indicate seizure here. Myoclonic-like jerks are well-recognized during syncope ("convulsive syncope") and do not require an epileptic mechanism. Features distinguishing these from seizure include their **brief duration** (seconds), **onset after loss of consciousness**, and crucially the **absence of postictal confusion** — this patient was alert and fully oriented immediately upon regaining consciousness.[3][4]

Why not the other choices:

- **B. Orthostatic syncope** — The patient was **seated**, not transitioning from supine to standing. Orthostatic syncope requires a positional change with a sustained drop in systolic BP ≥20 mmHg or diastolic BP ≥10 mmHg, which is not the mechanism here.[5]
- **C. Cardiac arrhythmia** — Cardiac syncope in young adults accounts for a small minority of cases. The **incomplete RBBB** on ECG can be a **benign finding** in young adults and does not indicate arrhythmia in isolation. There were no features suggestive of cardiac syncope such as exertional onset, palpitations, absence of prodrome, or abnormal cardiac exam.[3][5][6][7][8]
- **D. Cardiac structural abnormality** — Normal cardiopulmonary examination with no murmur, no exertional symptoms, and an isolated incomplete RBBB do not suggest structural heart disease.[3][7]

Would you like to explore evidence-based management strategies for recurrent vasovagal syncope?

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Question 654

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?

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

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The answer is **B. Direct activation of dopamine receptors**.

This patient's **pathological gambling** is a classic **impulse control disorder (ICD)** — a well-recognized adverse effect of **dopamine agonists** such as pramipexole and ropinirole, which act by **directly stimulating dopamine D2/D3 receptors**. In the DOMINION study (n=3,090), ICDs were identified in **17% of patients treated with a dopamine agonist** versus 6.9% on other dopaminergic medications (OR 2.72).[1] FDA adverse event data confirm the strongest signal with pramipexole (PRR 455.9) and ropinirole (PRR 152.5), both of which have preferential D3 receptor affinity.[2] The FDA label for pramipexole specifically warns about intense urges to gamble, increased sexual urges, and compulsive spending.[3]

Dopamine agonists are commonly initiated in younger Parkinson disease patients (typically <65 years, as in this 51-year-old) to delay levodopa-associated motor complications such as dyskinesias.[4] This prescribing pattern, combined with the temporal onset (months after treatment initiation), makes a dopamine agonist the most likely causative drug.

The other options describe different drug classes:

- **A (peripheral DOPA decarboxylase inhibition)** — carbidopa, used as an adjunct to levodopa but not strongly linked to ICDs
- **C (MAO-B inhibition)** — selegiline or rasagiline; associated with a lesser ICD risk than dopamine agonists[5]

- **D (COMT inhibition)** — entacapone or tolcapone; extends levodopa effect, not primarily linked to ICDs

Would you like to explore the management of dopamine agonist-induced impulse control disorders in Parkinson disease?

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Question 655

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?

A. Metoprolol
B. Verapamil
C. Nifedipine
D. Hydrochlorthiazide

https://openevidence.com/ask/b1f808d5-ba5a-4c1f-8213-c5715748f609

C. Nifedipine. Dose-dependent peripheral edema is the classic adverse effect of dihydropyridine calcium channel blockers, and nifedipine ranks highest among them for inducing it. The FDA label reports mild-to-moderate peripheral edema in approximately 10% of patients on immediate-release nifedipine, rising in a dose-dependent manner from ~10% to ~30% at the highest extended-release dose studied (180 mg).[1][2] In a network meta-analysis of 71 RCTs (56,283 patients), nifedipine had the highest edema risk of any dihydropyridine (RR 6.03 vs placebo, 95% CI 2.89–12.61) and ranked first by SUCRA (81.8%).[3]

Mechanism: Preferential precapillary arteriolar dilation without corresponding postcapillary venodilation raises intracapillary hydrostatic pressure, driving fluid extravasation into the interstitium.[3] This is a **localized vasodilatory phenomenon, not fluid retention or left ventricular dysfunction** — an important distinction, since it does not respond well to diuretics and treating it as volume overload is a well-described prescribing cascade leading to overdiuresis, AKI, electrolyte disturbance, and falls.[1][4]

Why the other options are wrong:

- **Metoprolol (A)** — beta-blockers cause fatigue, bradycardia, and bronchospasm; peripheral edema is not a characteristic effect.

- **Verapamil (B)** — a non-dihydropyridine with less peripheral arteriolar selectivity. Edema incidence with non-DHPs is 3.1% versus 12.3% with DHPs ($p < 0.0001$). Its hallmark adverse effects are constipation, bradycardia, and AV block.[5]
- **Hydrochlorothiazide (D)** — a diuretic that reduces volume; it treats edema rather than causing it. Its adverse effects are hypokalemia, hyponatremia, hyperuricemia/gout, hyperglycemia (relevant in this diabetic patient), and hypercalcemia.[6][7]

Clinical management if this occurs: Dose reduction, switching to a more lipophilic later-generation dihydropyridine (lipophilic DHPs carry 57% lower edema risk than traditional DHPs, RR 0.43), or switching to a non-dihydropyridine.[5] Notably, in this network meta-analysis, adding a RAS blocker mitigated amlodipine-associated edema but did not prevent nifedipine-associated edema — relevant here, since the patient is already on enalapril.[3]

Would you like to explore management strategies for CCB-induced peripheral edema while maintaining blood pressure control?

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Question 656

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?

A. Plasmodium ovale
B. Plasmodium falciparum
C. Chikungunya virus
D. Hepatitis A virus

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The answer is **B. Plasmodium falciparum**.

Several features of this case converge on *P. falciparum* malaria:

- **Ring-shaped inclusion bodies within erythrocytes** are the hallmark peripheral smear finding of *P. falciparum*. Microscopy characteristically shows early ring-stage (young trophozoite) forms, which account for ~80–95% of parasitized cells on thin smear, frequently with multiple parasites per erythrocyte.[1][2]
- **Chloroquine resistance is widespread in *P. falciparum* throughout India**, rendering the patient's already inadequate prophylaxis (only two doses rather than weekly dosing starting 1–2 weeks before travel and continuing 8 weeks after) completely ineffective. Proper prophylaxis for India requires agents effective against chloroquine-resistant strains (e.g., atovaquone-proguanil, doxycycline, or mefloquine).[3][4][5][6]
- **Jaundice, anemia (Hb 10 g/dL), and fragmented erythrocytes** reflect the hemolysis and microvascular pathology characteristic of *P. falciparum* severe malaria. *P. falciparum*

uniquely infects erythrocytes of all ages (unlike other species that preferentially infect reticulocytes or older RBCs), leading to higher parasitemia and more severe hemolysis.[1]

Why not the other options:

- **P. ovale** — Less common in India and, importantly, remains **chloroquine-sensitive**, so even the patient's limited prophylaxis would have offered some protection.[3][7]
- **Chikungunya virus** — Presents with prominent **arthralgia/arthritis**, not ring-form inclusions in erythrocytes; smear findings would be unremarkable.
- **Hepatitis A virus** — Can cause jaundice but would not produce **intraerythrocytic parasites** or fragmented red cells on smear.

Would you like to explore the treatment approach for severe P. falciparum malaria in a returning traveler?

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Question 657

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?

A. Glucose
B. Triiodothyronine (T3)
C. Thyroxine (T4)
D. Thyroid-stimulating hormone (TSH)

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The answer is **D. Thyroid-stimulating hormone (TSH)**.

This patient presents with a classic constellation of **primary hypothyroidism**: unexplained weight gain despite regular exercise, fatigue, constipation, **bradycardia** (pulse 52/min), and dry skin — all reflecting systemic metabolic slowing from thyroid hormone deficiency.[1][2] In primary hypothyroidism, the failing thyroid gland produces insufficient T4 and T3, which removes negative feedback on the anterior pituitary, resulting in **elevated TSH**.[3][4]

Why the other options are incorrect:

- **A. Glucose** — While hypothyroidism can impair insulin sensitivity, hyperglycemia is not a hallmark finding and would not be the most likely elevated value in this presentation.[1]
- **B. Triiodothyronine (T3)** — T3 is typically **low or low-normal** in hypothyroidism. Circulating T3 concentrations are usually maintained within the reference range until profound hypothyroidism develops, due to preferential T3 secretion and increased peripheral T4-to-T3 conversion as a compensatory mechanism.[4][5]
- **C. Thyroxine (T4)** — T4 is **low** in overt primary hypothyroidism, as the thyroid gland is the sole source of T4 production.[1]

TSH is the most sensitive initial diagnostic test for primary hypothyroidism (sensitivity ~98%), and an elevated TSH with low free T4 confirms overt disease.[1][6] This patient's demographic profile — a young woman — is also consistent with the higher prevalence of autoimmune thyroiditis (Hashimoto thyroiditis), which accounts for up to 85% of primary hypothyroidism in iodine-sufficient areas.[1]

Would you like to explore the initial levothyroxine dosing and monitoring approach for this patient?

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Question 658

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?

A. Trial of diphenhydramine
B. Stop evening exercise
C. Alcoholic beverage prior to bedtime
D. Scheduled afternoon naps

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B. Stop evening exercise is the best of the four options. It is the only choice consistent with behavioral sleep management: the other three (diphenhydramine, bedtime alcohol, scheduled afternoon naps) are each either recommended against or actively perpetuating his sleep-onset problem.

Why the other options are wrong

- **Diphenhydramine (A):** The American Academy of Sleep Medicine issued a recommendation against diphenhydramine 50 mg for sleep-onset or sleep-maintenance insomnia — reductions in sleep latency and increases in total sleep time fell below clinical significance thresholds, and the task force judged that most well-informed patients would not choose it over no treatment. The 2025 VA/DoD guideline likewise explicitly does not suggest diphenhydramine for chronic insomnia disorder, noting tolerance to the sedative effect within 3–4 days and next-day impairment — in one driving-simulator study, diphenhydramine 50 mg for one week impaired lane keeping more than alcohol at ~0.1% BAC, and self-reported drowsiness did not predict impairment. In a patient already falling asleep in class, this risks worsening daytime somnolence.[1][2][3]

- **Alcohol before bed (C):** Alcohol is initially sedating but substantially degrades sleep architecture, increasing fragmentation — the first half of the night is more consolidated at the cost of disturbed second-half sleep, with REM suppression at higher doses. Sleep hygiene guidance is to limit alcohol, not add it.[4][5]

- **Scheduled afternoon naps (D):** He is already napping more than an hour, which dissipates homeostatic sleep drive and directly worsens sleep-onset latency. Naps of 90 minutes or longer should be avoided because of their detriment to the next night's sleep, and those with sleep difficulties should avoid napping altogether. Nap avoidance is a standard component of sleep hygiene education.[4][6]

Caveat on the evidence for option B

The evidence that his specific 8 p.m. exercise is causing the problem is weaker than the exam framing implies. Meta-analyses in healthy adults do not support a general harm from evening exercise; impairment in sleep-onset latency, total sleep time, and sleep efficiency is seen mainly with **vigorous exercise ending ≤1 hour before bedtime**.[7][8] A large wearable-device cohort (14,689 individuals, >4 million person-nights) found later timing and higher exercise strain associated with delayed sleep onset and lower sleep quality, but **no association when exercise ended ≥4 hours before sleep onset**.[9] Given a bedtime of 11 p.m.–1 a.m. and actual sleep onset around 1–4 a.m., his 8 p.m. session already falls well outside that window. The American Heart Association similarly notes physical activity generally improves sleep regardless of timing, with reduced sleep efficiency only in some individuals exercising vigorously within an hour of bedtime.[10]

What actually warrants attention clinically

- **Caffeine:** 2–3 cups daily with afternoon dosing — caffeine can keep a person awake 6 or more hours after consumption; limit it after lunch.[4]

- **Fixed wake time and stimulus control** rather than sleep hygiene alone. Sleep hygiene education as monotherapy is inferior to CBT-I for sleep-onset latency, wake after sleep onset, and sleep efficiency, and the VA/DoD work group concluded it should not be first-line and may be harmful if it displaces referral for effective behavioral treatment. **CBT-I is the first-line definitive treatment**, with sleep restriction the most effective single component.[6][11]

- **Consider delayed sleep-wake phase disorder** — plausible in a 21-year-old with a 2–3 hour sleep-onset delay and morning grogginess, though not established here (only 2 months, and no data on sleep when following an unconstrained schedule). If pursued, melatonin failure at bedtime doesn't exclude it: for phase advance, low-dose melatonin is timed

several hours before desired sleep onset and combined with morning bright light, not taken at bedtime as a hypnotic.

- **Do not attribute the sleepiness entirely to insomnia.** Falling asleep in class and skipping class merit screening for depression, drowsy driving, stimulant or other substance use, and — if sleepiness persists after the schedule stabilizes — OSA, restless legs, and narcolepsy. Excessive daytime sleepiness is listed as a condition requiring adaptation or delay of CBT-I. [2]

Would you like to explore the diagnostic criteria and treatment protocol for delayed sleep-wake phase disorder in young adults?

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Question 659

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?

A. Social anxiety disorder
B. Avoidant personality disorder
C. Schizotypal personality disorder
D. Schizophrenia

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The most likely diagnosis is **C. Schizotypal personality disorder**.

This patient's presentation maps closely onto multiple DSM-5 diagnostic criteria for schizotypal personality disorder (SPD), a pervasive pattern of **social and interpersonal deficits**, **cognitive or perceptual distortions**, and **eccentricities of behavior** beginning by early adulthood:[1][2]

- **Odd beliefs/magical thinking** (Criterion A2): Preoccupation with paranormal phenomena (demons) and interpreting a breeze in an enclosed room as the "breath of a demon" — this is magical thinking, not a fixed delusion.[1]
- **Odd, eccentric appearance** (Criterion A7): Dressing exclusively in black with a long black coat year-round.[1]
- **Odd speech** (Criterion A4): Laborious speech on mental status exam, consistent with the vague, circumstantial, or idiosyncratic speech patterns described in SPD.[1]
- **No close friends** (Criterion A8): Social isolation, spending time alone playing games.[1]

- **Excessive social anxiety that does not diminish with familiarity** (Criterion A9): Discomfort around others at college.[1]
- **Interpersonal stiffness** (Criterion A6): Avoidance of eye contact.[1]

Why not the other choices:

- **Social anxiety disorder (A)**: SAD would explain the social discomfort but does not account for the **magical thinking, eccentric dress, odd speech**, and preoccupation with paranormal phenomena — these are the hallmarks that distinguish SPD.[1][3]
- **Avoidant personality disorder (B)**: In AvPD, there is an **active desire for relationships constrained by fear of rejection**, whereas this patient shows **persistent detachment and lack of desire** for relationships. AvPD also lacks the cognitive-perceptual distortions and eccentricity seen here.[1]
- **Schizophrenia (D)**: This patient lacks **frank psychotic symptoms** — he explicitly denies seeing demons, his beliefs are subthreshold (magical thinking, not delusions), and there are no hallucinations or formal thought disorder. SPD shares features with schizophrenia on a spectrum but **lacks persistent psychotic symptoms**.[1][4]

Would you like to explore the risk factors for progression from schizotypal personality disorder to schizophrenia?

References

1. Diagnostic and Statistical Manual of Mental Disorders. Dilip V. Jeste, Jeffrey A. Lieberman, David Fassler, et al. American Psychiatric Association (2022)
2. A diagnostic classification version of Schizotypal Personality Questionnaire using diagnostic classification models. Xi C, Cai Y, Peng S, Lian J, Tu D.. International Journal of Methods in Psychiatric Research. 2020;29(1):e1807. doi:10.1002/mpr.1807.
3. Personality Disorders. Sharp C.. The New England Journal of Medicine. 2022;387(10):916-923. doi:10.1056/NEJMra2120164.
4. Costs of schizotypal disorder: A matched-controlled nationwide register-based study of patients and spouses. Hastrup LH, Jennum P, Ibsen R, Kjellberg J, Simonsen E.. Acta Psychiatrica Scandinavica. 2021;144(1):60-71. doi:10.1111/acps.13292.

Question 660

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?

A. Asthma
B. Lymphangioleiomyomatosis
C. Chronic obstructive pulmonary disease (COPD)
D. Heart failure

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The answer is **C. Chronic obstructive pulmonary disease (COPD)**.

This presentation is classic for **COPD**: a 79-year-old with a **25-year heavy smoking history** presenting with **exertional dyspnea and productive cough**, physical exam findings of **hyperresonance, decreased breath sounds, and basilar crackles**, **pulmonary hyperinflation on chest radiography**, and spirometry showing an **obstructive pattern** with an FEV1/FVC ratio of 56% (< 0.7).[1]

Spirometric confirmation: Per the 2026 GOLD guidelines, a post-bronchodilator **FEV1/FVC < 0.7** in the appropriate clinical context (symptoms plus risk factor exposure) confirms the diagnosis of COPD.[1] This patient's FEV1/FVC of 56% clearly meets this threshold. The **FEV1 of 48% predicted** classifies the airflow obstruction as **GOLD grade 3 (severe)**, corresponding to FEV1 30–49% predicted.[1][2]

Radiographic correlation: The GOLD report notes that radiological changes associated with COPD include **signs of lung hyperinflation** (flattened diaphragm, increased retrosternal air space), hyperlucency, and rapid tapering of vascular markings — consistent with this patient's imaging.[1]

Why not the other options:

- **A. Asthma** — Typically presents with episodic, reversible airflow obstruction, often with atopy. The fixed obstruction pattern, long smoking history, and hyperinflation favor COPD.
- **B. Lymphangioleiomyomatosis (LAM)** — A rare disease predominantly affecting premenopausal women; exceedingly unlikely in a 79-year-old male smoker.
- **D. Heart failure** — Can cause dyspnea and basilar crackles, but would not produce hyperresonance, decreased breath sounds, or an obstructive spirometric pattern. Heart failure typically shows a **restrictive** pattern on spirometry, not obstruction with FEV1/FVC < 0.7.

Would you like to explore the recommended pharmacotherapy approach for severe (GOLD 3) COPD?

References

1. 2026 GOLD Report and Pocket Guide: Global Strategy for Prevention, Diagnosis, and Management of COPD – 2026 Report. . Global Initiative for Chronic Obstructive Lung Disease
2. FEV1/FVC Severity Stages for Chronic Obstructive Pulmonary Disease. Bhatt SP, Nakhmani A, Fortis S, et al.. American Journal of Respiratory and Critical Care Medicine. 2023;208(6):676-684. doi:10.1164/rccm.202303-0450OC.