A 22-year-old primigravida at 34 weeks gestation is brought to the emergency department by ambulance for sudden loss of consciousness followed by generalized shaking. The paramedics started an intravenous magnesium sulfate bolus, which was running wide open when the patient arrived at the hospital. She says she is very tired and has blurry vision and a headache. The patient also has muscle pain and sore joints and is not able to move her right arm. Blood pressure is 145/98 mm Hg, pulse is 112/min, and respirations are 16/min. The patient holds the right arm adducted and internally rotated. Examination shows loss of external rotation of the right arm but no sensory deficits. Deep tendon reflexes are 2+ bilaterally, and handgrip and wrist strength is preserved on both sides. Urinalysis shows 3+ protein. Which of the following is the most likely cause of this patient's arm weakness?

- A. Anterior shoulder dislocation
- B. Magnesium toxicity
- C. Posterior shoulder dislocation
- D. Postictal (Todd) paralysis
- E. Radial nerve compression

Submit

A 22-year-old primigravida at 34 weeks gestation is brought to the emergency department by ambulance for sudden loss of consciousness followed by generalized shaking. The paramedics started an intravenous magnesium sulfate bolus, which was running wide open when the patient arrived at the hospital. She says she is very tired and has blurry vision and a headache. The patient also has muscle pain and sore joints and is not able to move her right arm. Blood pressure is 145/98 mm Hg, pulse is 112/min, and respirations are 16/min. The patient holds the right arm adducted and internally rotated. Examination shows loss of external rotation of the right arm but no sensory deficits. Deep tendon reflexes are 2+ bilaterally, and handgrip and wrist strength is preserved on both sides. Urinalysis shows 3+ protein. Which of the following is the most likely cause of this patient's arm weakness?

- ✗ A. Anterior shoulder dislocation [21%]
- B. Magnesium toxicity [4%]
- ✓ C. Posterior shoulder dislocation [48%]
- D. Postictal (Todd) paralysis [22%]
- E. Radial nerve compression [2%]

Incorrect
Correct answer
C

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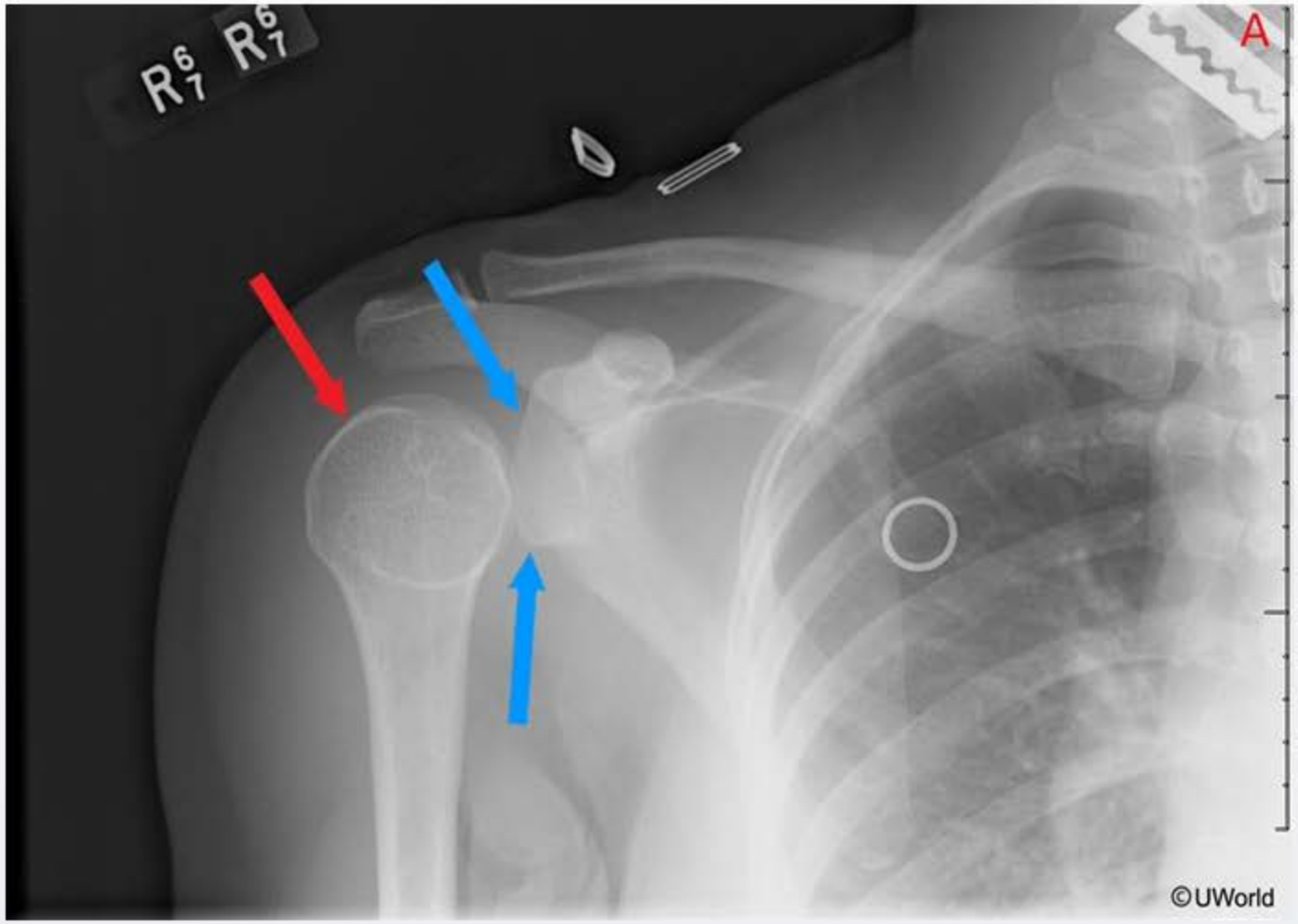
11/08/2018
Last Updated



This pregnant patient has hypertension, proteinuria, and a generalized tonic-clonic **seizure**, findings consistent with eclampsia. Violent muscle contractions, as seen in a seizure or electrocution injury, are a common cause of

This pregnant patient has hypertension, proteinuria, and a generalized tonic-clonic **seizure**, findings consistent with eclampsia. Violent muscle contractions, as seen in a seizure or electrocution injury, are a common cause of **posterior shoulder dislocation**.

In a posterior dislocation, the arm is typically held in **adduction** and **internal rotation**, with impaired external rotation, visible flattening of the anterior aspect of the shoulder, and prominence of the coracoid process. Radiographic findings may include:

- Loss of the normal overlap between the humeral head (red arrow) and the glenoid (blue arrows); a **normal shoulder x-ray** with normal overlap is given for comparison
- Internal rotation of the humeral head, which causes a circular appearance (light bulb sign) on anterior views (red arrow)
- Widened joint space >6 mm (rim sign) or 2 parallel cortical bone lines on the medial aspect of the humeral head (trough line sign)

Potential complications include fractures of the proximal humerus, labral injuries, and tears to the rotator cuff system. Most posterior dislocations are managed with closed reduction.

(Choice A) Anterior dislocation is the most common form of shoulder dislocation and is usually caused by a direct blow or fall on an outstretched arm. In anterior dislocations, the patient holds the arm slightly abducted and externally rotated.

(Choice B) Common adverse effects of magnesium sulfate include headache, nausea, fatigue, and diaphoresis.

externally rotated.

(Choice B) Common adverse effects of magnesium sulfate include headache, nausea, fatigue, and diaphoresis. Signs of magnesium toxicity include somnolence, loss of deep tendon reflexes, and respiratory depression but not focal weakness. This patient's reflexes are normal.

(Choice D) Todd paralysis refers to transient unilateral weakness following a tonic-clonic seizure that usually spontaneously resolves. Adduction and internal rotation of the arm are not seen.

(Choice E) Radial nerve compression from trauma can occasionally be seen in shoulder dislocations but most commonly occurs in the forearm. It often results in hand weakness and decreased handgrip, which are not seen in this patient.

Educational objective:
Violent muscle contractions (eg, seizure, electrocution injury) can cause posterior shoulder dislocation. On examination, the arm is held in adduction and internal rotation, with flattening of the anterior aspect of the shoulder. X-rays show loss of the normal relation between the humeral head and glenoid and internal rotation of the humeral head. Most posterior dislocations are managed with closed reduction.

References

- Neglected bilateral posterior shoulder fracture dislocation in an uncontrolled seizure patient.

A 28-year-old primigravida is admitted to the hospital at 10 weeks gestation. Her temperature is 36.7 C (98.2 F), pulse is 96/min, and respirations are 12/min. Arterial blood gas testing results are as follows:

pH	7.49
$PaCO_2$	54 mm Hg
Bicarbonate	44 mEq/L

Which of the following is the most likely cause of this patient's abnormal arterial blood gas?

- A. Asthma exacerbation
- B. Diarrhea
- C. Hyperemesis gravidarum
- D. Normal phenomenon of pregnancy
- E. Obesity hypoventilation
- F. Pulmonary embolism

Submit

A 28-year-old primigravida is admitted to the hospital at 10 weeks gestation. Her temperature is 36.7 C (98.2 F), pulse is 96/min, and respirations are 12/min. Arterial blood gas testing results are as follows:

pH	7.49
$PaCO_2$	54 mm Hg
Bicarbonate	44 mEq/L

Which of the following is the most likely cause of this patient's abnormal arterial blood gas?

- A. Asthma exacerbation [1%]
- B. Diarrhea [0%]
- ✔ C. Hyperemesis gravidarum [76%]
- D. Normal phenomenon of pregnancy [15%]
- E. Obesity hypoventilation [3%]
- F. Pulmonary embolism [1%]

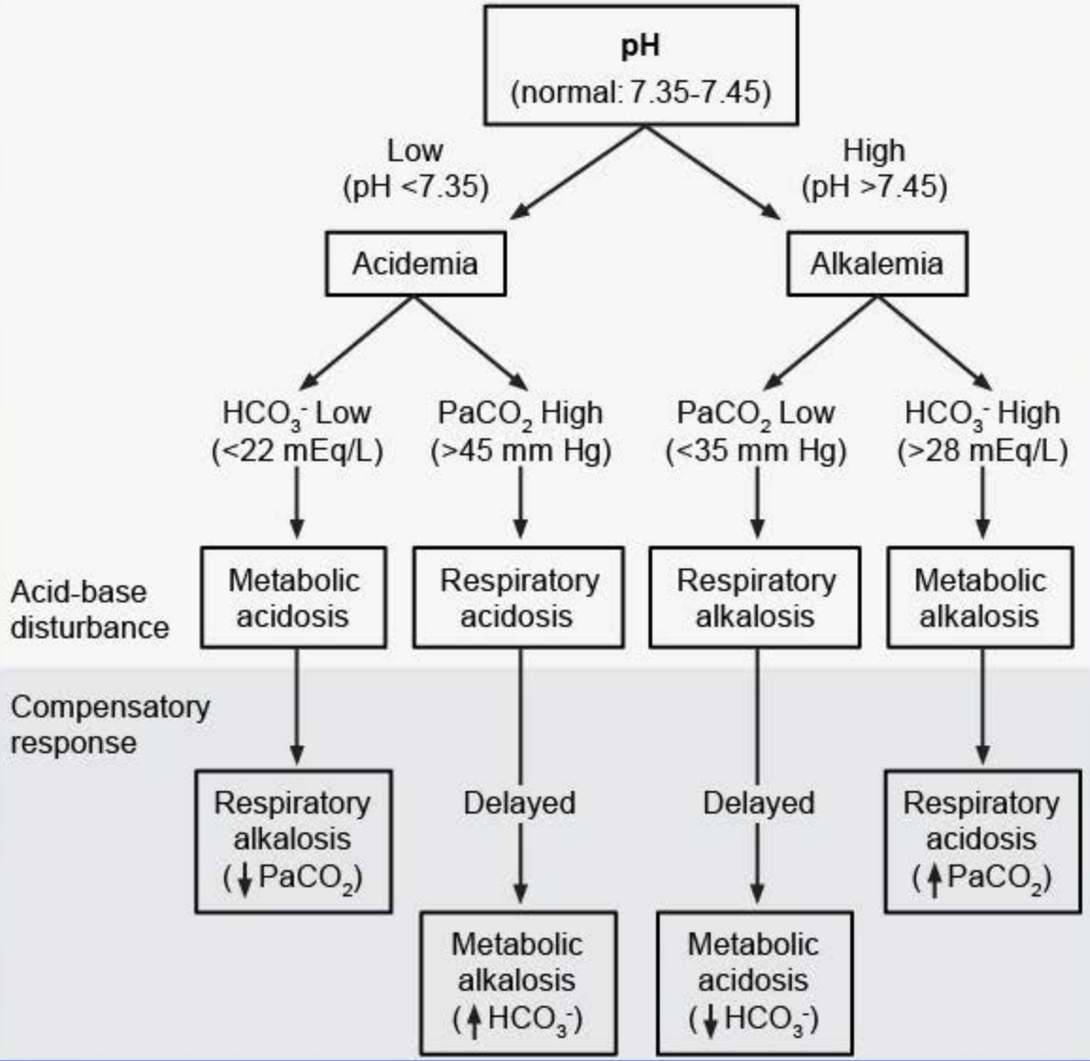
Correct

76%
Answered correctly

4 Seconds
Time Spent

07/17/2018
Last Updated

Arterial blood gas interpretation of primary acid-base disorders



The first step in assessing arterial blood gas is to look at the pH, with acidemia defined as <7.35 and alkalemia defined as >7.45. This patient's pH of 7.49 indicates alkalemia. The next step is to determine the **primary process**. Because this patient has elevated bicarbonate and $PaCO_2$ on arterial blood gas testing, it is most likely a primary metabolic alkalosis. The next step is to determine the degree of respiratory **compensation** (ie, retaining $PaCO_2$ through hypoventilation). This can be done using the following formula:

$$PaCO_2 = (0.9 \times \text{bicarbonate}) + 16 \pm 2$$

The expected $PaCO_2$ in this patient would be 53-57 [$(0.9 \times 44) + 16 \pm 2$], so she has a compensated metabolic alkalosis. Winter's formula ($PaCO_2 = [1.5 \times \text{bicarbonates}] + 8 \pm 2$) is used to assess respiratory compensation in primary metabolic acidosis, not alkalosis.

Hyperemesis gravidarum is characterized by severe vomiting during the first to early second trimesters and is associated with weight loss, volume depletion, and ketonuria. Metabolic alkalosis is often present due to loss of gastric acid. Volume depletion also causes a contraction metabolic alkalosis with activation of the renin-angiotensin-aldosterone system.

(Choice A) The most common acid-base disturbance in asthma is respiratory alkalosis (due to tachypnea). Respiratory or metabolic (lactic) acidosis may also occur and suggests a more severe exacerbation. Metabolic alkalosis is not a common finding in asthma.

(Choice B) Diarrhea is commonly associated with metabolic acidosis (due to loss of organic anions and bicarbonate), hyponatremia, and hypokalemia. Metabolic alkalosis is only rarely seen with diarrhea.

(Choice A) The most common acid-base disturbance in asthma is respiratory alkalosis (due to tachypnea). Respiratory or metabolic (lactic) acidosis may also occur and suggests a more severe exacerbation. Metabolic alkalosis is not a common finding in asthma.

(Choice B) Diarrhea is commonly associated with metabolic acidosis (due to loss of organic anions and bicarbonate), hyponatremia, and hypokalemia. Metabolic alkalosis is only rarely seen with diarrhea.

(Choice D) Hypocapnia is a normal phenomenon of late pregnancy caused by a direct stimulatory effect of progesterone on the central respiratory center. This leads to increased respiratory drive, relative hyperventilation, and primary respiratory alkalosis.

(Choice E) Obesity can cause hypoventilation (ie, Pickwickian syndrome), leading to chronic respiratory acidosis.

(Choice F) The most common acid-base disorder seen in pulmonary embolus (PE) is primary respiratory alkalosis from hyperventilation rather than metabolic alkalosis. PE is also usually associated with tachypnea.

Educational objective:
Hyperemesis gravidarum may cause significant volume depletion and loss of gastric acid, leading to primary metabolic alkalosis.

References

- Hyperemesis gravidarum—assessment and management
- Management strategies for hyperemesis.

A 1-day-old girl is evaluated in the newborn nursery due to swollen hands and feet. She was born at term via an emergency cesarean because her mother had preeclampsia with severe features complicated by pulmonary edema. The newborn's vital signs are normal. Examination shows a short, webbed neck; dysplastic nails; and bilateral, nonpitting carpal and pedal edema. Ultrasound of the abdomen shows a horseshoe kidney. Which of the following is the most likely cause of the edema in this patient?

- A. Capillary hyperpermeability
- B. Decreased albumin synthesis
- C. Excessive sodium retention
- D. Increased urinary loss of protein
- E. Left ventricle hypocontractility
- F. Lymphatic network dysgenesis

Submit

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- A. Capillary hyperpermeability [3%]
- B. Decreased albumin synthesis [2%]
- C. Excessive sodium retention [9%]
- D. Increased urinary loss of protein [9%]
- E. Left ventricle hypocontractility [4%]
- ✔ F. Lymphatic network dysgenesis [69%]

Correct

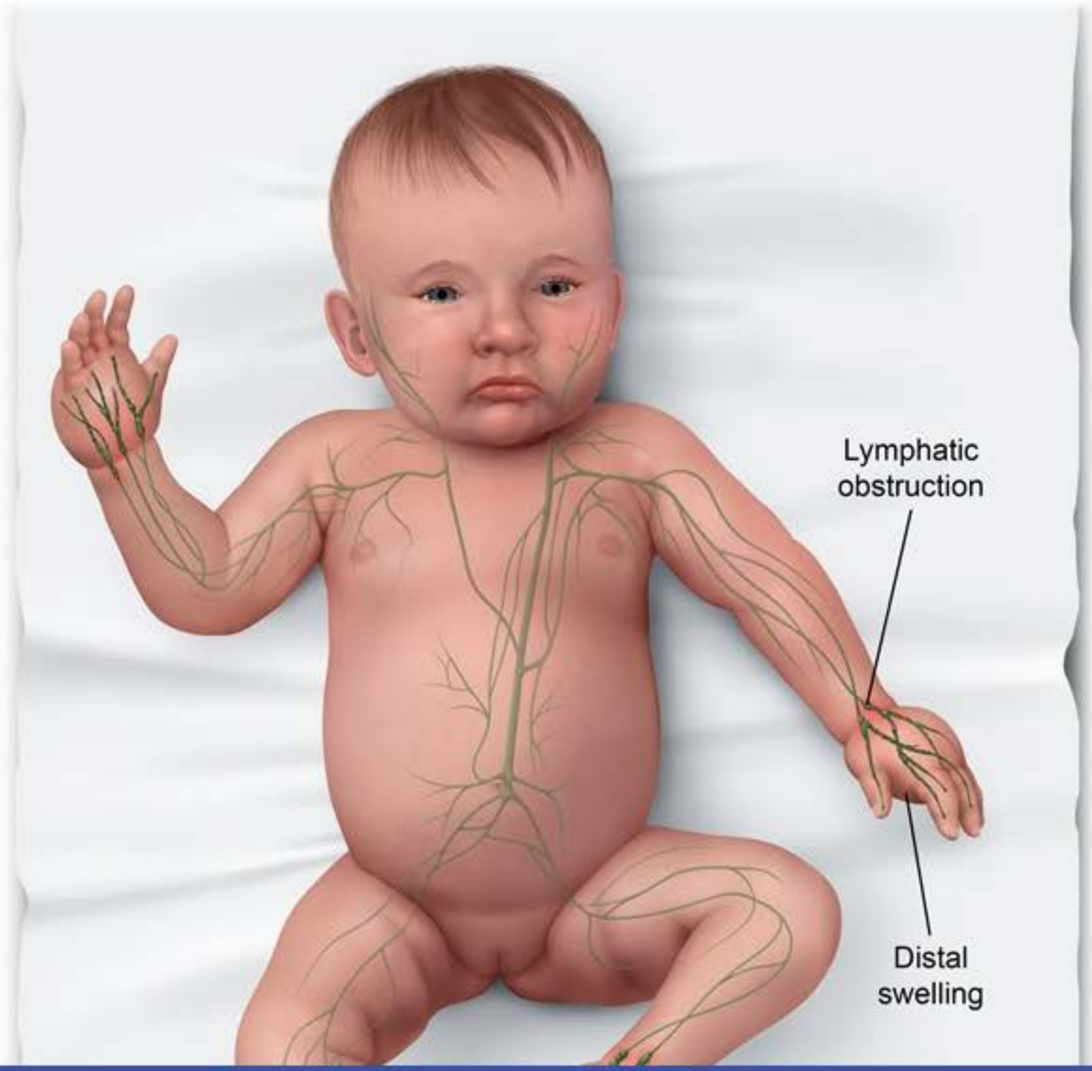
69% Answered correctly

9 Seconds Time Spent

11/08/2018 Last Updated

Explanation

Congenital lymphedema



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This infant has clinical features (eg, **webbed neck**, carpal and pedal edema, nail dysplasia, **horseshoe kidney**) consistent with Turner syndrome (TS), a congenital disorder caused by complete or partial deletion of an X chromosome. Swelling is due to **congenital lymphedema**, which occurs in over half of patients with TS and results from **lymphatic network dysgenesis**. The dysfunctional lymphatic system causes accumulation of protein-rich interstitial fluid in the hands, feet, and neck. Severe obstruction of lymphatic vessels can result in cystic hygroma of the neck and fetal hydrops.

Congenital lymphedema typically presents at birth with **edema** that is generally **nonpitting** due to the high protein content in the interstitial fluid. In contrast, the pitting edema seen with liver failure (hypoalbuminemia), nephrotic syndrome (proteinuria), and congestive heart failure (ventricular hypocontractility) is caused by low protein concentration in the interstitial fluid **(Choices B, D, and E)**.

(Choice A) Preeclampsia can exacerbate extremity swelling in pregnancy due to capillary hyperpermeability, decreased albumin, and renal dysfunction; however, these mechanisms are not the primary cause of congenital lymphedema.

(Choice C) Sodium retention occurs with renal and cardiac pathology. Horseshoe kidney may increase the risk of urinary infections, but renal function is typically normal. Aortic coarctation is also associated with TS and, if severe, can decrease renal perfusion and lead to kidney failure over time. However, an open ductus arteriosus during the first few days of life is protective against renal damage.

Educational objective:
Characteristic features of Turner syndrome include webbed neck, horseshoe kidney, and nail dysplasia.

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chromosome. Swelling is due to **congenital lymphedema**, which occurs in over half of patients with TS and results from **lymphatic network dysgenesis**. The dysfunctional lymphatic system causes accumulation of protein-rich interstitial fluid in the hands, feet, and neck. Severe obstruction of lymphatic vessels can result in cystic hygroma of the neck and fetal hydrops.

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Educational objective:
Characteristic features of Turner syndrome include webbed neck, horseshoe kidney, and nail dysplasia. Congenital lymphedema occurs due to dysgenesis of the lymphatic system and presents at birth with nonpitting carpal and pedal edema.

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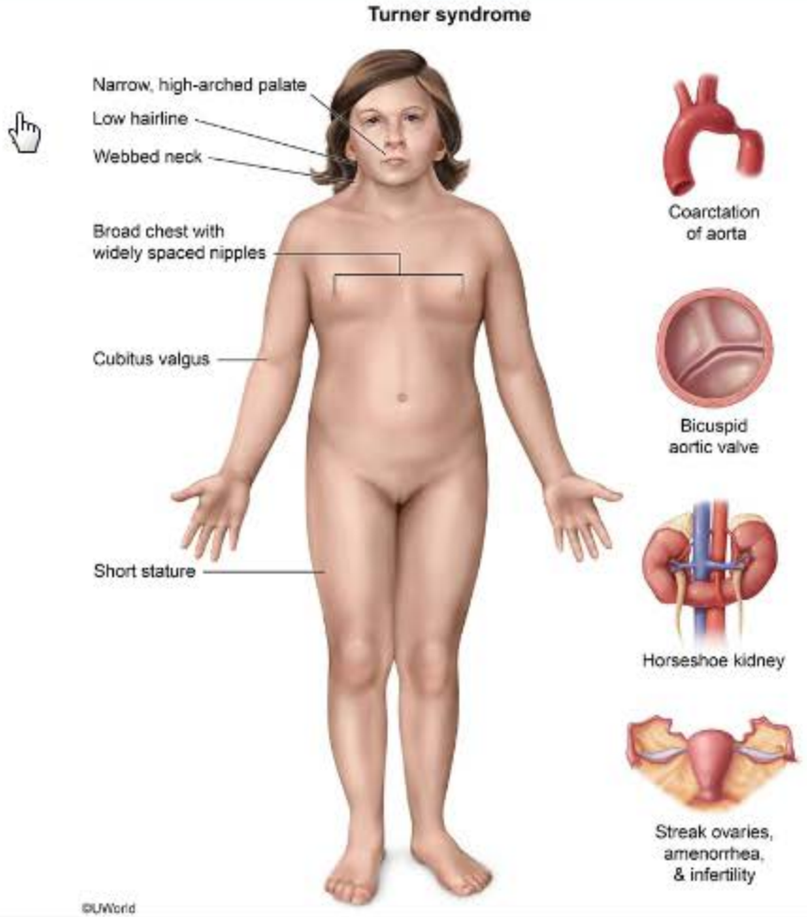

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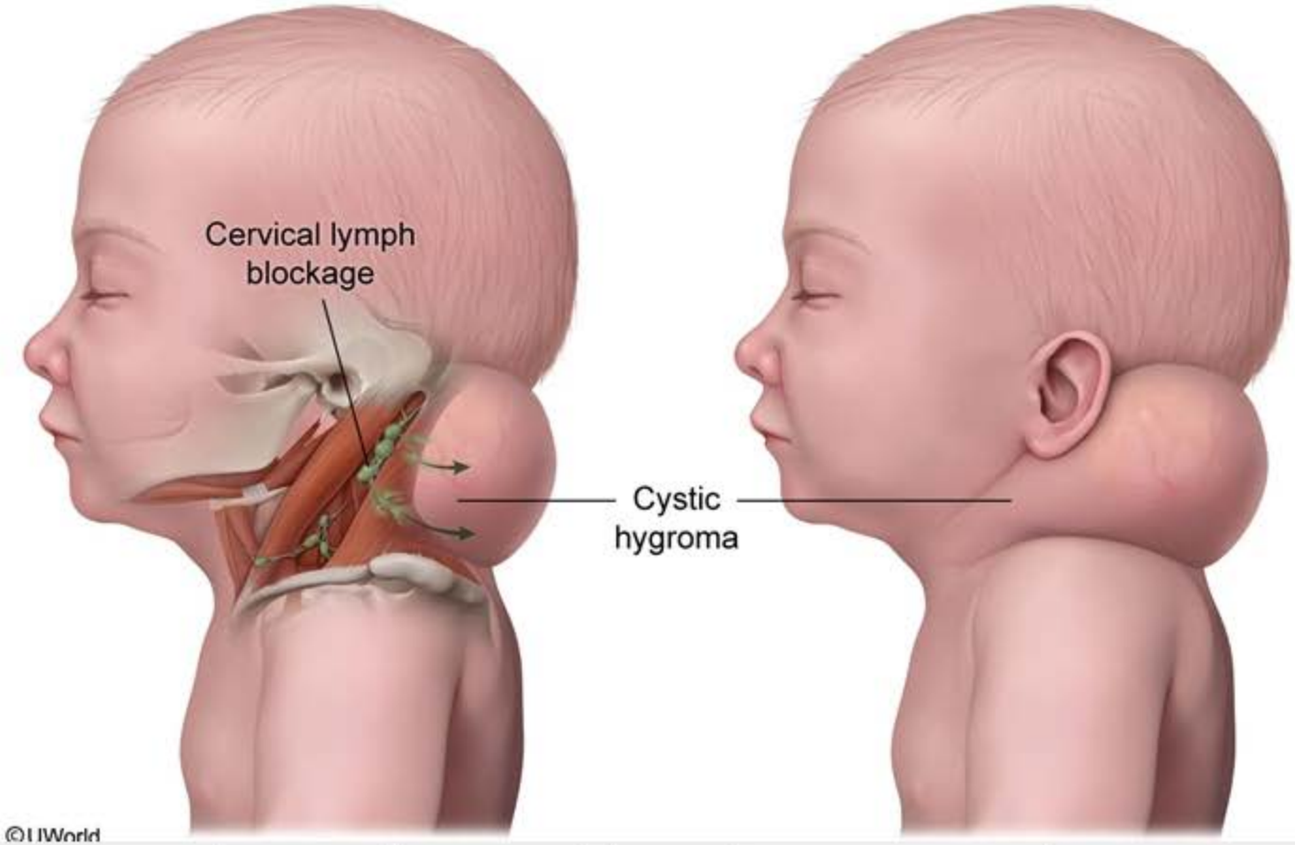
Cystic hygroma



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A 4-year-old boy is brought to the office by his parents for difficulty walking. The child started walking at age 17 months. He often falls while walking and has a tendency to walk on his toes. His maternal uncle had similar symptoms and died in his teens. Examination shows weakened hip muscles, thigh atrophy, bilateral calf enlargement, and positive Gower sign. What is the best test to confirm this patient's diagnosis?

- A. Electromyography
- B. Genetic testing
- C. Muscle biopsy
- D. Nerve conduction studies
- E. Serum aldolase levels
- F. Serum creatine kinase levels

Submit

A 4-year-old boy is brought to the office by his parents for difficulty walking. The child started walking at age 17 months. He often falls while walking and has a tendency to walk on his toes. His maternal uncle had similar symptoms and died in his teens. Examination shows weakened hip muscles, thigh atrophy, bilateral calf enlargement, and positive Gower sign. What is the best test to confirm this patient's diagnosis?

- ✗ A. Electromyography [1%]
- ✓ B. Genetic testing [39%]
- C. Muscle biopsy [56%]
- D. Nerve conduction studies [0%]
- E. Serum aldolase levels [0%]
- F. Serum creatine kinase levels [1%]

Incorrect
Correct answer
B

39%
Answered correctly

5 Seconds
Time Spent

11/03/2018
Last Updated

Explanation

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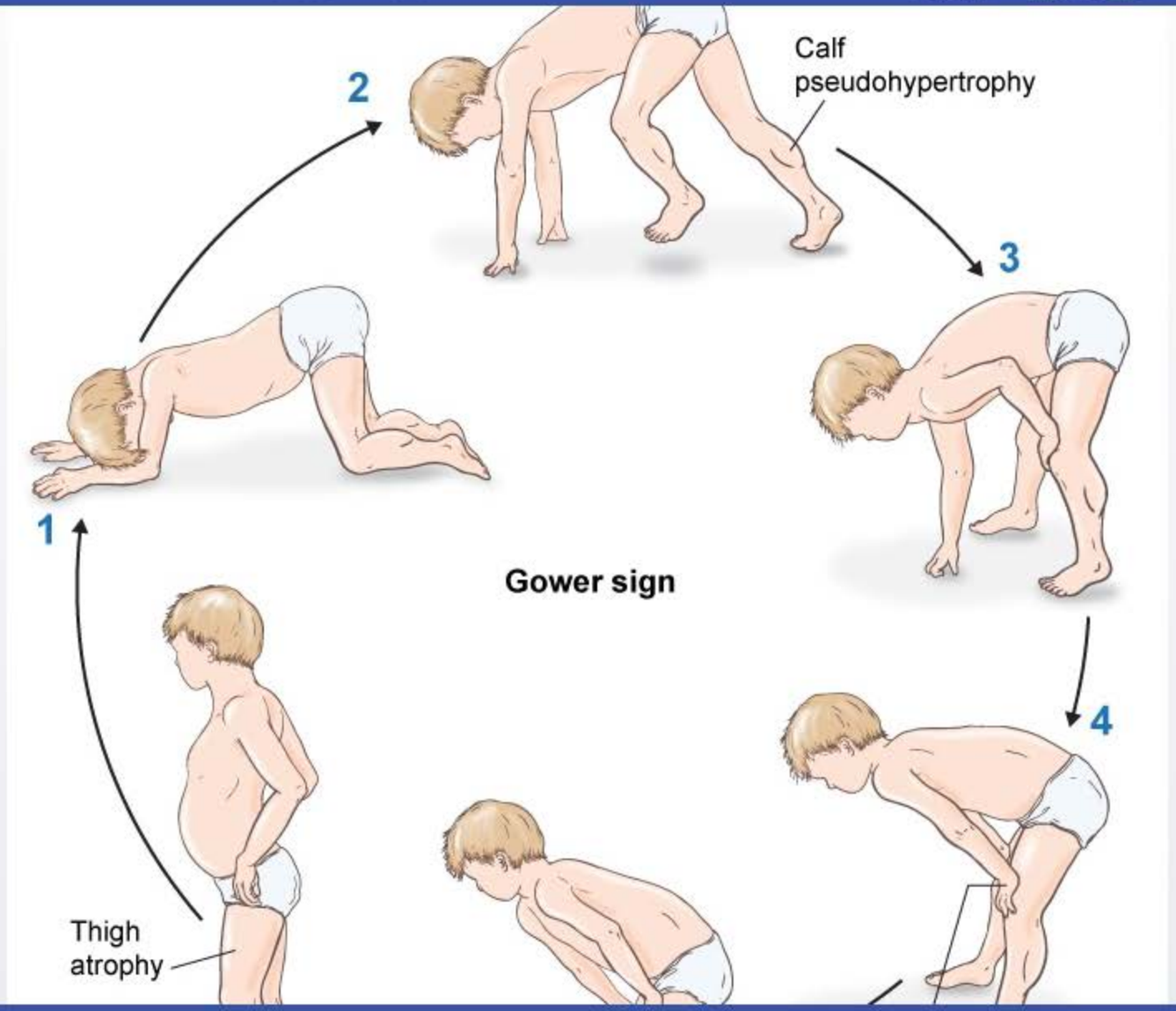

The patient most likely has Duchenne muscular dystrophy (DMD), the most common muscular dystrophy in children. The myopathy typically presents at age 2-5 with **bilateral calf pseudohypertrophy** and **Gower sign**, as seen in this patient. Similar symptoms in the maternal uncle are consistent with an **X-linked recessive** transmission. The gold standard for diagnosis is genetic testing, which would show deletion of the **dystrophin gene** on Xp21.

(Choices A and D) In DMD, electromyography demonstrates a myopathic pattern with normal nerve conduction velocities. However, these tests are supportive and not confirmatory.

(Choice C) Muscle biopsy would show fibrosis and fatty infiltration and can support the diagnosis in this patient. Immunochemistry staining of muscle tissue would show absent dystrophin.

(Choices E and F) Serum creatine kinase and aldolase levels are elevated as early as infancy even before clinical manifestations. These elevations reflect muscle damage and release of these enzymes in the serum. As the disease progresses and more muscle is replaced by fat and fibrosis, these levels eventually drop. These tests are typically used for screening, as elevations can be seen in other myopathies.

Educational objective:
Serum creatine phosphokinase and aldolase levels are elevated in screening for muscular dystrophies. Fibrosis and fatty infiltration on calf muscle biopsy support the diagnosis. Genetic studies are the gold standard for confirmation.

References

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A 15-year-old boy is brought to the office by his parents due to worsening articulation and gait instability. His parents say that his speech has been increasingly difficult to understand over the last 2 months, but he has had no difficulty with comprehension. The patient has also had progressive gait instability over the last month. He is falling more frequently and had to quit his basketball team. He has no chronic medical problems or allergies. The patient takes no medications and does not use alcohol or illicit drugs. Blood pressure is 120/70 mm Hg and pulse is 80/min. Musculoskeletal examination shows scoliosis. Neurologic examination reveals dysarthria and a wide-based, unstable gait. There are absent deep tendon reflexes of the bilateral lower extremities. MRI of the brain and spinal cord shows marked atrophy of the medulla and dorsal columns of the spinal cord. This patient is at greatest risk of mortality from which of the following conditions?

- A. Cardiac dysfunction
- B. Diabetic nephropathy
- C. Malignancy
- D. Respiratory failure
- E. Status epilepticus

Submit

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A 15-year-old boy is brought to the office by his parents due to worsening articulation and gait instability. His parents say that his speech has been increasingly difficult to understand over the last 2 months, but he has had no difficulty with comprehension. The patient has also had progressive gait instability over the last month. He is falling more frequently and had to quit his basketball team. He has no chronic medical problems or allergies. The patient takes no medications and does not use alcohol or illicit drugs. Blood pressure is 120/70 mm Hg and pulse is 80/min. Musculoskeletal examination shows scoliosis. Neurologic examination reveals dysarthria and a wide-based, unstable gait. There are absent deep tendon reflexes of the bilateral lower extremities. MRI of the brain and spinal cord shows marked atrophy of the medulla and dorsal columns of the spinal cord. This patient is at greatest risk of mortality from which of the following conditions?

- ✔ A. Cardiac dysfunction [55%]
- B. Diabetic nephropathy [0%]
- C. Malignancy [1%]
- D. Respiratory failure [41%]
- E. Status epilepticus [1%]

Correct

55% Answered correctly

4 Seconds Time Spent

06/10/2018 Last Updated

Friedreich ataxia	
Genetics	• Autosomal recessive • Loss-of-function, trinucleotide repeat (GAA) in *frataxin* gene

Clinical features	• Neurologic deficits
	  ◦ Cerebellar ataxia
	  ◦ Dysarthria
	  ◦ Loss of vibration and/or position sense
	  ◦ Absent deep tendon reflexes
	• Hypertrophic cardiomyopathy
	• Skeletal deformities (eg, scoliosis)
	• Diabetes mellitus

Prognosis	• Mean survival age 30-40 • Mortality due to cardiac dysfunction (eg, arrhythmia, congestive heart failure)

Friedreich ataxia (FA) classically presents as **progressive gait ataxia** and dysarthria in **adolescents** or young adults. FA is an autosomal recessive disorder caused by a trinucleotide repeat (GAA) expansion that results in a loss-of-function mutation in the *frataxin* gene. Neurologic manifestations (eg, ataxia, **dysarthria**, loss of vibration/position sense) result from degeneration of the spinal tracts (ie, spinocerebellar tracts, posterior columns). Other clinical features include **hypertrophic cardiomyopathy**, diabetes mellitus, and skeletal deformities (eg, scoliosis)

Treatment typically involves multidisciplinary supportive care and monitoring for complications; there is no specific disease-modifying therapy. After disease onset, survival rarely exceeds 20 years. The most common **cause of death** is **cardiac dysfunction** related to cardiomyopathy, typically a fatal arrhythmia or congestive heart failure.

(Choice B) Diabetes mellitus develops in a minority of patients with FA but is a rare cause of death.

(Choice C) Ataxia-telangiectasia is an autosomal recessive disorder that presents with immunodeficiency, progressive cerebellar ataxia, and ocular and cutaneous telangiectasias. Patients with ataxia-telangiectasia have deficits in DNA repair that increase the risk of malignancy. FA does not predispose to cancer.

(Choice D) Guillain-Barré syndrome (GBS) is an immune-mediated polyneuropathy that classically presents as ascending paralysis and can progress to respiratory failure, but the overall risk of mortality is relatively low. GBS is associated with absent reflexes, but it typically follows an infection, is not commonly associated with dysarthria, and would not cause abnormal medullary or dorsal column findings on MRI. Although patients with FA can have aspiration pneumonia and respiratory complications due to bulbar weakness, mortality is most commonly due to cardiac dysfunction.

(Choice E) Status epilepticus can result in mortality from cerebral anoxia, aspiration, and respiratory failure. Patients with FA do not have an increased risk of seizures.

Educational objective:
Friedreich ataxia is a neurodegenerative disorder that classically presents in adolescence with progressive ataxia and dysarthria. The most common cause of death is cardiac dysfunction (eg, arrhythmia, congestive heart failure) due to hypertrophic cardiomyopathy.

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- Absent deep tendon reflexes

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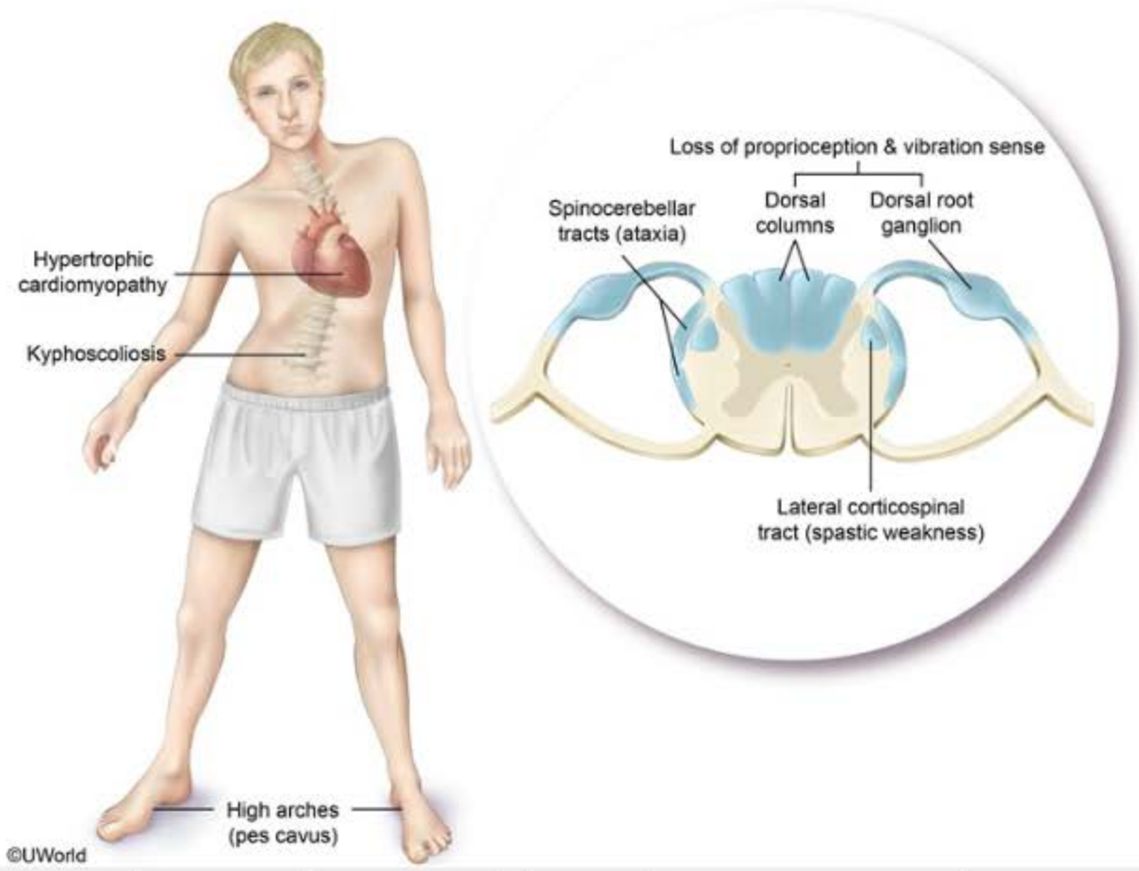
Friedreich ataxia



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A 2-year-old boy is brought to the physician because he has difficulty keeping up with other children at day care. Over the past couple of months, he has been more fatigued than usual and seems weak. The boy has had some difficulty climbing stairs, which he has never experienced before. He also has difficulty rising from the floor and often has to use his hands to help him stand up. His mother thinks that she had a relative with a disorder that caused weakness but is unsure of the diagnosis. His temperature is 37 C (98.6 F), pulse is 94/min, blood pressure is 90/50 mm Hg, and respirations are 18/min. Examination shows an alert and cooperative child. Auscultation shows normal first and second heart sounds with no murmurs. The patient's lungs are clear to auscultation and his abdominal examination is within normal limits. Neurologic examination demonstrates 1+ patellar and Achilles reflexes bilaterally. Both calves appear enlarged. Diagnostic workup would most likely show which of the following findings?

A. Decreased serum aldolase
B. Decreased serum creatine kinase
C. Elevated antinuclear antibodies
D. Muscle biopsy with absent dystrophin
E. Muscle biopsy with reduced dystrophin
F. Myotonic discharges on electromyography

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Over the past couple of months, he has been more fatigued than usual and seems weak. The boy has had some difficulty climbing stairs, which he has never experienced before. He also has difficulty rising from the floor and often has to use his hands to help him stand up. His mother thinks that she had a relative with a disorder that caused weakness but is unsure of the diagnosis. His temperature is 37 C (98.6 F), pulse is 94/min, blood pressure is 90/50 mm Hg, and respirations are 18/min. Examination shows an alert and cooperative child. Auscultation shows normal first and second heart sounds with no murmurs. The patient's lungs are clear to auscultation and his abdominal examination is within normal limits. Neurologic examination demonstrates 1+ patellar and Achilles reflexes bilaterally. Both calves appear enlarged. Diagnostic workup would most likely show which of the following findings?

✗ A. Decreased serum aldolase [0%]

B. Decreased serum creatine kinase [0%]

C. Elevated antinuclear antibodies [0%]

✓ D. Muscle biopsy with absent dystrophin [75%]

E. Muscle biopsy with reduced dystrophin [22%]

F. Myotonic discharges on electromyography [0%]

Incorrect
Correct answer

75%
Answered correctly

18 Seconds
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10/29/2018
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Exhibit Display

Muscular dystrophies

Diagnosis	Duchenne	Becker	Myotonic
Genetics	X-linked recessive deletion of dystrophin gene on chromosome Xp21		Autosomal dominant expansion of a CTG trinucleotide repeat in DMPK gene on chromosome 19q 13.3
Clinical presentation	• Onset: age 2-3 • Progressive weakness, Gower maneuver, calf pseudohypertrophy	• Onset: age 5-15 • Milder weakness compared to Duchenne muscular dystrophy	• Onset: age 12-30 • Facial weakness, hand grip myotonia, dysphagia
Comorbidities	• Scoliosis • Cardiomyopathy	• Cardiomyopathy	• Arrhythmias • Cataracts • Balding • Testicular atrophy/ infertility
Prognosis	• Wheelchair-dependent by adolescence • Death by age 20-30 from respiratory or heart failure	Death by age 40-50 from heart failure	Death from respiratory or heart failure depending on age of onset

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This patient's age, sex, presentation, and family history are consistent with Duchenne muscular dystrophy (DMD). DMD is caused by **dystrophin gene deletion**, which disrupts the amino acid coding sequence for dystrophin, a protein found on the plasma membrane of muscle fibers. The result is severe **proximal lower-extremity weakness** that includes difficulty walking and climbing stairs, and Gower sign (patient uses hands to "walk up" the legs in order to stand up). It progressively worsens to involve respiratory and cardiac muscles, eventually causing death by **respiratory or heart failure**. Diagnosis is confirmed by genetic testing, biopsy that shows muscle replacement by fat and fibrosis, and absent dystrophin on immunochemistry staining.

(Choices A and B) Muscle degeneration in the muscular dystrophies releases muscle enzymes into the blood, resulting in markedly elevated serum creatine phosphokinase and aldolase.

(Choice C) Increased antinuclear antibodies and myositis-specific antibodies can be seen in autoimmune myositis (dermatomyositis, polymyositis). Although autoimmune myositis symmetrically weakens proximal muscles, interstitial pulmonary disease, dysphagia, and polyarthritis are usually seen. In addition, bilateral calf enlargement is unique to DMD and Becker muscular dystrophy (BMD).

(Choice E) BMD is a similar but milder version of DMD. In BMD, the dystrophin gene deletion preserves the reading frame for dystrophin, resulting in decreased (but not absent) dystrophin and muscle weakness later in childhood.

(Choice F) Myotonic dystrophy is an autosomal dominant disease that generally presents in the teenage years with muscle weakness, myotonia, cataracts, and cardiac conduction abnormalities. The muscular groups that are most affected include the facial muscles, intrinsic hand muscles, and ankle dorsiflexors. Myotonia, or delayed muscle relaxation, is a prominent feature of the disease and manifests as a myotonic pattern on

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is unique to DMD and Becker muscular dystrophy (BMD).

(Choice E) BMD is a similar but milder version of DMD. In BMD, the dystrophin gene deletion preserves the reading frame for dystrophin, resulting in decreased (but not absent) dystrophin and muscle weakness later in childhood.

(Choice F) Myotonic dystrophy is an autosomal dominant disease that generally presents in the teenage years with muscle weakness, myotonia, cataracts, and cardiac conduction abnormalities. The muscular groups that are most affected include the facial muscles, intrinsic hand muscles, and ankle dorsiflexors. Myotonia, or delayed muscle relaxation, is a prominent feature of the disease and manifests as a myotonic pattern on electromyography. In contrast, a myopathic pattern would be seen in DMD and BMD.

Educational objective:
Duchenne muscular dystrophy should be suspected in a boy age <5 with proximal muscle weakness, Gower sign, and bilateral calf pseudohypertrophy. Serum creatine phosphokinase and aldolase levels are elevated even before the manifestation of weakness. An absent dystrophin gene on genetic testing and undetectable dystrophin protein on muscle biopsy confirm the diagnosis.

References

- Entries in the Leiden Duchenne muscular dystrophy mutation database: an overview of mutation types and paradoxical cases that confirm the reading-frame rule.

A 4-year-old boy is brought to the physician for evaluation of binge-eating. He complains constantly of hunger and has temper tantrums when his parents refuse to give him additional snacks. Past medical history is significant for hospitalization during the first month of life for nasogastric feeding due to weak suck and hypotonia. The patient is status post orchiopexy for bilateral cryptorchidism at age 1 year. He also receives physical and speech therapies twice a week. His height is <5th percentile and weight is >99th percentile. On examination, he has a narrow forehead, a down-turned mouth, almond-shaped eyes, and small hands and feet. He has low muscle tone and a microphallus. Which of the following is the most likely cause of this patient's condition?

A. Disregulation of imprinted gene expression in chromosome 11p15
B. Loss of the maternal copy of 15q11-q13
C. Loss of the paternal copy of 15q11-q13
D. Nondisjunction resulting in an extra X chromosome
E. X-linked mutation of the fragile X mental retardation 1 gene
F. X-linked mutation of the hypoxanthine-guanine phosphoribosyl transferase gene

Submit

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A 4-year-old boy is brought to the physician for evaluation of binge-eating. He complains constantly of hunger and has temper tantrums when his parents refuse to give him additional snacks. Past medical history is significant for hospitalization during the first month of life for nasogastric feeding due to weak suck and hypotonia. The patient is status post orchiopexy for bilateral cryptorchidism at age 1 year. He also receives physical and speech therapies twice a week. His height is <5th percentile and weight is >99th percentile. On examination, he has a narrow forehead, a down-turned mouth, almond-shaped eyes, and small hands and feet. He has low muscle tone and a microphallus. Which of the following is the most likely cause of this patient's condition?

- A. Disregulation of imprinted gene expression in chromosome 11p15 [3%]
- B. Loss of the maternal copy of 15q11-q13 [13%]
- ✔ C. Loss of the paternal copy of 15q11-q13 [76%]
- D. Nondisjunction resulting in an extra X chromosome [1%]
- E. X-linked mutation of the fragile X mental retardation 1 gene [3%]
- F. X-linked mutation of the hypoxanthine-guanine phosphoribosyl transferase gene [1%]

Correct

76% Answered correctly

4 Seconds Time Spent

10/01/2018 Last Updated

Prader-Willi syndrome	

Clinical features	• Hypotonia
	• Weak suck/feeding problems in infancy
	• Hyperphagia/obesity
	• Short stature
	• Hypogonadism
	• Intellectual disability
	• Dysmorphic facies
	  • Narrow forehead
	  • Almond-shaped eyes
	  • Downturned mouth

Diagnosis	• Deletions on paternal 15q11-q13
Complications	• Sleep apnea (70%) • Type 2 diabetes mellitus (25%) • Gastric distension/rupture • Death by choking (8%)

This patient has the characteristic features of Prader-Willi syndrome (PWS), a sporadic disorder due to **maternal uniparental disomy**. Normally, people inherit 2 active copies of each gene - 1 from the mother and 1 from the father. Patients with PWS inherit both copies of a section of chromosome 15 from their mother. The **deletion of the paternal copy of chromosome 15q11-q13** results in **poor suck and feeding problems in infancy** followed

This patient has the characteristic features of Prader-Willi syndrome (PWS), a sporadic disorder due to **maternal uniparental disomy**. Normally, people inherit 2 active copies of each gene - 1 from the mother and 1 from the father. Patients with PWS inherit both copies of a section of chromosome 15 from their mother. The **deletion of the paternal copy of chromosome 15q11-q13** results in **poor suck and feeding problems in infancy** followed by a life of compulsive **binge-eating** and obesity-related problems. Other common manifestations are shown in the table.

Genetic testing is required to confirm diagnosis and begins with karyotype and methylation studies, followed by fluorescence in-situ hybridization, and then microsatellite probes. Management revolves around **obesity** and its complications. Patients benefit from a structured eating environment and strict limitation of food intake (eg, locks on refrigerator, close supervision). They should be screened for **sleep apnea** (central and obstructive) as well as **type 2 diabetes mellitus**. Some patients undergo growth hormone therapy to improve linear growth and body composition, including fat-free mass and bone density.

(Choice A) Beckwith-Wiedemann syndrome is a congenital disorder due to disregulation of imprinted gene expression in chromosome 11p15. Characteristic physical findings include macroglossia, rapid growth, hemihyperplasia, and umbilical hernia or omphalocele.

(Choice B) Patients with **Angelman syndrome** suffer from paternal uniparental disomy (eg, deletion of the maternal copy of chromosome 15q11-q13). As in PWS, these patients may have short stature and intellectual disability. However, other unique features include frequent **smiling/laughter**, hand-flapping, ataxia, and seizures.

(Choice D) Klinefelter syndrome (XXY) is the most common sex chromosome abnormality causing primary

maternal copy of chromosome 15q11-q13). As in PWS, these patients may have short stature and intellectual disability. However, other unique features include frequent **smiling/laughter**, hand-flapping, ataxia, and seizures.

(Choice D) Klinefelter syndrome (XXY) is the most common sex chromosome abnormality causing primary hypogonadism. However, newborns typically have normal male external genitalia and no apparent dysmorphic features. After puberty, small testes and tall stature become apparent.

(Choice E) Fragile X syndrome is the most common X-linked inherited cause of intellectual disability. Affected boys have a prominent forehead and macroorchidism in contrast to PWS.

(Choice F) Lesch-Nyhan syndrome results from a deficiency of the hypoxanthine-guanine phosphoribosyl transferase enzyme, resulting in marked hyperuricemia. It is characterized by self-mutilation, mental retardation, and extrapyramidal symptoms (eg, dystonia, choreoathetosis).

Educational objective:
The main features of Prader-Willi syndrome are hypotonia, hyperphagia, and obesity. Patients are at risk for sleep apnea, type 2 diabetes mellitus, and gastric rupture.

References

- Prader-Willi syndrome: an update and review for the primary pediatrician.
- Recommendations for the diagnosis and management of Prader-Willi syndrome.
- Clinical report—health supervision for children with Prader-Willi syndrome.

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A 6-year-old girl is brought to the office for evaluation of pubic hair development. The girl's mother reports first noticing axillary hair a few weeks ago while dressing her for school. The patient has also had breast and pubic hair development but no vaginal bleeding, headaches, emesis, or visual disturbances. She has no medical conditions and takes no daily medications. The patient had 2 long bone fractures at ages 4 and 5. Family history is unremarkable. Physical examination reveals 2 large hyperpigmented macules with irregular contours on the left side of her back and chest. Axillae have secondary hair; there is no freckling. Bilateral breasts have budding and enlargement of the areola. There is coarse, dark pubic hair along the labia and the pubic junction. Which of the following is the most likely diagnosis in this patient?

- A. Adrenal tumor
- B. McCune-Albright syndrome
- C. Neurofibromatosis type 1
- D. Peutz-Jeghers syndrome
- E. Sturge-Weber syndrome
- F. Tuberous sclerosis

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- A. Adrenal tumor [12%]
- ✔ B. McCune-Albright syndrome [75%]
- C. Neurofibromatosis type 1 [4%]
- D. Peutz-Jeghers syndrome [1%]
- E. Sturge-Weber syndrome [2%]
- F. Tuberous sclerosis [2%]

Correct

75% Answered correctly

7 Seconds Time Spent

08/21/2018 Last Updated

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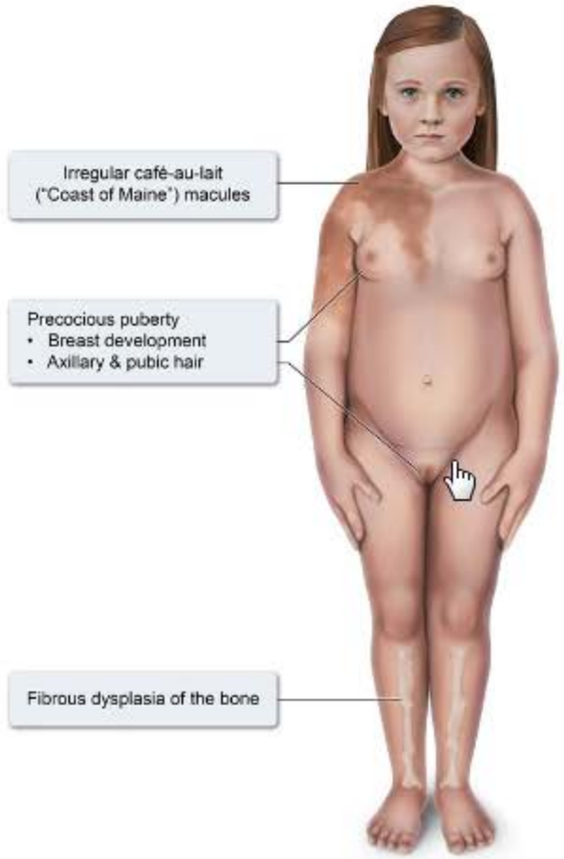
McCune-Albright Syndrome



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This child has early breast and pubic hair development consistent with **precocious puberty**, the onset of secondary sexual characteristics in girls age <8 or boys age <9. Central precocious puberty is due to early activation of the hypothalamic-pituitary-gonadal axis. Peripheral precocity is attributed to premature secretion of sex hormones independent of GnRH.

In addition to precocious puberty, this patient has **irregular café-au-lait macules** confined to one side of the body and recurrent fractures due to **polyostotic fibrous dysplasia**, characteristic of **McCune-Albright syndrome** (MAS). MAS is a rare cause of precocious puberty due to a mutation in the *GNAS* gene, which results in constant G protein activation and overproduction of pituitary hormones. Therefore, in addition to **GnRH-independent (ie, peripheral)** precocious puberty (FSH, LH), MAS can also lead to thyrotoxicosis (TSH), acromegaly (GH), and Cushing syndrome (ACTH).

(Choice A) An adrenal tumor typically causes isolated premature adrenarche (eg, pubic/axillary hair, acne, body odor) and is unlikely in this patient with concomitant breast development.

(Choice C) Neurofibromatosis type 1 (NF1) can cause precocious puberty (due to optic glioma affecting the hypothalamus) and long-bone dysplasia (eg, fractures). However, café-au-lait macules in NF1 are typically more numerous (≥6) with regular borders and have associated axillary freckling.

(Choice D) Peutz-Jeghers syndrome is characterized by gastrointestinal tract hamartomatous polyposis. The associated skin lesions are small (1-5 mm), perioral, mucocutaneous pigmented macules. Patients do not undergo precocious puberty.

(Choice E) Sturge-Weber syndrome is characterized by intellectual disability, seizures, and visual impairment due

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(Choice E) Sturge-Weber syndrome is characterized by intellectual disability, seizures, and visual impairment due to capillary-venous malformations. The associated skin lesion is a port-wine stain over the territory of the trigeminal nerve. There is no associated precocious puberty.

(Choice F) Tuberous sclerosis is a neurocutaneous disorder that can cause central precocious puberty due to brain hamartomas. However, associated skin lesions include hypopigmented ash-leaf spots and shagreen patches.

Educational objective:
McCune-Albright syndrome is characterized by peripheral precocious puberty, irregular café-au-lait macules, and polyostotic fibrous dysplasia (eg, recurrent fractures).

References

- McCune-Albright syndrome.
- Fibrous dysplasia/McCune-Albright syndrome: clinical and translational perspectives.

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(MAS). MAS is a rare cause of precocious puberty due to a mutation in the *GNAS* gene, which results in constant

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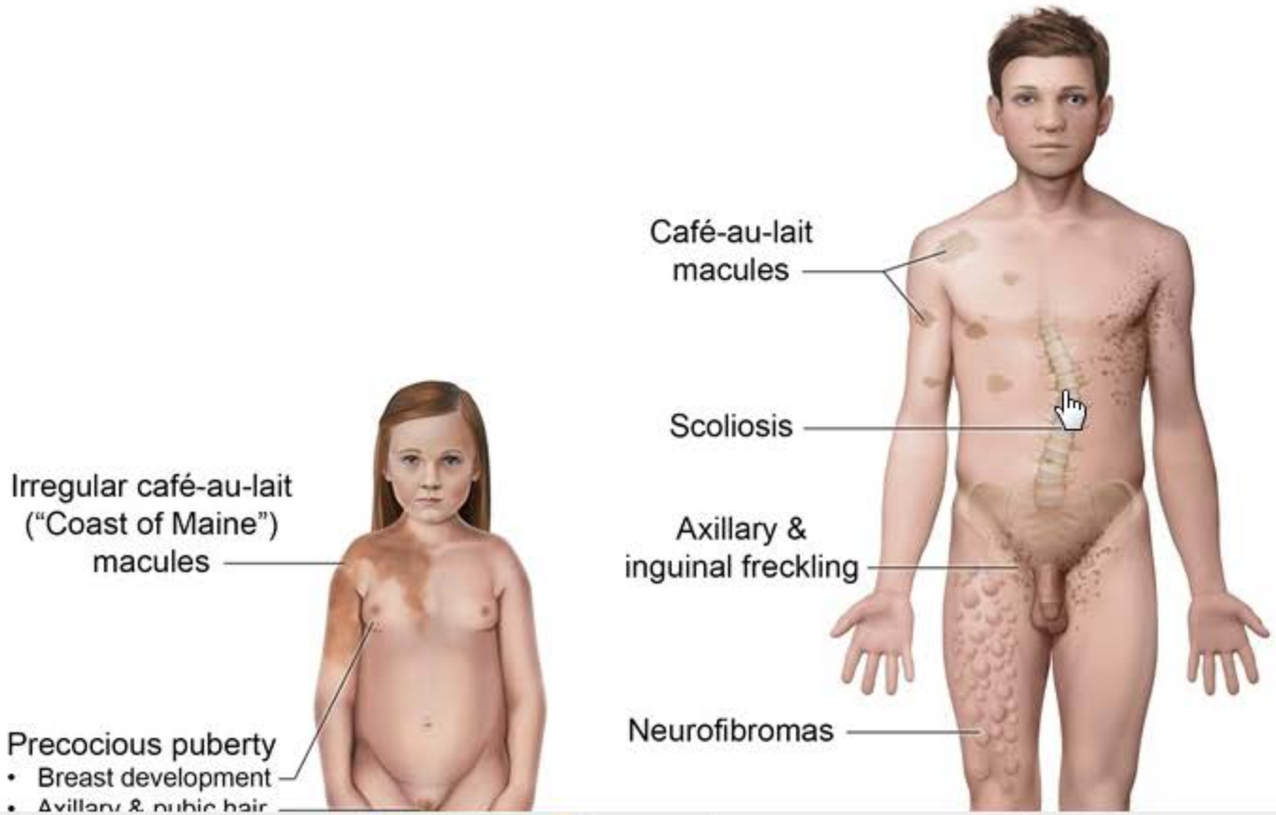
McCune-Albright Syndrome vs. Neurofibromatosis type I



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Educational objective:

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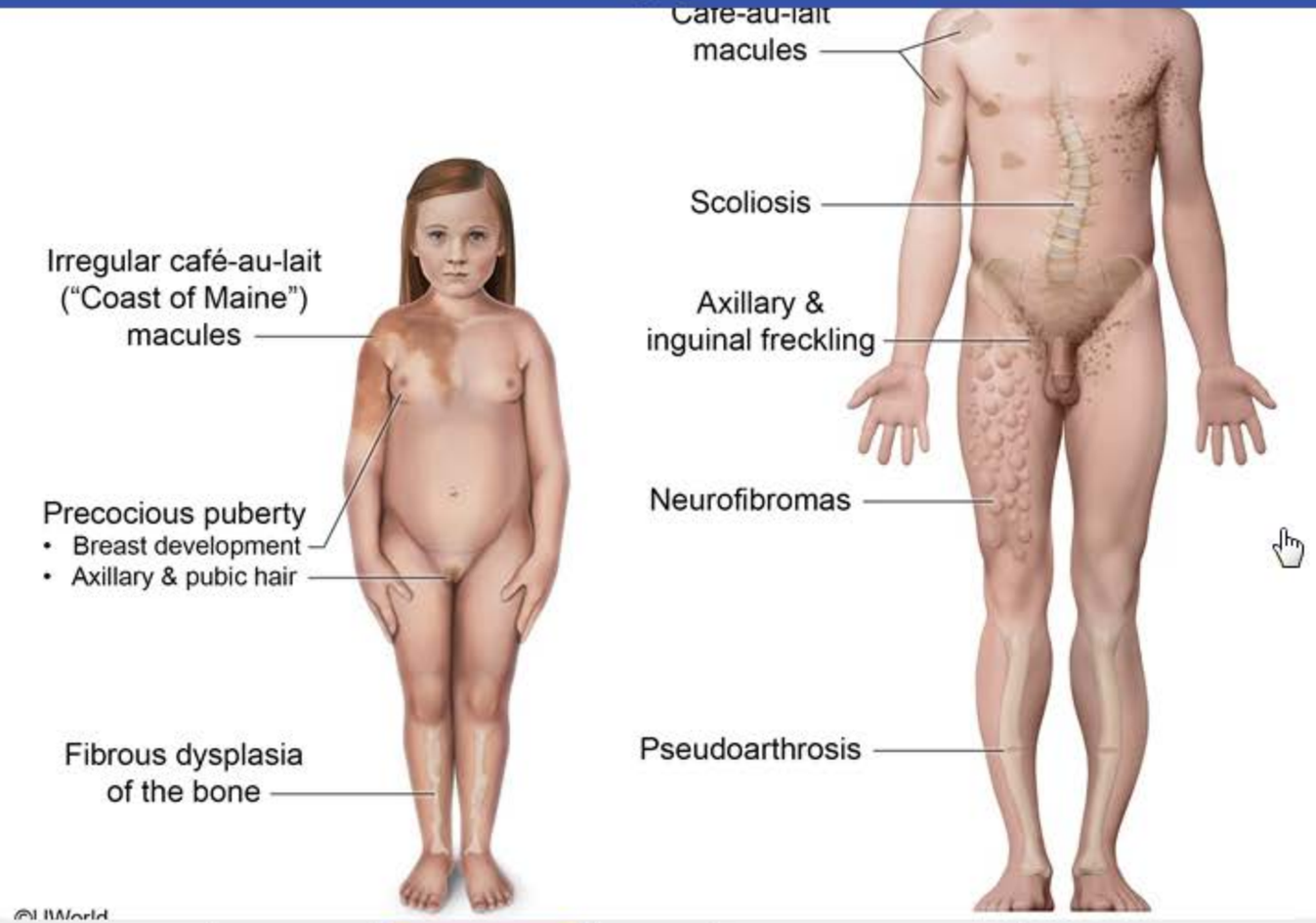

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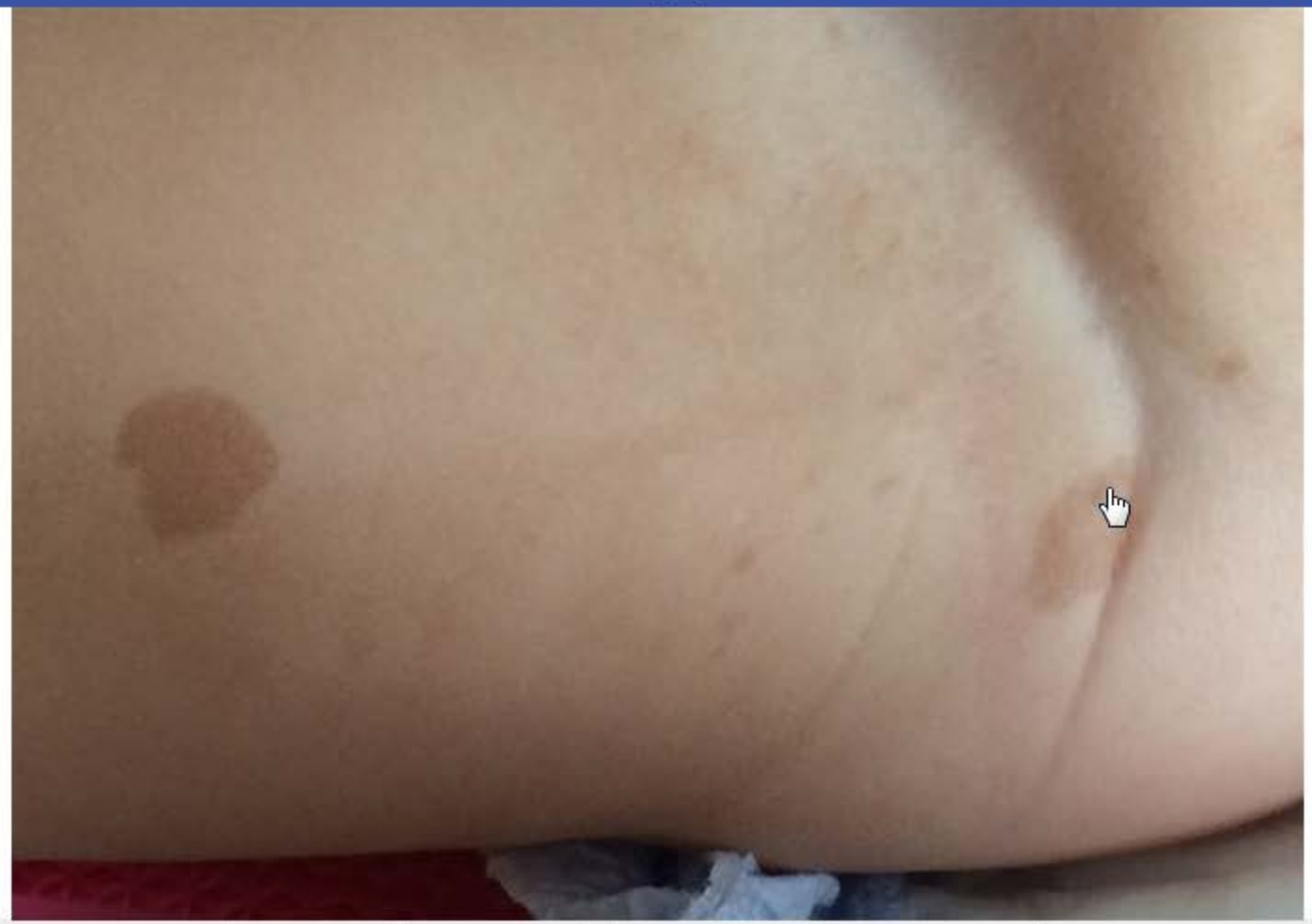

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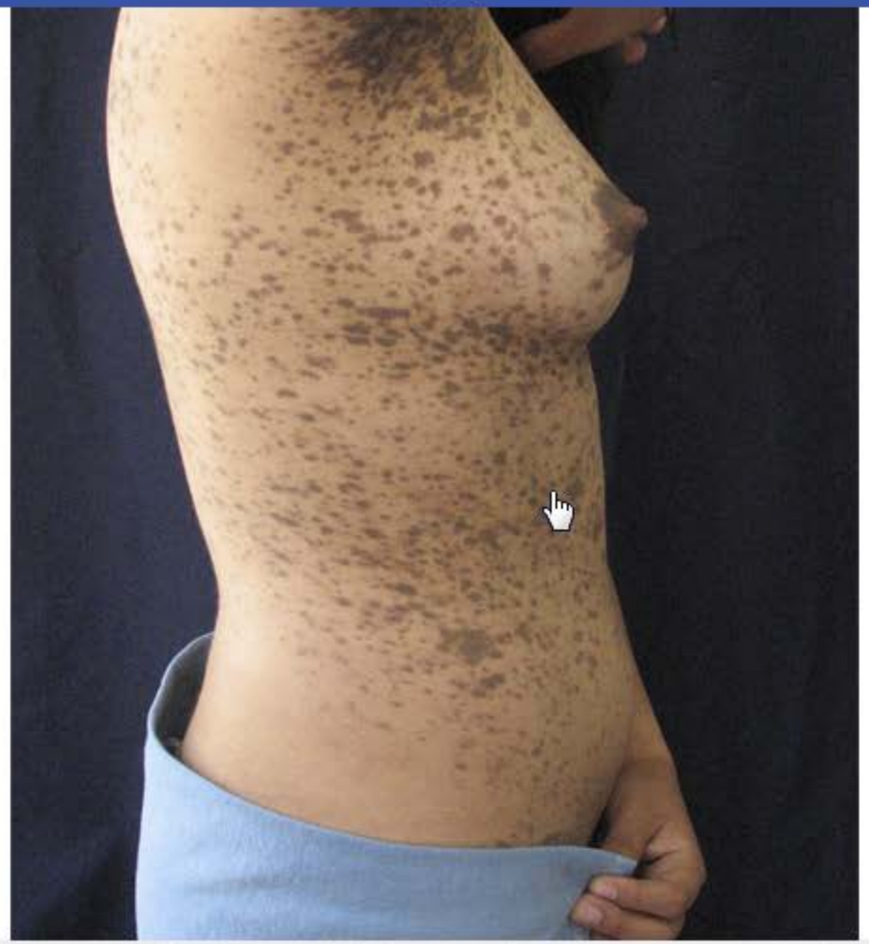

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Educational objective:

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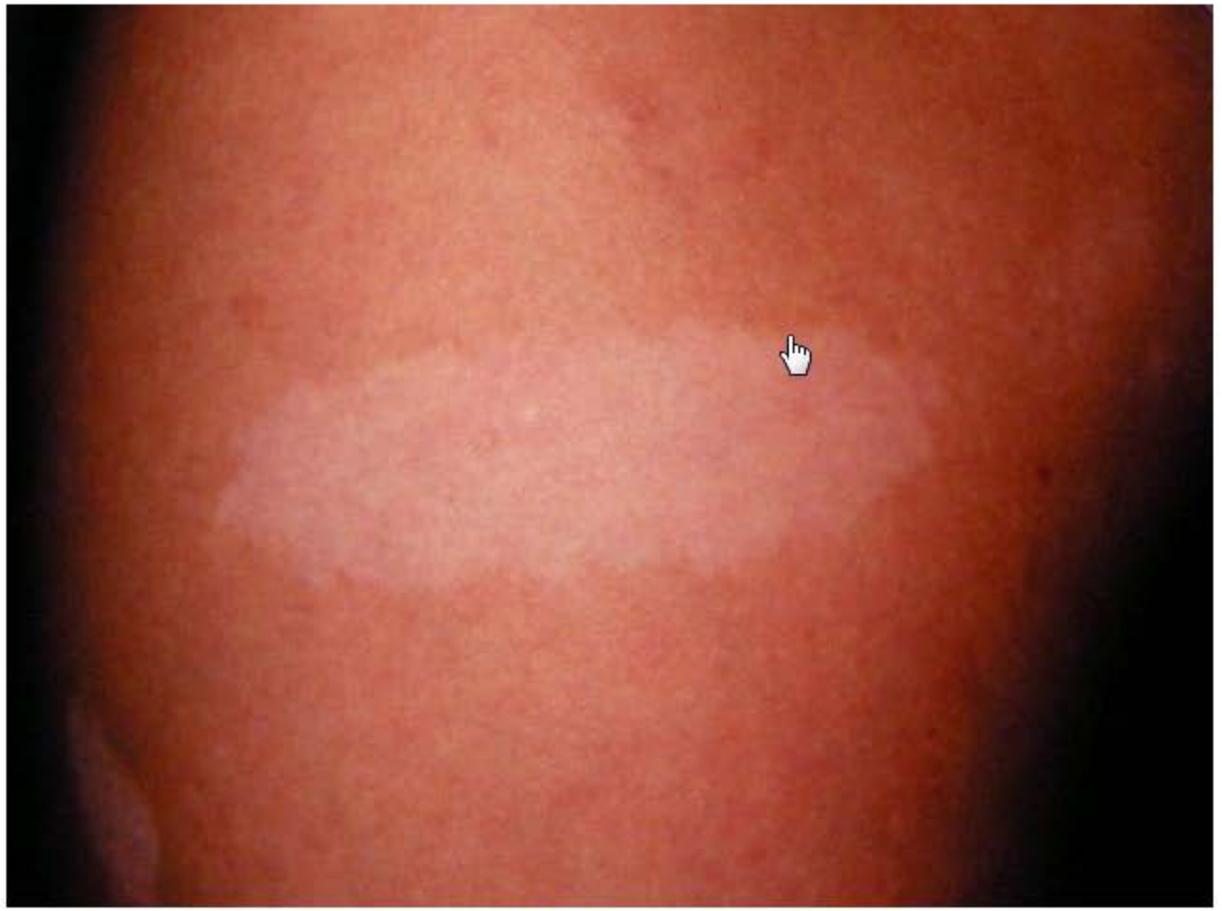

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Educational objective:

A healthy 15-year-old girl comes to the physician for a routine health maintenance examination. She feels well and has no concerns. Her menstrual cycles are regular and last 3-4 days; her last menses was 1 week ago. The patient has been sexually active with one partner for the past year and takes oral contraceptive pills daily. She has no vaginal discharge or pain. She is an honors student in 10th grade and plays varsity soccer. The patient has tried marijuana "a few times" but does not use tobacco or alcohol. Her parents are healthy. Her maternal grandfather died of a myocardial infarction at age 68. The patient's body mass index is 23 kg/m^2. Vital signs and physical examination are normal. What is the best next step in the evaluation of this patient?

- A. *Chlamydia trachomatis* testing
- B. Complete blood count
- C. Echocardiography
- D. Fasting lipid panel
- E. Urine culture
- F. Urine toxicology screen

Submit

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- ✔ A. *Chlamydia trachomatis* testing [70%]
- B. Complete blood count [12%]
- C. Echocardiography [0%]
- D. Fasting lipid panel [7%]
- E. Urine culture [1%]
- F. Urine toxicology screen [7%]

Correct

70%
Answered correctly

4 Seconds
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The purpose of screening tests is to identify individuals at increased risk for a particular disease who would benefit from diagnosis and treatment. All **sexually active women age ≤24** should undergo testing for *Chlamydia trachomatis* and *Neisseria gonorrhoeae*, 2 of the most common sexually transmitted infections. Screening is also recommended for any person with a new partner in past 2 months, multiple partners, history of sexually transmitted infections, illicit drug use, incarceration, and contact with sex workers.

Cervicitis is a common manifestation of chlamydia and gonorrhea, but many patients are asymptomatic. Undetected and untreated infection can lead to **pelvic inflammatory disease** and its associated complications (eg, infertility, ectopic pregnancy, chronic pelvic pain). In addition, these chlamydial and gonorrheal infections can facilitate HIV transmission.

The best screening test is the **nucleic acid amplification test**, which has high sensitivity and specificity. The test can be performed on urine, endocervical, vaginal, or urethral specimens with similar accuracy. Patients diagnosed with infection should receive antibiotics immediately and refrain from sexual intercourse until treatment is complete and symptoms have resolved. All sex partners from the preceding 2 months should also be tested and treated for infection.

(Choice B) Patients who have no symptoms (eg, fatigue, pallor, dyspnea) and no menorrhagia do not require routine complete blood count testing.

(Choice C) Electrocardiogram, echocardiography, and exercise testing should be performed in athletes at risk for sudden cardiac death. High-risk patients include those with a history of Marfan syndrome, chest pain, or dyspnea on exertion; family history of cardiomyopathy or long-QT syndrome; and premature cardiac death or disability in a

on exertion; family history of cardiomyopathy or long-QT syndrome; and premature cardiac death or disability in a close relative age <50. Routine screening is otherwise not recommended due to risk of false-positive results and lack of cost efficiency.

(Choice D) Universal screening for dyslipidemia is recommended at age 9-11 and at age 17-21, as lipid levels are relatively stable just prior to and after puberty. Screening outside of these periods should occur in patients at high risk for cardiovascular disease (eg, history of obesity/diabetes mellitus/tobacco exposure, family history of premature coronary disease) and men age ≥35.

(Choice E) Routine screening for asymptomatic bacteriuria is not recommended in men and nonpregnant women. However, pregnant women should be screened for asymptomatic bacteriuria due to the increased incidence of pyelonephritis and low birth weight.

(Choice F) A basic drug test can detect amphetamine, cocaine, marijuana, opioids, and phencyclidine that have been used within a few days of the test. Testing may be useful if the patient is in a drug abuse rehabilitation or pain management program or is receiving psychiatric care. Random drug screening is not recommended, but adolescents should be counseled on the increased risk of unintentional injuries, motor vehicle crashes, abuse, and dependence.

Educational objective:

All sexually active women age ≤24 should be screened for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* by nucleic acid amplification testing. Athletes with risk factors for sudden death should undergo cardiac evaluation, but routine screening is not recommended otherwise. Random urine toxicology is generally not recommended, but the risks of short- and-long term drug use should be discussed.

A newborn girl is examined in the delivery room immediately after induced vaginal delivery for intrauterine growth restriction (IUGR). She was born to a 40-year-old woman with no significant medical history. In addition to IUGR, prenatal ultrasound demonstrates a ventricular septal defect. Her parents decline additional prenatal testing. The patient's weight and head circumference are <5th percentile. Examination shows hypertonia and closed fists, with the second digit overlapping the third and the fifth overlapping the fourth. Based on this patient's presumed chromosomal abnormality, which of the following additional physical findings is most likely to be present on examination?

- A. Cat-like cry
- B. Cutis aplasia
- C. Micrognathia
- D. Microphthalmia
- E. Transverse palmar crease
- F. Webbed neck

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- A. Cat-like cry [9%]
- ✗ B. Cutis aplasia [6%]
- ✓ C. Micrognathia [65%]
- D. Microphthalmia [7%]
- E. Transverse palmar crease [9%]
- F. Webbed neck [1%]

Incorrect
Correct answer
C

65%
Answered correctly

5 Seconds
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09/10/2018
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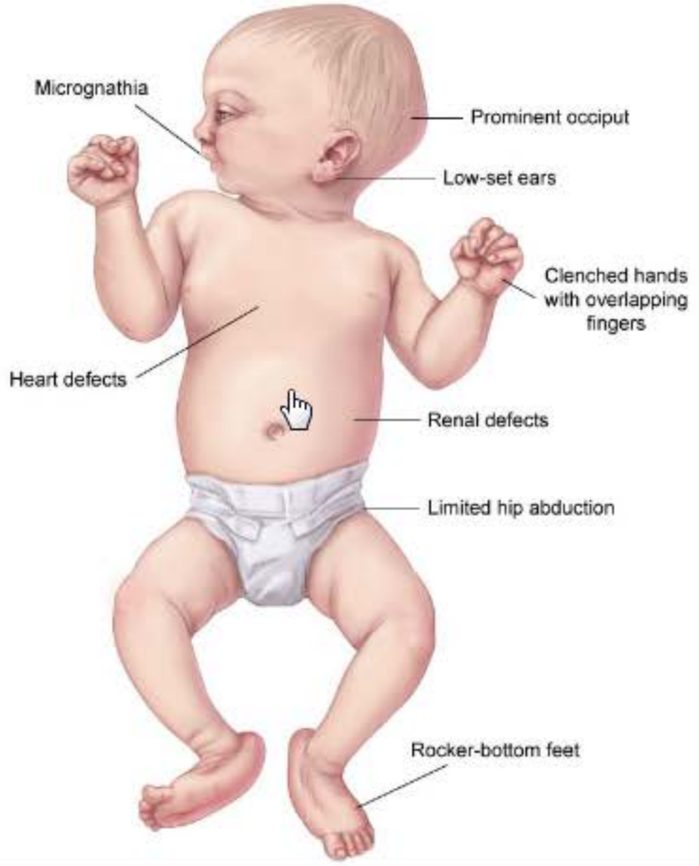
Trisomy 18 (Edwards syndrome)



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This newborn's low birth weight due to **intrauterine growth restriction**, microcephaly, ventricular septal defect, and **closed fists with overlapping fingers** are all classic physical examination features seen in **trisomy 18** (**Edwards syndrome**). Other findings include **micrognathia, prominent occiput, rocker-bottom feet**, and severe intellectual disability.

After trisomy 21, trisomy 18 is the second most common autosomal trisomy observed in live births. The risk of trisomies increases with maternal age due to meiotic nondisjunction within maternal oocytes. Diagnosis is suspected based on prenatal ultrasonography, and karyotype (prenatal or postnatal) confirms the diagnosis. Approximately 95% of trisomy 18 patients die during their first year of life, most commonly due to cardiac failure from congenital heart disease or respiratory failure from hypoventilation or aspiration.

(Choice A) A cat-like cry is seen in cri-du-chat (5p deletion) syndrome. Infants with this syndrome may also have microcephaly; however, a characteristic protruding metopic suture is present. Other manifestations are hypotonia, short stature, hypertelorism, wide and flat nasal bridge, and intellectual disability.

(Choices B and D) Cutis aplasia (absence of epidermis over the skull) and microphthalmia are both classically seen in trisomy 13 (Patau syndrome). This condition also associated with other midline defects, including holoprosencephaly and omphalocele. Closed fists with overlapping fingers are not seen.

(Choice E) A transverse palmar crease can be a normal variant but is also strongly associated with trisomy 21 (Down syndrome). Infants with Down syndrome also have hypotonia, upward and slanted palpebral fissures, epicanthal folds, Brushfield spots, cardiac malformations, and intestinal atresia.

(Choice F) A webbed neck is a classic feature of Turner syndrome (45,XO). Other features include a low

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(Choices B and D) Cutis aplasia (absence of epidermis over the skull) and microphthalmia are both classically seen in **trisomy 13 (Patau syndrome)**. This condition also associated with other midline defects, including holoprosencephaly and omphalocele. Closed fists with overlapping fingers are not seen.

(Choice E) A transverse palmar crease can be a normal variant but is also strongly associated with **trisomy 21 (Down syndrome)**. Infants with Down syndrome also have hypotonia, upward and slanted palpebral fissures, epicanthal folds, Brushfield spots, cardiac malformations, and intestinal atresia.

(Choice F) A webbed neck is a classic feature of **Turner syndrome** (45,XO). Other features include a low hairline, broad chest with widely spaced nipples, cubitus valgus, and short stature.

Educational objective:
Infants with Edwards syndrome (trisomy 18) commonly have microcephaly, prominent occiput, intrauterine growth restriction, and micrognathia, as well as closed fists with overlapping digits and rocker-bottom feet. The mortality rate in the first year of life approaches 95%.

References

- Trisomy 18: review of the clinical, etiologic, prognostic, and ethical aspects.
- Anatomy of trisomy 18.

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from congenital heart disease or respiratory failure from hypoventilation or aspiration.

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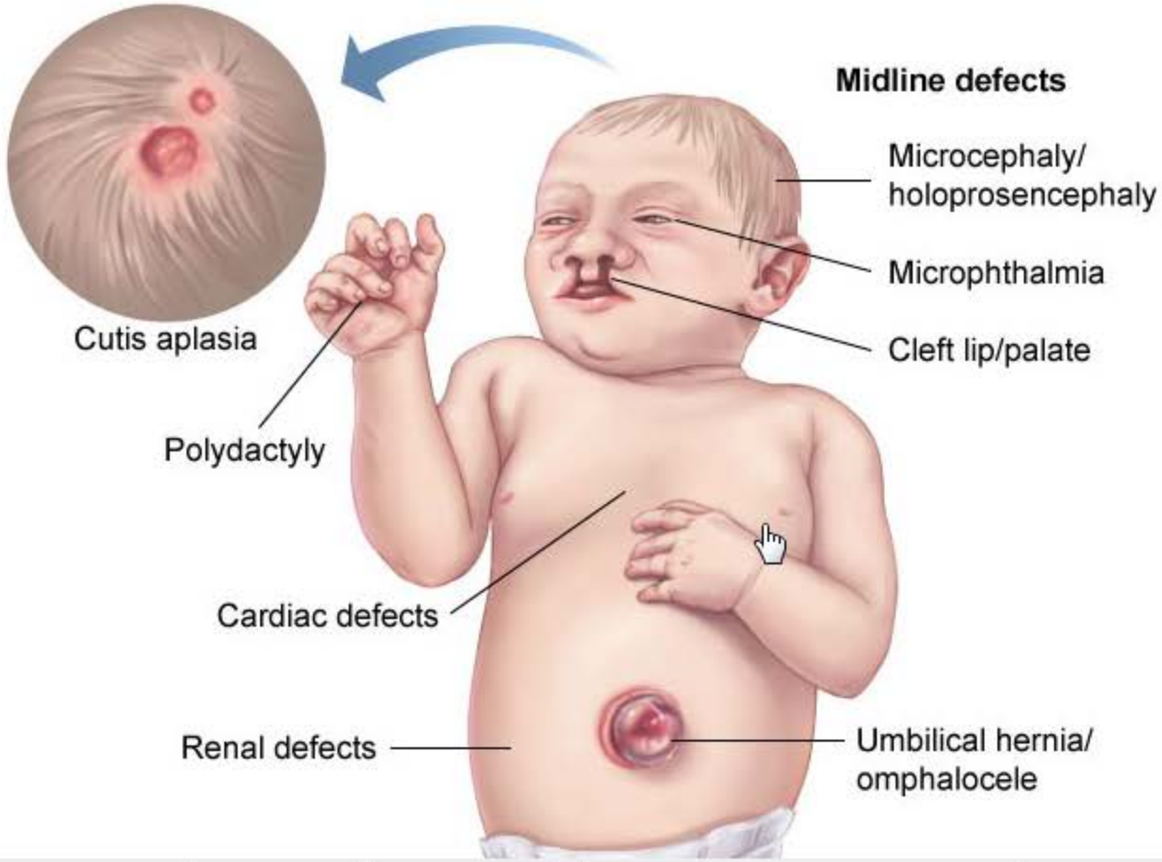

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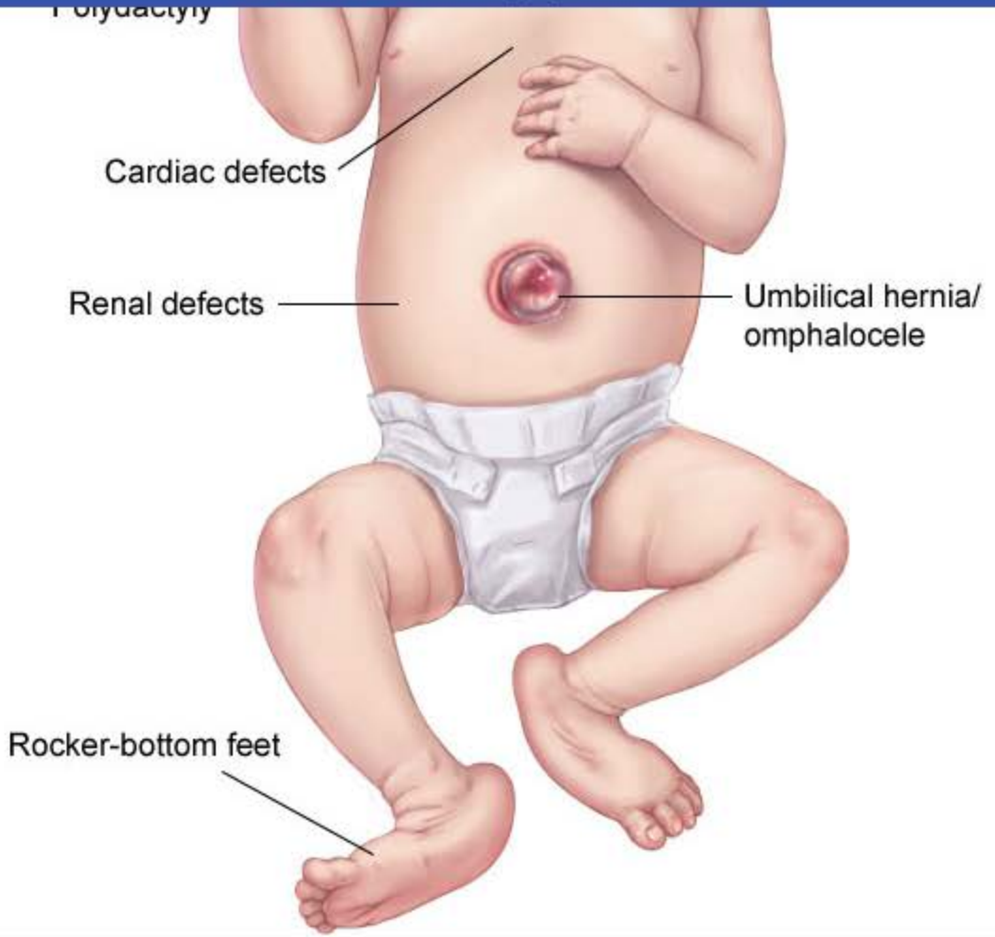

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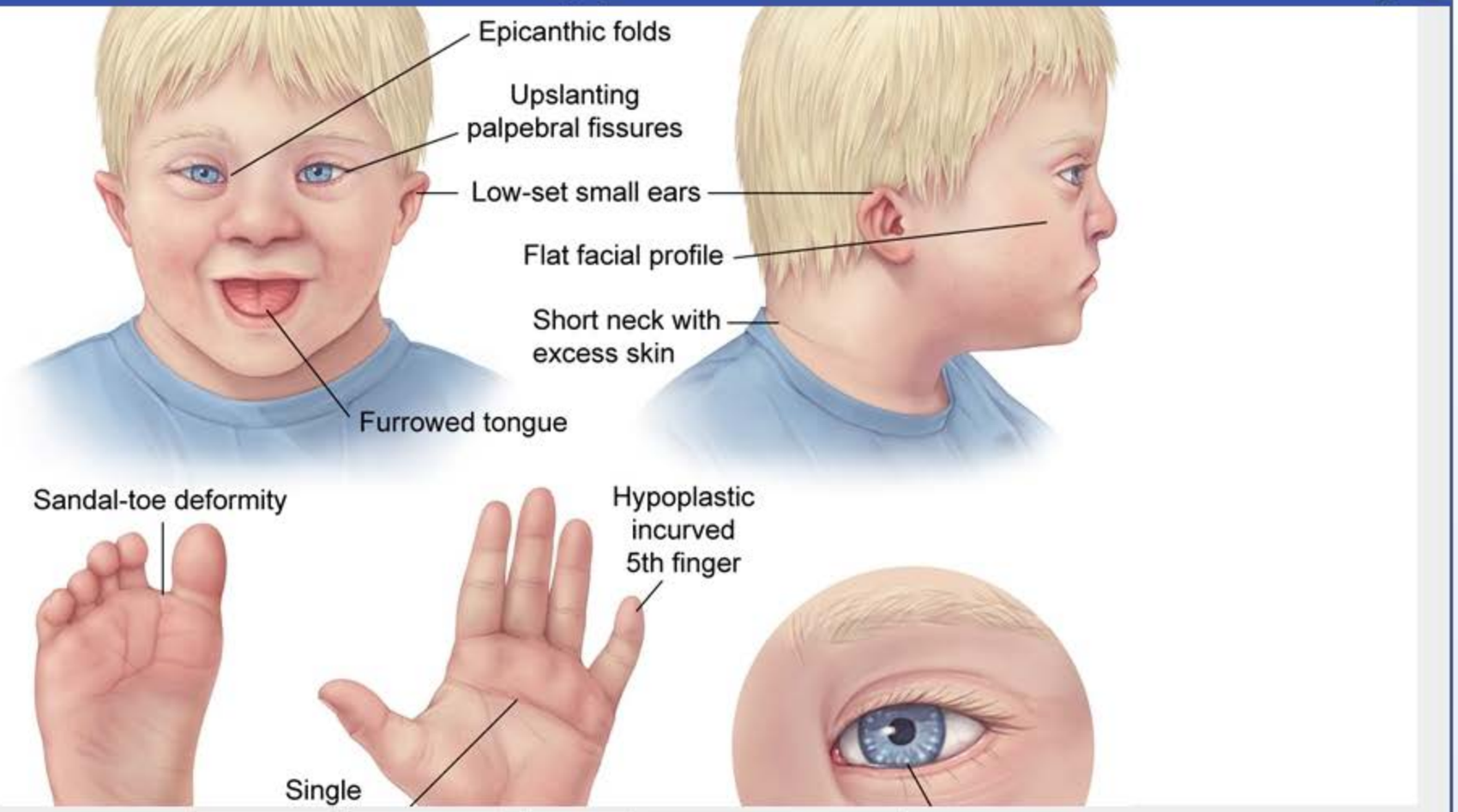

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- Trisomy 18: review of the clinical, etiologic, prognostic, and ethical aspects.

A 5-year-old boy is brought to the emergency department by his parents for difficulty walking. The patient has had pain in his legs since the morning and "wouldn't even get out of bed." The father says that his son played 2 soccer games yesterday with no pain or trauma. One week ago, the patient had a low-grade fever and cough that have since resolved. Review of systems is positive for a nonpruritic rash on his back and legs for the past 2 days that the parents attribute to a new laundry detergent. He has had no nausea, emesis, weight loss, or night sweats. The patient has no significant medical history and takes no daily medications. Temperature is 36.7 C (98 F), blood pressure is 90/40 mm Hg, pulse is 138/min, and respirations are 20/min. Physical examination shows an uncomfortable-appearing boy lying in bed who cries with any attempt to move his legs. A purplish, nonblanching rash is noted over his buttocks and posterior thighs. Abdominal examination is soft with active bowel sounds and mild diffuse tenderness to palpation without rebound or guarding. Lower extremity joints demonstrate no deformity, erythema, swelling, or warmth. The patient refuses to walk due to pain in his legs. Laboratory results from urinalysis are as follows:

Specific gravity	1.016
pH	7.0
Protein	trace
Blood	large
Glucose	negative
Ketones	negative

Protein	trace
Blood	large
Glucose	negative
Ketones	negative
Leukocyte esterase	negative
Nitrites	negative

The patient is admitted to the hospital for further management. Which of the following complications of the underlying disease is he most likely to develop?

- A. Hemolytic anemia
- B. Intussusception
- C. Joint destruction
- D. Urethritis
- E. Uveitis
- F. Volvulus

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Protein	trace
Blood	large
Glucose	negative
Ketones	negative
Leukocyte esterase	negative
Nitrites	negative

The patient is admitted to the hospital for further management. Which of the following complications of the underlying disease is he most likely to develop?

- A. Hemolytic anemia [31%]
- ✔ B. Intussusception [41%]
- C. Joint destruction [12%]
- D. Urethritis [4%]
- E. Uveitis [8%]
- F. Volvulus [1%]

Henoch-Schönlein purpura	
Pathogenesis	• IgA-mediated leukocytoclastic vasculitis
Clinical manifestations	• Palpable purpura • Arthritis/arthralgia • Abdominal pain, intussusception • Renal disease similar to IgA nephropathy
Laboratory findings	• Normal platelet count & coagulation studies • Normal to ↑ creatinine • Hematuria ± RBC casts ± proteinuria
Treatment	• Supportive (hydration & NSAIDs) for most patients • Hospitalization & systemic glucocorticoids in patients with severe symptoms

NSAIDs = nonsteroidal anti-inflammatory drugs; **RBC** = red blood cell.

Henoch-Schönlein purpura (HSP) is an IgA-mediated vasculitis that occurs most commonly in children during the fall, winter, and spring months. Classic manifestations include **palpable purpura** on the lower extremities, **abdominal pain**, **arthralgia/arthritis**, and renal disease (**hematuria** ± proteinuria). Symptoms are often preceded by a mild upper respiratory tract infection, as seen in this child.

Although the majority of patients with HSP develop colicky abdominal pain due to localized bowel wall

Although the majority of patients with HSP develop colicky abdominal pain due to localized bowel wall inflammation, the presence of severe abdominal pain should prompt further workup for complications such as gastrointestinal (GI) hemorrhage, bowel perforation, or intussusception.

Intussusception is the most common GI complication, as **intestinal edema** and **bleeding** associated with HSP act as a lead point for the intestines to telescope into the adjacent bowel. In contrast to most idiopathic intussusception in children, which is typically ileocolic, intussusception in HSP is usually confined to the small bowel (ileoileal). Presentation typically involves severe, episodic abdominal pain and "**currant jelly**" or **bloody stools**; the presence of a **"target" sign on ultrasound** is diagnostic. Although ileocolic intussusceptions are treated with air or contrast enema, ileoileal intussusceptions that do not reduce spontaneously often require surgical management.

(Choice A) Hemolytic anemia may occur in patients with systemic lupus erythematosus. Although this disease causes rash, arthralgia/arthritis, and renal disease, skin manifestations typically include a malar or discoid rash rather than palpable purpura on the buttocks.

(Choice C) Septic arthritis, which presents with fever and joint pain/swelling, can result in joint destruction if left untreated. In contrast, arthritis associated with HSP is self-limiting and does not cause long-term joint damage.

(Choice D) Urethritis occurs with reactive arthritis, which presents with joint swelling and is typically preceded by an enteric infection (eg, *Campylobacter*, *Shigella*) causing diarrhea rather than an upper respiratory illness.

(Choice E) Uveitis is a complication of juvenile idiopathic arthritis, which typically presents with chronic joint swelling, often involving multiple joints. This patient with joint pain but no swelling has arthralgia, not arthritis.

causes rash, arthralgia/arthritis, and renal disease; skin manifestations typically include a malar or discoid rash rather than palpable purpura on the buttocks.

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(Choice D) Urethritis occurs with reactive arthritis, which presents with joint swelling and is typically preceded by an enteric infection (eg, *Campylobacter*, *Shigella*) causing diarrhea rather than an upper respiratory illness.

(Choice E) Uveitis is a complication of juvenile idiopathic arthritis, which typically presents with chronic joint swelling, often involving multiple joints. This patient with joint pain but no swelling has arthralgia, not arthritis.

(Choice F) Volvulus, or intestinal malrotation, presents with abdominal pain, distension, and vomiting (often bilious). A nonblanching rash and arthralgia are not associated, and volvulus is not a typical complication of HSP.

Educational objective:
Henoch-Schönlein purpura (HSP) is an IgA-mediated vasculitis that presents most commonly in children with palpable purpura, abdominal pain, arthralgia/arthritis, and hematuria. Children with HSP are at increased risk for ileoileal intussusception due to intestinal edema and bleeding.

References

- Henoch-Schönlein purpura from vasculitis to intestinal perforation: a case report and literature review.
- Henoch-Schönlein purpura.

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act as a lead point for the intestines to telescope into the adjacent bowel. In contrast to most idiopathic

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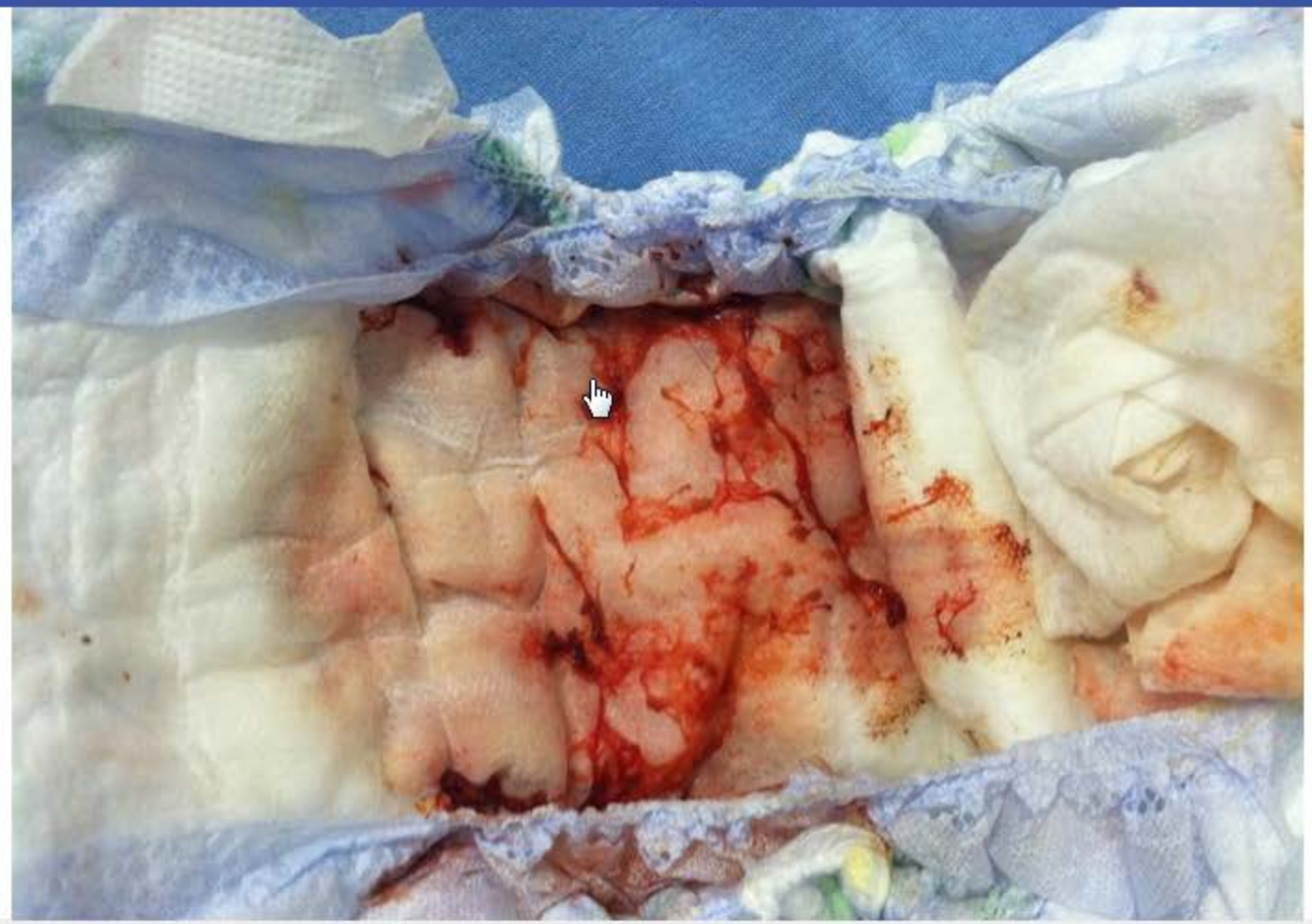

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Henoch-Schönlein purpura (HSP) is an IgA mediated vasculitis that presents most commonly in children with

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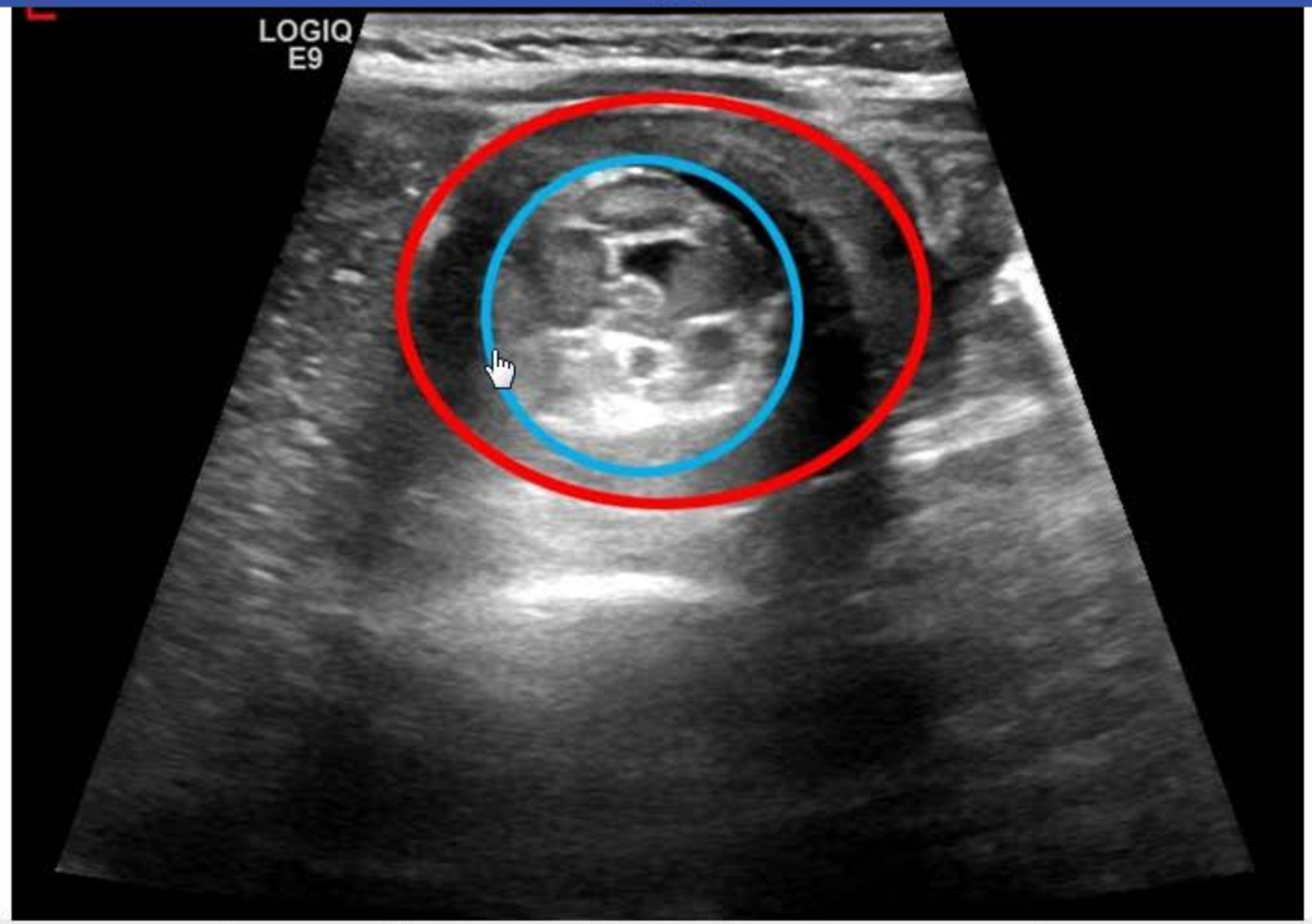

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Henoch-Schönlein purpura (HSP) is an IgA mediated vasculitis that presents most commonly in children with

A 15-year-old girl is brought to the office for evaluation of primary amenorrhea. The patient's mother and older sisters underwent menarche around age 13. The patient has had no changes in weight or nipple discharge but has difficulty identifying various odors. She has no known medical conditions and has had no surgery. The patient takes no daily medications and does not use tobacco, alcohol, or illicit drugs. She is not sexually active. Height is at the 3rd percentile for age, with 4.8 cm (1.9 in) of growth noted in the last year. Visual fields are intact. No breast tissue is present, and there is no axillary or pubic hair. Ultrasound confirms the presence of a uterus and 2 normal-appearing ovaries. Serum FSH level is 2 mU/mL (normal: 4-30 mU/mL) and LH is 3 mU/mL (normal: 5-25 mU/mL). Karyotype analysis of this patient is most likely to show which of the following?

- A. 45,XO
- B. 46,XX
- C. 46,XY
- D. 47,XXX
- E. 47,XXY

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A 15-year-old girl is brought to the office for evaluation of primary amenorrhea. The patient's mother and older sisters underwent menarche around age 13. The patient has had no changes in weight or nipple discharge but has difficulty identifying various odors. She has no known medical conditions and has had no surgery. The patient takes no daily medications and does not use tobacco, alcohol, or illicit drugs. She is not sexually active. Height is at the 3rd percentile for age, with 4.8 cm (1.9 in) of growth noted in the last year. Visual fields are intact. No breast tissue is present, and there is no axillary or pubic hair. Ultrasound confirms the presence of a uterus and 2 normal-appearing ovaries. Serum FSH level is 2 mU/mL (normal: 4-30 mU/mL) and LH is 3 mU/mL (normal: 5-25 mU/mL). Karyotype analysis of this patient is most likely to show which of the following?

- ✗ A. 45,XO [13%]
- ✓ B. 46,XX [69%]
- C. 46,XY [6%]
- D. 47,XXX [4%]
- E. 47,XXY [6%]

Incorrect
Correct answer
B

69%
Answered correctly

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06/08/2018
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Kallmann syndrome

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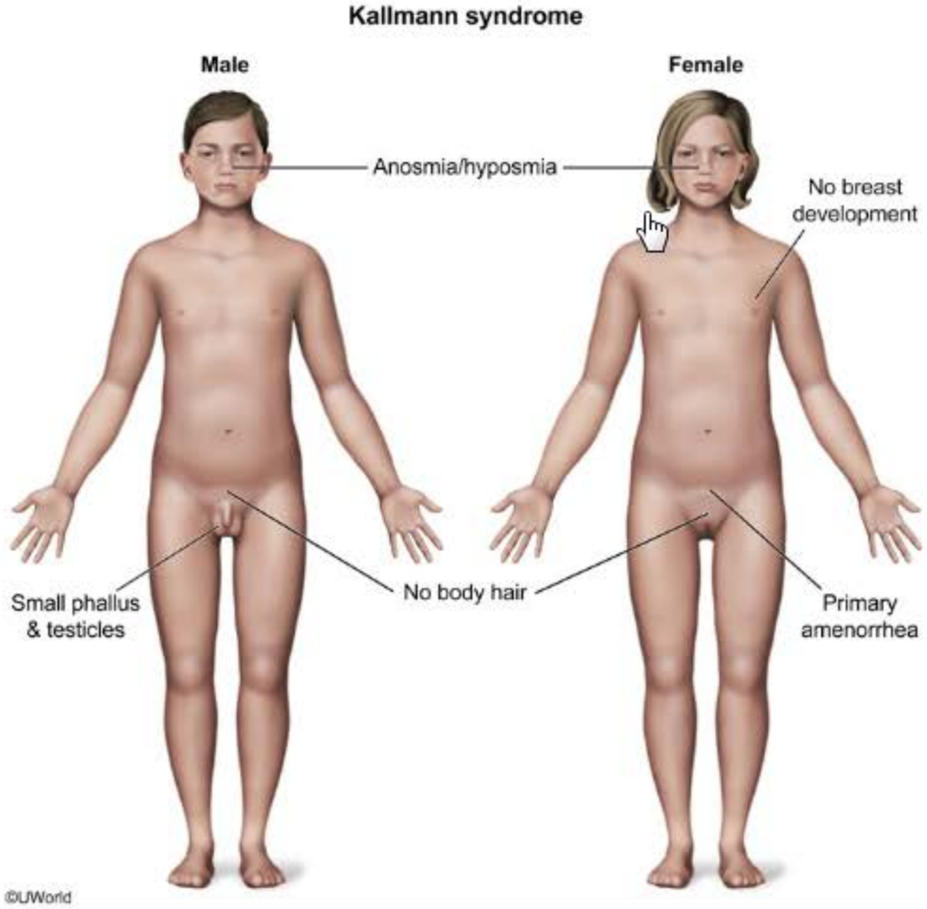

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Delayed puberty is diagnosed based on the lack of secondary sexual characteristics in girls age ≥12. This patient's pubertal delay and **anosmia** (ie, inability to distinguish odors) are suggestive of **Kallmann syndrome**, a disorder of migration of fetal olfactory and GnRH-producing neurons, resulting in rhinencephalon hypoplasia and **hypogonadotropic hypogonadism**. Most cases are X-linked recessive; however, girls can be affected via sporadic, autosomal dominant, and autosomal recessive mutations.

Due to the lack of GnRH production and release from the hypothalamus, the pituitary does not release gonadotropins; therefore, patients have **low FSH and LH levels**. The low gonadotropin levels do not stimulate the ovary to produce estrogen; therefore, girls have short stature, primary amenorrhea, and no breast development. Boys and girls have a **karyotype/genotype consistent with phenotype** (**46,XX** in this girl) and normal internal reproductive organs. Management of these patients includes facilitating development of secondary sexual characteristics in adolescents and improving fertility in adults.

(Choice A) Patients with Turner syndrome (45,XO) are phenotypically female and may present with delayed puberty (eg, short stature, no breast development, amenorrhea). However, due to gonadal dysgenesis and resultant primary ovarian insufficiency, patients have hypergonadotropic hypogonadism (elevated FSH and LH).

(Choice C) Patients with androgen insensitivity syndrome (AIS) or 5-alpha-reductase deficiency are genotypic males (46,XY) who present as phenotypic females. Patients with AIS have breast development but no pubic and axillary hair. Patients with 5-α-reductase deficiency have virilization (eg, clitoromegaly) at puberty and no breast development. In both cases, patients have primary amenorrhea (no uterus) but normal to high FSH and LH levels.

(Choice D) Patients with a 47,XXX genotype typically have normal secondary sexual characteristic development

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resultant primary ovarian insufficiency; patients have hypergonadotropic hypogonadism (elevated FSH and LH).

(Choice C) Patients with androgen insensitivity syndrome (AIS) or 5-alpha-reductase deficiency are genotypic males (46,XY) who present as phenotypic females. Patients with AIS have breast development but no pubic and axillary hair. Patients with 5-α-reductase deficiency have virilization (eg, clitoromegaly) at puberty and no breast development. In both cases, patients have primary amenorrhea (no uterus) but normal to high FSH and LH levels.

(Choice D) Patients with a 47,XXX genotype typically have normal secondary sexual characteristic development and tall stature. FSH and LH levels are normal.

(Choice E) Patients with **Klinefelter syndrome** (47,XXY) are phenotypically male and present with hypergonadotropic hypogonadism (elevated FSH and LH) due to testicular damage during development.

Educational objective:

Kallmann syndrome is a disorder of migration of fetal GnRH and olfactory neurons that results in delayed puberty (ie, primary amenorrhea) and anosmia. Due to the lack of GnRH secretion, patients have hypogonadotropic hypogonadism (low FSH). In these patients, karyotype (genotype) is consistent with phenotype.

References

- Isolated gonadotropin-releasing hormone (GnRH) deficiency.
- Kallmann syndrome: phenotype and genotype of hypogonadotropic hypogonadism.

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Item 12 of 15
Question Id: 3912

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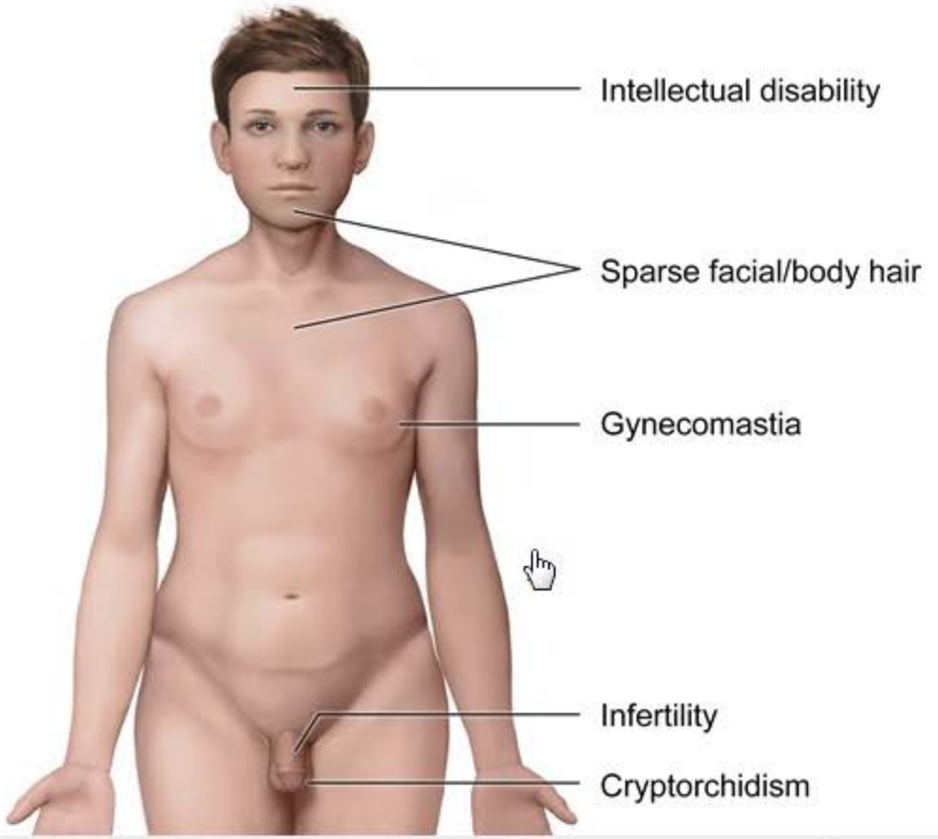
Klinefelter syndrome (47,XXY)



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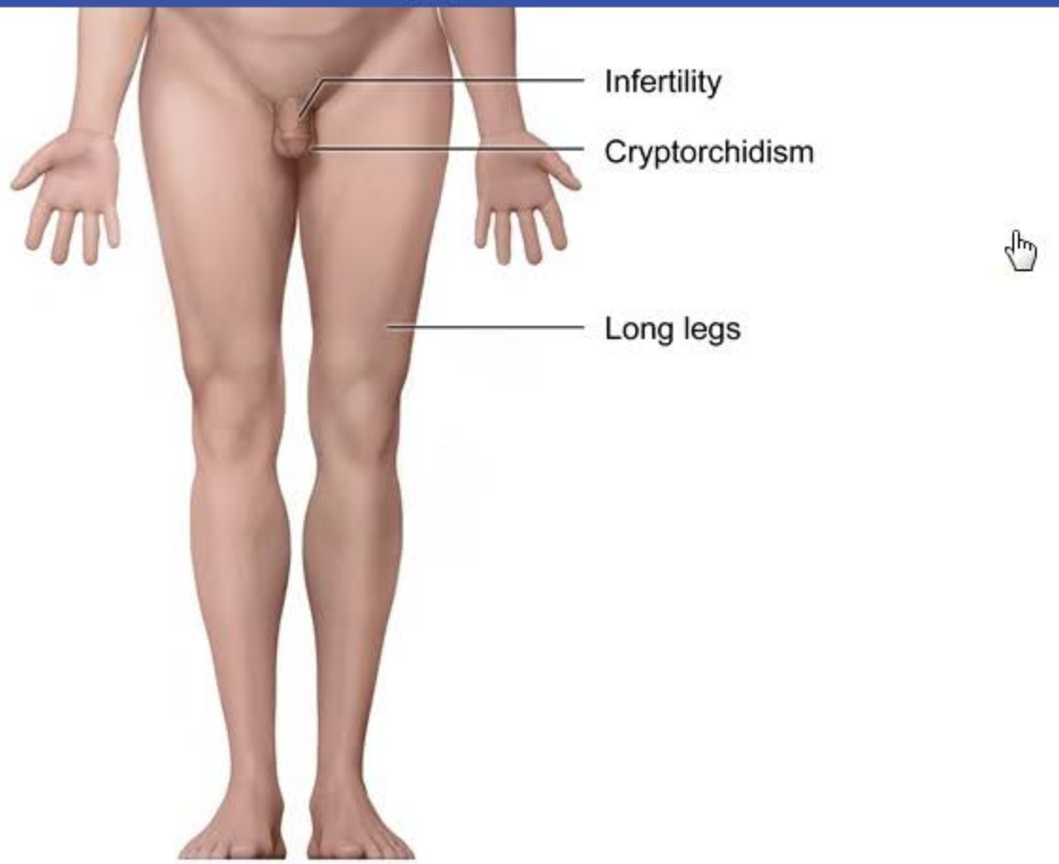

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A 6-year-old girl is brought to the office due to pallor and decreased energy. Ten days ago, the patient developed fever, emesis, and bloody diarrhea, and these symptoms resolved after a few days. However, over the past 2 days she has been less active, uninterested in playing, and sleeping throughout the day. She has no chronic medical conditions. Her older sister had a sore throat a few days ago, but no other family members have been ill. Temperature is 37.1 C (98.8 F), blood pressure is 120/70 mm Hg, and pulse is 134/min. Physical examination shows a pale, tired-appearing girl. Cardiac examination reveals tachycardia; there are no rubs or murmurs. The lungs are clear to auscultation bilaterally. The abdomen is soft, nontender, and nondistended; bowel sounds are normal. Laboratory results are as follows:

Complete blood count	
Hemoglobin	6.4 g/dL
Platelets	45,000/mm^3
Leukocytes	15,200/mm^3
Serum chemistry	
Creatinine	2.4 mg/dL
Liver function studies	
Total bilirubin	3.3 mg/dL

Total bilirubin	3.3 mg/dL
Direct bilirubin	0.1 mg/dL

Urinalysis

Specific gravity	1.025
Protein	+2
Blood	moderate
Leukocyte esterase	negative
Nitrites	negative
Red blood cells	20-30/hpf

Which of the following is the most likely diagnosis in this patient?

A. Acute lymphocytic leukemia
B. Glucose-6-phosphate dehydrogenase deficiency
C. Hemolytic uremic syndrome
D. Immune thrombocytopenic purpura
E. Poststreptococcal glomerulonephritis

Specific gravity	1.025
Protein	+2
Blood	moderate
Leukocyte esterase	negative
Nitrites	negative
Red blood cells	20-30/hpf

Which of the following is the most likely diagnosis in this patient?

- A. Acute lymphocytic leukemia [1%]
- ✗ B. Glucose-6-phosphate dehydrogenase deficiency [0%]
- ✓ C. Hemolytic uremic syndrome [88%]
- D. Immune thrombocytopenic purpura [3%]
- E. Poststreptococcal glomerulonephritis [5%]

Incorrect
Correct answer

88%
Answered correctly

17 Seconds
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09/29/2018
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Hemolytic uremic syndrome	
Pathogenesis	• Initial insult from Shiga toxin (*Escherichia coli* serotype O157:H7) • Vascular damage & microthrombi formation
Clinical features	• Preceding bloody diarrhea • Fatigue, pallor • Bruising, petechiae • Oliguria, edema
Laboratory findings	• Hemolytic anemia (schistocytes, ↑ bilirubin) • Thrombocytopenia • Acute kidney injury (↑ BUN, ↑ creatinine)
Treatment	• Fluid & electrolyte management • Blood transfusions • Dialysis

BUN = blood urea nitrogen.

This patient's presentation is consistent with **hemolytic uremic syndrome** (HUS), which is characterized by the triad of **hemolytic anemia**, thrombocytopenia, and acute kidney injury. Most commonly seen in children, HUS usually occurs due to Shiga toxin-producing diarrheogenic pathogens such as *Escherichia coli* O157:H7 or *Shigella*.

Children with HUS often have fatigue and pallor following resolution of a bloody diarrheal illness. Fever is uncommon at the time of presentation. Laboratory findings include **thrombocytopenia** and anemia with evidence of microangiopathic hemolysis (eg, elevated indirect bilirubin, schistocytes). **Renal injury** is evident by elevated creatinine and may present with hematuria, proteinuria, oliguria/anuria, and secondary hypertension.

Management of HUS is **supportive**, including correction of fluid/electrolyte disturbances and management of hypertension. Profound anemia (hemoglobin <6 g/dL) requires transfusion, and dialysis is indicated for severe kidney injury (eg, anuria). Most patients improve within 2-3 weeks.

(Choice A) Acute lymphocytic leukemia frequently presents with leukocytosis, anemia, and thrombocytopenia. Patients with acute lymphoblastic leukemia do not typically present with acute kidney injury, and physical examination usually reveals hepatosplenomegaly and lymphadenopathy due to extramedullary leukemic infiltration.

(Choice B) Glucose-6-phosphate dehydrogenase deficiency often presents as an acute hemolytic anemia following exposure to oxidative stress (eg, sulfa drugs, infection). It does not cause thrombocytopenia or acute kidney injury, which are seen in this patient.

(Choice D) Immune thrombocytopenic purpura presents with isolated thrombocytopenia often after a viral infection. Anemia and acute kidney injury are not seen.

(Choice E) Poststreptococcal glomerulonephritis may also present with hematuria, hypertension, and acute kidney injury. Thrombocytopenia and anemia are atypical, and preceding symptoms include a group A streptococcal skin or throat infection, not bloody diarrhea.

Educational objective:

(Choice B) Glucose-6-phosphate dehydrogenase deficiency often presents as an acute hemolytic anemia following exposure to oxidative stress (eg, sulfa drugs, infection). It does not cause thrombocytopenia or acute kidney injury, which are seen in this patient.

(Choice D) Immune thrombocytopenic purpura presents with isolated thrombocytopenia often after a viral infection. Anemia and acute kidney injury are not seen.

(Choice E) Poststreptococcal glomerulonephritis may also present with hematuria, hypertension, and acute kidney injury. Thrombocytopenia and anemia are atypical, and preceding symptoms include a group A streptococcal skin or throat infection, not bloody diarrhea.

Educational objective:
Hemolytic uremic syndrome is characterized by the triad of hemolytic anemia, thrombocytopenia, and acute kidney injury. Presentation typically occurs after resolution of prodromal bloody diarrhea caused by *Escherichia coli* O157:H7 or *Shigella*.

References

- HUS and TTP in children.
- Shiga toxins and the pathophysiology of hemolytic uremic syndrome in humans and animals.

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A 14-year-old girl is brought to the clinic for a routine well-child visit. The girl has been healthy and her only concern is that she has not yet had a menstrual period. Most of her friends have undergone menarche, and she wants to know when she will start menstruating. She wears corrective glasses for myopia. Her father is 190.5 cm (6 ft 3 in) tall, and her mother is 183 cm (6 ft) tall. On examination, the patient's height and weight are at the 5th and 55th percentiles, respectively. Blood pressure is 140/90 mm Hg in the right upper arm and 90/40 mm Hg in the lower extremities. Multiple pigmented nevi are scattered on the face and chest. Which of the following complications is this patient most at risk of developing?

- A. Chronic constipation
- B. Endometrial hyperplasia
- C. Intellectual disability
- D. Mitral valve prolapse
- E. Osteoporotic fracture
- F. Visual field defects

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Item 14 of 15
Question Id: 4765

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A 14-year-old girl is brought to the clinic for a routine well-child visit. The girl has been healthy and her only concern is that she has not yet had a menstrual period. Most of her friends have undergone menarche, and she wants to know when she will start menstruating. She wears corrective glasses for myopia. Her father is 190.5 cm (6 ft 3 in) tall, and her mother is 183 cm (6 ft) tall. On examination, the patient's height and weight are at the 5th and 55th percentiles, respectively. Blood pressure is 140/90 mm Hg in the right upper arm and 90/40 mm Hg in the lower extremities. Multiple pigmented nevi are scattered on the face and chest. Which of the following complications is this patient most at risk of developing?

- A. Chronic constipation [1%]
- ✗ B. Endometrial hyperplasia [4%]
- C. Intellectual disability [8%]
- D. Mitral valve prolapse [20%]
- ✓ E. Osteoporotic fracture [58%]
- F. Visual field defects [6%]

Incorrect
Correct answer
E

58%
Answered correctly

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11/01/2018
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This patient's **short stature**, signs of **aortic coarctation** (blood pressure differential), and absent menarche are most likely due to **Turner syndrome** (TS), a chromosomal abnormality caused by complete or partial loss of an X chromosome (**45,X karyotype**).

Patients with TS typically have **ovarian dysgenesis**, leading to "streak ovaries" (small ovaries with little to no follicles) and primary ovarian insufficiency. Because ovaries normally produce estrogen, patients with TS are **estrogen deficient**, which leads to **amenorrhea** and minimal or no breast development (thelarche). Estrogen also inhibits osteoclast-mediated bone resorption; therefore, patients with TS have increased bone resorption, decreased bone mineral density, and increased risk of **osteoporotic fracture**. Estrogen replacement therapy is given to girls with TS to promote normal sexual maturation and reduce the risk of osteoporotic fractures.

(Choice A) Chronic constipation is common in patients with hypothyroidism. Although hypothyroidism can cause delayed menstruation and hypertension, there is no associated blood pressure differential (ie, no associated aortic coarctation).

(Choice B) Patients with polycystic ovarian syndrome (PCOS) have high, unopposed estrogen levels that increase the risk of endometrial hyperplasia. Patients with PCOS can have amenorrhea due to anovulation; however, they are typically post-menarche and have associated hirsutism and obesity. The low estrogen levels in TS are likely protective against endometrial hyperplasia.

(Choice C) Most patients with TS have normal cognitive abilities. However, there is an increased risk of impaired nonverbal skills (eg, mathematics), attention-deficit hyperactivity disorder, and problems with executive functioning.

(Choice D) Mitral valve prolapse is more common in patients with connective tissue disorders (eg, Marfan

TS are likely protective against endometrial hyperplasia.

(Choice C) Most patients with TS have normal cognitive abilities. However, there is an increased risk of impaired nonverbal skills (eg, mathematics), attention-deficit hyperactivity disorder, and problems with executive functioning.

(Choice D) Mitral valve prolapse is more common in patients with connective tissue disorders (eg, Marfan syndrome). Patients do not have menstrual abnormalities and typically have tall stature.

(Choice F) Visual field defects (eg, bitemporal hemianopsia) can occur with a prolactinoma compressing the optic chiasm. Excess prolactin causes galactorrhea and suppresses GnRH, resulting in amenorrhea; however, prolactinomas are not associated with aortic coarctation.

Educational objective:
Short stature, amenorrhea, and aortic coarctation are features of Turner syndrome. Patients are at increased risk of osteoporotic fracture due to estrogen deficiency from ovarian dysgenesis.

References

- Effect of estrogen replacement therapy on bone and cardiovascular outcomes in women with Turner syndrome: a systematic review and meta-analysis.
- Bone health in children and adolescent with Turner syndrome.

An 11-year-old boy is brought to the physician for evaluation of scoliosis. His mother noticed that he always seems to be leaning even when he tries to sit or stand upright. The boy has a history of myopia and upward lens dislocation for which he wears corrective glasses. He otherwise has been healthy and doing well in school. His father had scoliosis and vision problems and died from "heart problems" last year. Physical examination shows a boy with a long face, high arched palate with crowded teeth, and upward dislocation of the lens. He has a tall stature for his age; long arms and legs with minimal subcutaneous fat; long, thin fingers; and a prominent sternum. Joint hypermobility, skin hyperelasticity, and 15 degrees of thoracic scoliosis are seen. A diastolic murmur is heard in the aortic area. Which of the following is the most likely etiology of this patient's condition?

- A. Cystathionine synthase deficiency
- B. Defective collagen production
- C. Mutation of the fibrillin-1 gene
- D. Mutation of the fibrillin-2 gene
- E. Nondisjunction resulting in an extra X chromosome

Submit

An 11-year-old boy is brought to the physician for evaluation of scoliosis. His mother noticed that he always seems to be leaning even when he tries to sit or stand upright. The boy has a history of myopia and upward lens dislocation for which he wears corrective glasses. He otherwise has been healthy and doing well in school. His father had scoliosis and vision problems and died from "heart problems" last year. Physical examination shows a boy with a long face, high arched palate with crowded teeth, and upward dislocation of the lens. He has a tall stature for his age; long arms and legs with minimal subcutaneous fat; long, thin fingers; and a prominent sternum. Joint hypermobility, skin hyperelasticity, and 15 degrees of thoracic scoliosis are seen. A diastolic murmur is heard in the aortic area. Which of the following is the most likely etiology of this patient's condition?

- A. Cystathionine synthase deficiency [3%]
- ✗ B. Defective collagen production [11%]
- ✓ C. Mutation of the fibrillin-1 gene [80%]
- D. Mutation of the fibrillin-2 gene [3%]
- E. Nondisjunction resulting in an extra X chromosome [0%]

Incorrect
Correct answer
C

80%
Answered correctly

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07/10/2018
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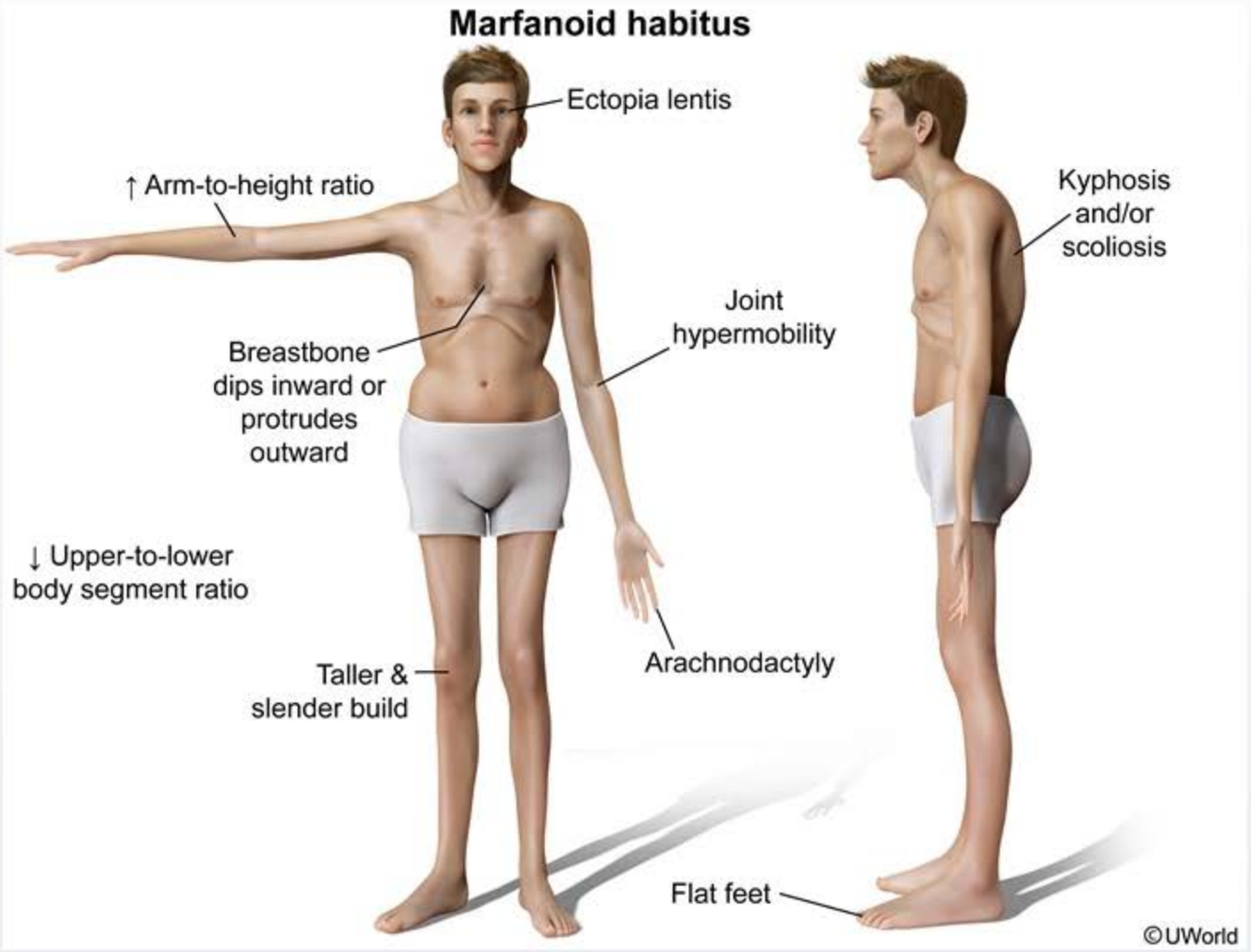

This patient's family history and physical appearance are very characteristic of Marfan syndrome. Marfan

This patient's family history and physical appearance are very characteristic of Marfan syndrome. Marfan syndrome is an autosomal dominant disorder of the fibrillin-1 gene that results in systemic weakening of connective tissue. Classic skeletal manifestations include **joint hypermobility**, skin hyperelasticity, long fingers (**arachnodactyly** ["thumb sign"]), **pectus excavatum**, and **scoliosis/kyphosis**. The face is long, the palate has a high arch, and the teeth are crowded. **Lens dislocation** (ectopia lentis), iridodonesis (a rapid contraction and dilation of the iris), and myopia (from elongation of the globe) are also typical.

The most life-threatening finding in Marfan syndrome is aortic root dilation. The diastolic murmur in this patient reflects **aortic regurgitation**. The syndrome requires close monitoring with echocardiography for the development of **aneurysms** and **aortic arch dissection**. Mitral valve prolapse is also common and manifests as a mid-systolic click and late systolic murmur. First-degree relatives should undergo genetic testing.

(Choice A) Homocystinuria is an autosomal recessive disorder that results from deficiency of cystathionine synthase, an enzyme involved in the metabolism of methionine. These patients share many features of Marfan syndrome (eg, pectus deformity, tall stature, arachnodactyly). However, they usually have a fair complexion, thromboembolic events, and intellectual disability. The other main differentiating feature is lens dislocation in homocystinuria that is downward rather than upward.

(Choice B) Ehlers-Danlos syndrome is a collagen disorder characterized by scoliosis, joint laxity, and aortic dilation. Patients with this disorder do not have the disproportionately tall stature, lens dislocation, or pectus carinatum seen in Marfan syndrome.

(Choice D) Congenital contractural arachnodactyly is an autosomal dominant condition resulting from mutations of

synthase, an enzyme involved in the metabolism of methionine. These patients share many features of Marfan syndrome (eg, pectus deformity, tall stature, arachnodactyly). However, they usually have a fair complexion, thromboembolic events, and intellectual disability. The other main differentiating feature is lens dislocation in homocystinuria that is downward rather than upward.

(Choice B) Ehlers-Danlos syndrome is a collagen disorder characterized by scoliosis, joint laxity, and aortic dilation. Patients with this disorder do not have the disproportionately tall stature, lens dislocation, or pectus carinatum seen in Marfan syndrome.

(Choice D) Congenital contractural arachnodactyly is an autosomal dominant condition resulting from mutations of the fibrillin-2 gene. These patients have tall stature, arachnodactyly, and multiple contractures involving large joints. Ocular and cardiovascular symptoms are not present in congenital contractural arachnodactyly. In addition, patients with Marfan syndrome do not have joint contractures.

(Choice E) A tall and slender stature, but not connective tissue problems, is seen in Klinefelter syndrome.

Educational objective:
Marfan syndrome is an autosomal dominant disorder that results from mutations of the fibrillin-1 gene. Affected patients have tall stature; long, thin extremities; arachnodactyly; joint hypermobility; upward lens dislocation; and aortic root dilation.

References

- Health supervision for children with Marfan syndrome.

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15

syndrome is an autosomal dominant disorder of the fibrillin-1 gene that results in systemic weakening of connective

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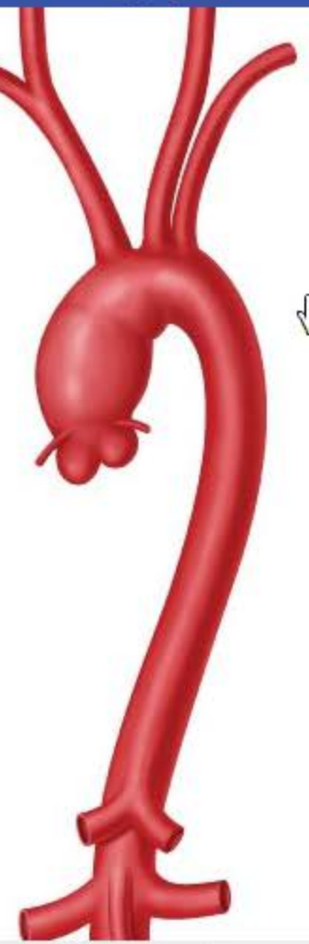

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