



NBME EXPLANATIONS

NBME 22 Block 1

from CrackNBME

22-Block 1

Q1

A 49-year-old man comes to the physician because of increasingly severe pain in his left hip during the past 2 months. He was recently discharged from a rehabilitation facility for treatment of alcoholism. He says, "The pain gets so bad at times that it even hurts my golf game." He has pain with weight bearing. Physical examination shows limited active and passive range of motion of the left hip. Hip x-rays show no abnormalities. A coronal T1-weighted MRI is shown. Which of the following is the most likely cause of this patient's pain?



- A. Avascular necrosis
- B. Hyperparathyroidism
- C. Osteitis deformans
- D. Septic arthritis
- E. Tuberculous osteomyelitis

▼ Explanation

• Answer is A (Avascular Necrosis)

◦ IMP Clues:

- Severe pain in his left hip (could be neuro, vascular, ortho...)
- Discharged from rehab facility for treatment of alcoholism (Important risk factor)
- Limited active & passive range of motion (if both active & passive are affected, this is not muscular etiology)
- X-ray shows no abnormalities (excludes choice B, C, and E)
- MRI shows head of femur crescent sign

◦ Dx → Femoral Head Avascular Necrosis

- Most common site is **head of femur**
 - Other common sites include **scaphoid bone [asked on NBME]** & **humeral head**
- **HY USMLE Etiologies:**
 - **Alcoholism**
 - **Corticosteroids**
 - **Trauma/Fractures**
 - **Sickle Cell Anemia**
 - **Gaucher's Disease**
 - SLE
- Presentation: **Chronic Progressive severe** pain with limitation in **both active & passive** range of motion

USMLE can be assholes and ask for disrupted nerve in cases of femoral head avascular necrosis

- Answer is **Medial Femoral Circumflex artery**

▪ Investigations:

- X-Ray: **normal** early
- **MRI: most sensitive (crescent sign: Dark on T1, Bright on T2)**

▼ Other Choices

• Choice B → Hyperparathyroidism

- Primary: **90% of the time is caused by a parathyroid adenoma**, while the remaining 10% is due to hyperplasia or tumor.
- Secondary: Due to Renal Failure, which causes hyperphosphatemia.

- Hyperparathyroidism would cause **Osteolytic lesions on X-ray**

- **Choice C → Paget's Disease (Osteitis deformans)**

- **Abnormal bone remodeling disorder** characterized by following 3 phases:
 1. **Lytic Phase** (*Increased* number & activity of **osteoclasts** = *increased* bone resorption)
 2. **Mixed Phase** (*Increased* activity of **osteoblast & osteoblasts** = **Woven hypervascularity bone** ⇒ **Mosaic pattern** "woven + lamellar bone")
 3. **Sclerotic Phase** (**Decreased** Osteoclast & Osteoblast activity)
- As a result of the disorganized bone remodeling, patients experience **bone pain**, **skull enlargement**, and the USMLE favorite **tinnitus** (due to involvement of the ossicles)
- Characterized by **HIGH ALP activity with all remaining labs found to be NORMAL**
- USMLE loves to give you the XRAY descriptions of **"Picture-Frame Vertebra"**, **"Mixed osteosclerotic and osteolytic areas"**, or **"Cortical thickening of vertebral endplates"**.
- HY Complications on the USMLE are **High-Output Heart Failure** (due to AV-Shunting in bone) & **Osteosarcoma**.



Paget Disease Presentations on the USMLE:

1. They give you a 55M + bone pain + high ALP+ normal calcium & phosphate.
 - a. Ask for Dx ⇒ **"Paget Disease"** or **"Osteitis Deformans"**
 - b. Ask for cause of shortness of breath ⇒ **"High Cardiac Output"** or **"high-output HF"** or **"AV Fistula"**
2. They give you an elderly patient with a hat that doesn't fit him anymore + tinnitus
 - a. Ask for Expected Labs ⇒ **HIGH** ALP + normal Calcium + normal Phosphate
 - b. Ask for Diagnosis ⇒ **"Paget Disease"** or **"Osteitis Deformans"**
 - c. Ask for expected bone complication ⇒ **Osteosarcoma**

- **Choice D → Septic Arthritis** presents as **ACUTE ONSET** severe pain + **fever** + **red swollen hot joint** (usually knee).

- **ASPIRATION IS DONE IMMEDIATELY. IT IS A MEDICAL EMERGENCY**

- **Choice E →** Usually affects the spine (**Pott's Disease**)

- **Osteolytic lesions that destroy intravertebral discs.**
- Hx of TB or Triad of night sweats, weight loss, and fever.

Q2

A 16-year-old girl has pain and tingling in her left hand when she goes backpacking. The symptoms resolve 5 minutes after she takes off her backpack. Which of the following abnormalities is the most likely cause?

- A. C-7 to T-1 congenital fusion
- B. Cervical rib
- C. Diastematomyelia
- D. Hemivertebra
- E. Spina bifida occulta of C-7

▼ **Explanation**

- **Answer is B (Cervical Rib)**

- **IMP Clues:**
 - Pain & Tingling in her hand when she goes backpacking (hand nerve affection is C8-T1 nerves compression maybe?)
 - Pain resolves 5 mins after she takes off her backpack (this means that these symptoms are caused by the bag, the compression of the bag)

- **Dx → Thoracic Outlet Syndrome 2ry to a Cervical Rib**

- **Abnormal Cervical Rib** that is when compressed by the bag, compresses what's underneath it.
 - **What's Underneath it?**
 - **Lower Trunk of Brachial plexus** which supplies the **hands (C8-T1)**
- What's another HY cause of Thoracic Outlet Syndrome?

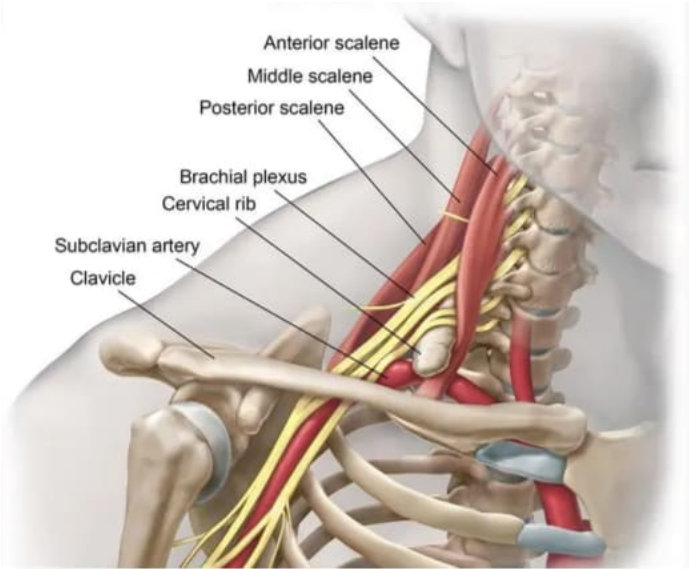
▪ **Anterior Scalene Muscle Hypertrophy**



Differential Diagnosis

Cervical Radiculopathy presents in the same way:

Feature	Cervical Disc Herniation	Foraminal Stenosis
Etiology	Herniated nucleus pulposus compressing nerve root	Narrowing of intervertebral foramen
Patient	Younger (20s–40s)	Older (>50)
Onset	Sudden (after trauma or activity)	Gradual , chronic neck arthritis history
Pain Increases with	Neck flexion or Valsalva	Neck extension or rotation to affected side
Pain Decreases with	Extension (opens disc space)	Flexion (opens foramina)
Imaging	MRI shows herniated disc impinging nerve	MRI shows narrowed spinal foramina



▼ **Other Choices**

- **Choice A** → presents as short neck with limited neck mobility since birth (LY)
- **Choice C** → Split spinal cord would present with progressive lower limb neurological deficits in a child (LY)
- **Choice D** → Hemivertebrae presents as congenital scoliosis with progressive back pain (LY)
- **Choice E** → usually asymptomatic + tuft of hair or dimple on skin overlying that area

Q3

A 48-year-old man comes to the physician because of fatigue, increasing shortness of breath on exertion, and decreased exercise tolerance over the past 4 months. An x-ray of the chest shows cardiac enlargement and prominent pulmonary vasculature. He is treated pharmacologically but subsequently develops glucose intolerance, evidence of liver dysfunction, and mild to moderate ascites. An older brother died at age 52 years with similar symptoms. Which of the following are the most important screening tests to perform on this patient and his family?

- A. Fasting serum gastrin and insulin measurements
- B. Hepatitis B and hepatitis C antibody assays
- C. HLA class I and class II typing
- D. Serum thyroid-stimulating hormone and thyroxine (T4) measurements
- E. Transferrin saturation and serum ferritin measurements

▼ **Explanation**

- **Answer is E (Transferrin saturation & serum ferritin measurement)**
 - **IMP Clues:**
 - Fatigue, increases SOB on exertion, and decreases exercise tolerance (okkk noted)
 - CXR shows cardiac enlargement & prominent pulmonary vasculature (cardiomegaly + pulmonary edema)
 - Develops glucose intolerance (pancreas also affected)
 - Liver dysfunction and ascites (liver also affected)
 - Older brother died at age 52 with similar symptoms (okay, so hereditary condition)
 - **Dx → Hemochromatosis**
 - **AR**; mutation of **HFE gene** on **chromosome 6** causing “increased intestinal iron absorption” [asked on NBME]
 - Increased Iron absorption causes increased iron deposition all over the body
 - Iron overload causes:
 - **Deposits in skin → Hyperpigmentation / Bronze skin**

USMLE loves giving you the below liver picture and asks for gene/mechanism/cause/complications:

- Deposition in liver → **Hepatitis & can progress to HCC**
- Deposits in tail of pancreas → **DM & hypoglycemia**
- Deposition in joints → **pseudogout (HY)**
- Deposition in heart → **Cardiomyopathy (Both dilated & restrictive cardiomyopathy)**
- Deposition in testes, pituitary, hypothalamus → **hypogonadism & infertility**

• Diagnosis:

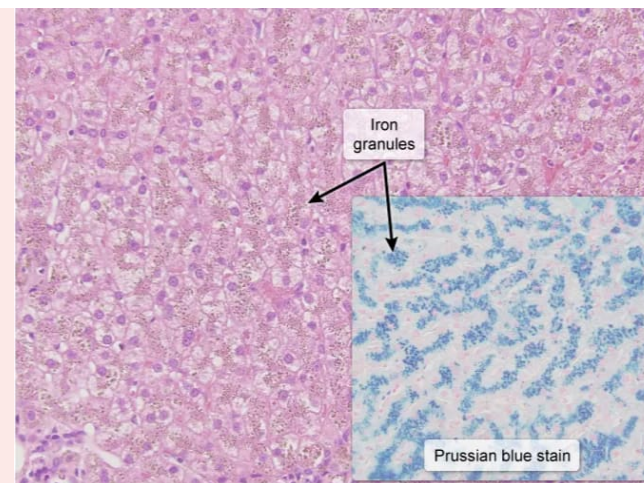
- **Ferritin** > 300 ng/dl
- **Transferrin** *decreased*

• Treatment:

- **Serial Phlebotomy**



Treatment of Secondary Hemochromatosis "Transfusion Siderosis" is *iron chelation therapy* (Deferoxamine)



- Gene → **HFE mutation**
- Mechanism → **Increased Intestinal Iron absorption**
- Cause → **Iron overload & deposition into hepatocytes**
- Complication → **Hepatitis/Cirrhosis/HCC**



Why does hemochromatosis appear earlier in men than women?

▼ **Answer**

Women are able to excrete iron by menstruation. Men don't menstruate. I hope.

▼ **Other Choices**

- **Choice A** → Serum gastrin screens for **Gastrinoma** (ZE syndrome) & Insulin for **Insulinoma**
 - **Gastrinoma** presents as **recurrent duodenal & jejunal ulcers resistant to treatment + diarrhea + abdominal pain**
 - **Insulinoma** presents as attacks of *severe hypoglycemia*
- **Choice B** → **HBV & HCV** assays for **viral hepatitis**, which is unlikely as they don't cause glucose intolerance nor cardiomyopathy. Also, his brother dying of the same symptoms hints that it is hereditary
- **Choice C** → used for autoimmune diseases screening.
- **Choice D** → TSH & T4 screens for *hypo or hyperthyroidism*. Irrelevant here.

Q4

A 32-year-old woman begins to hyperventilate and then develops blurred vision and numbness around her mouth after being told her best friend has suddenly died. Her pulse is 95/min and blood pressure is 120/80 mm Hg. Which of the following is most likely decreased in this woman?

- A. Arterial blood oxygen concentration
- B. Arterial blood PO₂
- C. Arterial pressure
- D. Cerebral blood flow
- E. Cerebral tissue pH

▼ **Explanation**

- **Answer is D (Cerebral Blood Flow)**
 - **IMP Clues:**
 - Hyperventilate + blurred vision + numbness around mouth after bad news (effects of hyperventilation)

- **Dx → Panic Attack**

- Panic Attacks cause **hyperventilation**
- Hyperventilation causes **increased washing-out of CO₂ = hypocapnia**:
 - **Brain Flow to decrease (vasoconstriction)** → Blurring of vision & dizziness
 - Less CO₂ causes **Respiratory Alkalosis** → less protons (H) bound to albumin → Calcium binds to albumin → less ionized (free) Calcium → **Hypocalcemia**
 - Hypocalcemia causes the **peri-oral numbness** in the vignette.
- 🧠 **Hypocalcemia can also cause Trousseau's sign & Chvostek's sign**
 - **Trousseau's sign** → Carpopedal spasm when BP is measured
 - **Chvostek's sign** → Facial twitching on percussion of facial nerve



? Patient had serious head trauma. The anesthesiologist mechanically ventilated the patient and set his RR to a high rate. What is the reasoning?

▼ **Answer**

To decreased Intracranial Pressure - Higher RR causes increased CO₂ washing, this causes cerebral vessels to constrict → less intracranial pressure.
The increased ICP can cause the brain to herniate, because of the edema caused by the head trauma.

▼ **Other Choices**

- **Choice A** → Arterial blood O₂ concentration would stay the same. O₂ Sat is usually maintained at 98-99%. The hemoglobin is already concentrated with as much O₂ as possible. More O₂ will do nothing extra.
- **Choice B** → Arterial PO₂ would increase. The amount of O₂ in plasma would increase. This will raise the arterial pressure of O₂ slightly.
- **Choice C** → Arterial Pressure would increase slightly. CO₂ causes vasodilation all over the body (except the lungs). Less CO₂ = more vasoconstriction = slightly higher BP.
- **Choice E** → pH would increase. Less CO₂ means alkalosis = Higher pH.

Q5

A 2-month-old boy is brought to the physician because of a 7-day history of hoarseness. His mother has AIDS and used cocaine throughout her pregnancy. Physical examination shows no abnormalities. A fiberoptic laryngoscopic examination shows a nodule on the left vocal cord. Which of the following viruses is the most likely cause of this nodule?

- A. Cytomegalovirus
- B. Herpes simplex virus
- C. HIV
- D. Human papillomavirus
- E. Varicella-zoster virus

▼ **Explanation**

- **Answer is D (Human Papillomavirus)**
 - **IMP Clues:**
 - Hoarseness (Vocal cords are affected)
 - Mother has AIDS & used cocaine in pregnancy (So plenty of infections expected to be transmitted to the poor baby)
 - Physical Examinations shows no abnormalities (excludes CMV & VZV)
 - Fiberoptic laryngoscopic examination shows a nodule on the left vocal cord (confirms the diagnosis)

- **Dx → Recurrent Respiratory Papillomatosis**
 - Caused by **HPV 6 & 11**
 - Acquired via **vertical transmission during vaginal delivery**
 - Child presents with **hoarseness, stridor, or life-threatening airway obstruction**
 - Diagnosis via **laryngoscopy**, showing **papilloma on the larynx / vocal cords**
- What would histological biopsy of a **skin wart** show?
 - **Papillary Architecture** (*Fibrovascular core* lined by thickened epithelium)
 - **Epidermal Thickening**
 - **Koilocytosis** (Irregular nucleus surrounded by *perinuclear vacuolization/halos*)



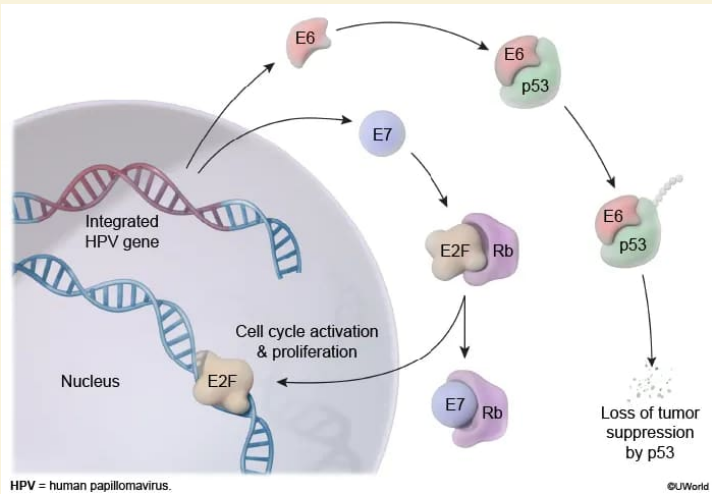
How does the papillae of HPV form?

E6 protein

- **Inactivation TP53** (tumor suppressor gene) via **Ubiquitin-mediated proteolysis**
 - **Decreased** apoptosis

E7 protein

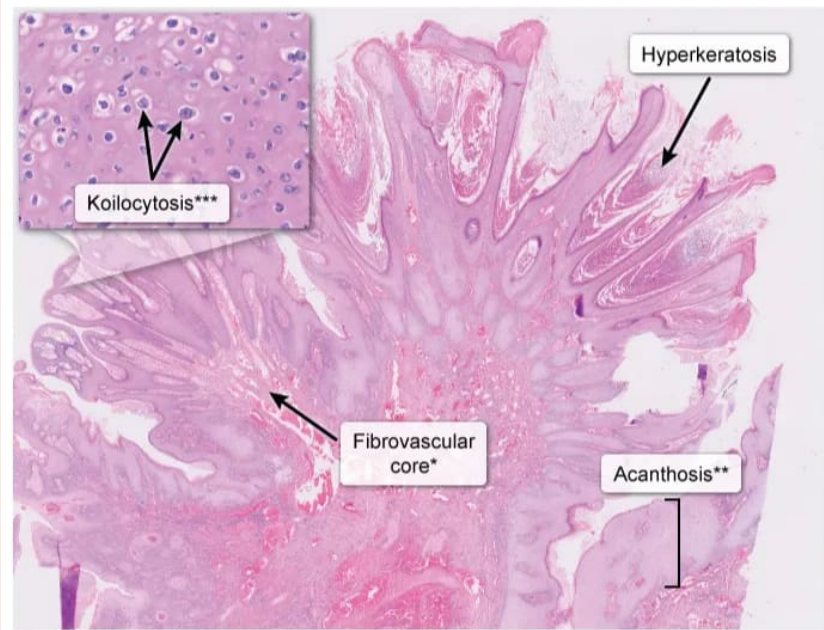
- **Increased phosphorylation of Rb**
 - Rb separates from EF-2 → EF-2 then causes **cell cycle activation & proliferation** (mitosis)



Laryngoscope findings below, showing multiple raspberry-shaped papillae all over vocal cords and larynx:



Histological Biopsy Findings:



▼ Other Choices

- **Choice A → Congenital CMV** features include **Microcephaly, Ventriculomegaly, SNHL, Periventricular Calcifications, and HSM, jaundice, and blueberry muffin rash.**
- **Choice B → Congenital HSV** is transmitted during vaginal birth. Can cause **keratoconjunctivitis, encephalitis, or even disseminated infection in severe cases.**
- **Choice C → HIV** makes the child have HIV too, so he will present with recurrent infections and failure to thrive.
- **Choice E → Congenital VZV** features include **cutaneous scaring in dermatomal distribution, limb hypoplasia,** cataracts, and microcephaly.

Q6

A 16-year-old girl is brought to the physician because of excessive dieting, constant studying, and social withdrawal during the past 3 weeks. She is 168 cm (5 ft 6 in) tall and weighs 48 kg (106 lb); BMI is 17 kg/m2. Her blood pressure is 95/66 mm Hg. Physical examination shows dry skin and fine hair growth. Laboratory studies show:

Serum	
Na+	138 mEq/L

Serum	
K+	2.2 mEq/L
Cl-	90 mEq/L
HCO3-	36 mEq/L
Urea nitrogen	25 mg/dL
Creatinine	1.2 mg/dL
Arterial blood gas analysis on room air	
pH	7.48
Pco2	48 mm Hg
Po2	97 mm Hg

This patient has most likely been abusing which of the following substances?

- A. Alcohol
- B. Amphetamines
- C. Diuretics
- D. Laxatives
- E. Thyroid hormone

▼ Explanation

- Answer is C (Diuretics)
 - IMP Clues
 - Blood Pressure is 95/66 mmHg (Hypotensive, so probably hypovolemic?)
 - Dry skin & Fine hair growth (electrolyte disturbances cause hypothyroidism-like state; this is also seen in eating disorders)
 - Low serum K (massive giveaway, what is infamous for cause hypokalemia? yes diuretics)
 - Low serum Cl (also, the combination of low K + low Cl getting excreted also hints at diuretics)
 - High HCO3 + High pH + high PCO2 (Metabolic alkalosis compensated by increase PCO2)
 - High Creatinine (Kidneys involved)
 - Dx → Loop Diuretics Abuse
 - Loops *inhibit the Na/K/2Cl transporter* on the *ascending loop of Henle*
 - Na & Cl excreted → Water follows = **Diuresis**
 - K is excreted → **Hypokalemia**
 - Diuresis = less blood volume = **Increased RAAS**
 - Increased AT-2 causes:
 1. **Vasoconstriction to increase Blood Pressure to balance hypovolemia**
 2. **Aldosterone production → Excretion of H & K and Reabsorption of Na**
 - Exacerbates Hypokalemia
 - Alkalosis
- This is why a side effect of diuretics is “Contraction Alkalosis”.

 - The “contraction” of blood volume causes compensatory mechanisms that results in “alkalosis”

▼ Other Choices

- Choice A → Alcohol abuse would cause CNS depression effects + Ataxia + Liver affection
- Choice B → Chronic amphetamines abuse would present as *loss of appetite* so *weight loss* & *pale mottled skin* due to severe prolonged VC (prolonged catecholamines stimulation)
- Choice D → Low K & Low HCO3 & Metabolic Acidosis
- Choice E → We would see palpitations, sweating, loss of weight, Dry Hot skin, increased activity, fast metabolism, and more. You know, classic Hyperthyroidism.

A 67-year-old woman comes to the physician because of a 1-year history of a nonproductive cough and progressive shortness of breath with exertion. She has not had fever or any other symptoms. She has no history of serious illness and takes no medications. She does not smoke. Vital signs are within normal limits. Pulse oximetry on room air shows an oxygen saturation of 92%. Fine, dry crackles are heard at both lung bases. Physical examination shows clubbing of the hands. There is no peripheral edema. A chest x-ray shows fine linear opacities in the lower third of the lungs bilaterally. A CT scan of the chest shows bibasilar interstitial reticulonodular markings with interlobular septal thickening. Pulmonary function tests show a normal FEV1, an FVC of 48% of predicted, and diffusion capacity of the lung for carbon monoxide of 55% of predicted. Which of the following is the most likely diagnosis?

- A. Allergic granulomatous angiitis (Churg-Strauss syndrome)
- B. Bronchoalveolar carcinoma
- C. Emphysema
- D. Idiopathic pulmonary fibrosis
- E. Lupus pneumonitis

▼ Explanation

• Answer is D (Idiopathic Pulmonary Fibrosis)

◦ IMP Clues:

- Non-productive cough & progressive SOB & no fever (probably a non-infection etiology)
- She doesn't smoke (Probably excludes cancer & COPD)
- CXR shows fine linear opacity bilaterally & CT scan shows interstitial reticulonodular markings with interlobular septal thickening (These phrases are so HY & buzzy for pulmonary fibrosis)
- PFTs show normal FEV1 & FVC of 48% (Restrictive pattern, normal expiratory flow with decreases capacity)
- DCLO 55% of predicted (diffusion across alveoli is affected)

• Dx → Idiopathic Pulmonary Fibrosis

◦ A type of **restrictive lung disease**

- (Normal FEV1, Low FVC, high/normal FEV1/FVC ratio)
- Low **DLCO** (alveoli-blood diffusion is affected because thickness of alveolar wall increased due to fibrosis)

◦ Symptoms: **Non-productive cough, progressive shortness of breath, fatigue, and clubbing**

◦ What causes the fibrosis? [asked on NBME]

- **Activation of macrophages + ROS damaging the epithelium + Cytokines (TGF- β) that activates fibroblasts & causes collagen deposition → Fibrosis**

◦ Imaging:

- CXR: **Fine Opacity**
- CT: **Reticulonodular pattern & honeycombing**



▼ Other Choices

• Choice A → Allergic granulomatous angiitis (Churg-Strauss syndrome)

- Presents as **asthma + eosinophilia + some sort of inflammation in the head (sinusitis, mastoiditis, nasal polyps, otitis, nasal perforation)**
- Associated with Mononeuritis Multiplex
- **p-ANCA & Anti-MPO positive**

• Choice B → Bronchoalveolar Carcinoma's greatest risk factor is smoking. She's not a smoker. **The most common subtype of lung cancer in non-smoker females is adenocarcinoma.**

• Choice C → **Emphysema's greatest risk factor is smoking too.** Emphysema is an obstructive lung disease. So, patterns will have low FEV1/FVC ratio.

? Most HY causes of Emphysema?

▼ Answers

Smoking & Alpha-1 Anti-Trypsin Deficiency -

1. Smoking causes Centrilobular / Centriacinar emphysema
2. alpha-1-antitrypsin deficiency causes Panacinar / Panlobular emphysema.

MOAs:

- Protease is an enzyme that breaks elastic fibers of alveoli
- Alpha-1-antitrypsin inhibits protease, so its deficiency causes increase protease activity = more elastic fibers breakdown = emphysema
- Smoking activates protease = increase protease activity = more elastic fibers breakdown = emphysema

- **Choice E** → Lupus pneumonitis is a complication of SLE. The pain is usually pleuritic + fever + cough + dyspnea +/- hemoptysis
 - Labs: Positive Anti-Smith, Positive Anti-dsDNA, Positive ANA, low C3, low C4

Q8

A 17-year-old boy is brought to the emergency department 45 minutes after he collapsed while competing in a high school wrestling competition. He is 178 cm (5 ft 10 in) tall and normally weighs 61 kg (135 lb), but he competes in the 58-kg (128-lb) weight class. On arrival, he is alert. His pulse is 104/min, and blood pressure is 90/55 mm Hg. Physical examination shows pallor and diaphoresis. After administration of intravenous fluids, he says he feels 'back to normal.' On further questioning, he says that he was afraid that he would not qualify to compete in his weight class, so he took a long steam bath and used a laxative prior to the match to quickly lose 2.3 kg (5 lb). Laboratory studies are most likely to show which of the following?

- A. Hypercalcemia
- B. Hyperuricemia
- C. Hypokalemia
- D. Hyponatremia
- E. Hypophosphatemia

▼ Explanation

- **Answer is C (Hypokalemia)**
 - **IMP Clues:**
 - Normally weighs 61 kg, but competes in the 58 kg class (athletes do this, dehydrate themselves to match into their weight class)
 - Pulse is 104 & BP is 90/55 mmHg + Pallor and diaphoresis (He's shocked)
 - Returns back to normal after IV fluids (He was hypovolemic apparently)
 - Long steam bath & used a laxative (so yah, he was trying to shed as much water as possible, but he got his electrolytes all over the place)
 - Q asks what labs would you expect?
 - Stool is rich in **potassium & Bicarb**
 - So, Diarrhea / Laxative abuses would cause **hypokalemic metabolic acidosis**.

? Vomiting vs Diarrhea arrows [K - Cl - Na - HCO3 - PCO2 - pH]

▼ Answer

Vomiting	Diarrhea
low K	low K
low Cl	normal Cl
normal/low Na	normal/low Na
high HCO3	low HCO3,
high PCO2	low Pco2,
high pH	low pH
"Hypokalemic Hypochloremic Metabolic Alkalosis"	"Non-Anion Gap Metabolic Acidosis"

Q9

A 12-year-old girl is referred to the emergency department by her physician because she has been unable to walk for 5 days. Her parents appear very anxious, but she seems unconcerned about her symptoms. Her temperature is 37.0°C (98.6°F), pulse is 70/min, and blood pressure is 115/70 mm Hg. Deep tendon reflexes in the lower extremities are equal bilaterally. Sensation to pain and to light touch is variable. Which of the following is the most likely diagnosis?

- A. Brief psychotic disorder
- B. Conversion disorder
- C. Depersonalization/derealization disorder
- D. Illness anxiety disorder (hypochondriasis)
- E. Post-traumatic stress disorder

▼ Explanation

- **Answer is B (Conversion Disorder)**

- **IMP Clues:**

- Unable to walk for 5 days (the loss of function)
 - She seems unconcerned about her symptoms (the characteristic feature)
 - Normal Vitals + Reflexes equal bilaterally (actually, the patient is intact)

- **Dx → Conversion Disorder**

- **Sudden “apparent/reversible” loss of function** due to some kind of **stressor**.
 - **The patient is UNBOTHERED BY HIS CONDITION. [Characteristic]**

USMLE can present it as a hoarseness of voice, blindness, inability to walk, paralysis, cannot move finger or a limb.

▼ Other Choices

- **Choice A** → Schizophrenia for < 1 month duration
- **Choice C** → Patient feels that he is “separated” from his body or the world around him is not real.
- **Choice D** → Patient is distressed & anxious about having a disease **despite having no** symptoms & all the investigations/examinations are normal
 - USMLE can give you a 50y old male that has a co-worker that died of cancer & he has anxiety that he might be next, despite him being perfectly fine with no symptoms & all the investigations being
- **Choice E** → Patient reliving trauma by flashbacks or dreams for > 1 month.

Q10

An 85-year-old woman is diagnosed with a fracture of the right femur and begins treatment with morphine by patient-controlled analgesic pump. Three days later, her respirations are 6/min. Physical examination shows pinpoint pupils. Her serum creatinine concentration is 1.8 mg/dL. Which of the following best explains this patient's clinical deterioration after the initiation of morphine therapy?

- A. Chronic dosing of morphine decreases its bioavailability
- B. Morphine bioavailability increases with chronic dosing
- C. Morphine downregulates μ -opioid receptors with chronic dosing
- D. Morphine inhibits its own metabolism
- E. Morphine is metabolized to active metabolites that accumulate

▼ Explanation

- **Answer is E (Morphine is metabolized to active metabolite that accumulates)**

- **IMP Clues:**

- Respirations are 6/min (severe respiratory depression from morphine overdose)
 - Pinpoint pupils (severe CNS depression from morphine overdose)
 - Creatinine concentration is 1.8 mg/dl (kidneys not working as they should, so probably the morphine is accumulating)

- **Dx → Morphine Overdose**
 - Morphine is **metabolized in the liver** into *morphine-3-glucuronide* & *morphine-6-glucuronid* and **excreted by the kidneys**.

- **Morphine Overdose/Toxicity** happens in one of 3 ways:

1. **Increased Intake**

2. **Decreased First pass metabolism**

- Less morphine metabolized → More active morphine → more profound effects.

3. **Decreased Renal Excretion** [this is what we have here]

- Renal Dysfunction → less excretion → accumulation of metabolites (morphine-3-glucuronide & morphine-6-glucuronid) → more profound effect

? 80-year-old patient underwent femur replacement & was placed on IV morphine. After a few days he was dismissed from the hospital & was prescribed oral morphine. A few days later, we was brought back to the ER with pinpoint pupils & severe respiratory depression. What is the cause?

▼ **Answer**

Decreased First Pass Metabolism - Patient is older & cannot metabolize the drugs at the same rate, so less morphine was metabolized → more profound effects.

Q11

A 50-year-old man who is a college professor has had an increasing cough for 6 months and hemoptysis for 1 week. He has smoked 1 pack of cigarettes per day for the past 32 years. He plays squash twice a week and swims 3 times a week. An x-ray of the chest shows a 3 × 4-cm hilar mass. Cytologic examination of sputum shows non-small cell carcinoma. The physician tells the patient he has lung cancer. The patient responds, 'How can this be happening to me? I eat right and exercise.' Which of the following responses by the physician is most appropriate?

- A. 'Don't worry. I will be there for you and make sure everything turns out the way you want.'
- B. 'Eating right and exercising will not help prevent cancer.'
- C. 'In fact, as you probably know, the major risk for lung cancer is smoking.'
- D. 'It must be difficult for you to accept this diagnosis when you feel healthy.'
- E. 'Regardless of your good habits, it's time to realize that you have lung cancer.'

▼ **Explanation**

- **Answer is D**

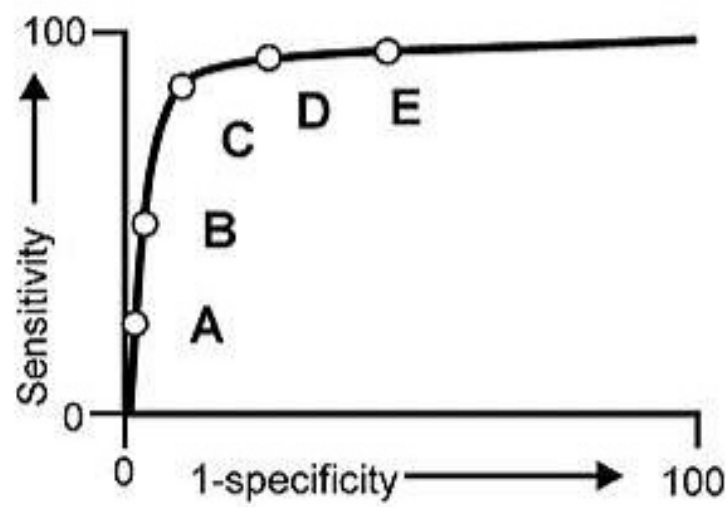
- Okay, the patient found out he has cancer & is freaking out. **You must empathize with the patient, listen to him, and acknowledge how he feels.**
- He is freaking out saying "How can this happen to me, I eat right & exercise."
- You should response with "It must be difficult for you," You are **empathizing** with him "to accept this diagnosis when you feel healthy." You are **actively listening to his concerns & acknowledging** how he feels.

▼ **Other Choices**

- **Choice A** → You are promising him a lie & giving him false hope. Nope.
- **Choice B** → Okay Dr. Knows It All. Have some empathy man.
- **Choice C** → Also being a douchebag.
- **Choice E** → Too direct. Be nice & listen to him. Acknowledging how he feels is important. It's cancer dude not a cold.

Q12

A screening test for cancer is developed and applied to 500 subjects known to have cancer and 500 patients without cancer. Using various cutoff points for the test (A, B, C, D, and E), the sensitivity and specificity of each cutoff point are plotted on a graph of sensitivity as a function of 1-specificity. Which of the following cutoff points will most effectively rule in cancer?



- A. A
- B. B
- C. C
- D. D
- E. E

▼ Explanation

- Answer is A
 - Q says which point most effectively rules in cancer.
 - **Specificity** = tries to confirm that **YOU HAVE** the disease
 - **Sensitivity** = tries to confirm you **NOT HAVING** the disease
 - So, we want to rule in, so we need the **highest specificity possible**.
 - Let's say A is 5, B is 10, C is 15, D is 20, and E is 25
 - A = $100 - 5 = 95$
 - B = $100 - 10 = 90$
 - C = $100 - 15 = 85$
 - D = $100 - 20 = 80$
 - E = $100 - 25 = 75$
 - So, the **highest value for specificity is A (1 - least amount) = greatest amount**.

Q13

A 49-year-old man has had the gradual onset of numbness and pain of the left index finger over the past 3 weeks. Pulses are full and equal bilaterally. The left index finger is mottled blue and pale. Laboratory studies show:

Hemoglobin	14.5 g/dL
Hematocrit	41.7%
Erythrocyte count	4.6 million/mm ³
Leukocyte count	8500/mm ³
Neutrophils	74%
Eosinophils	4%
Lymphocytes	20%
Monocytes	2%
Mean corpuscular volume	89 μm ³
Platelet count	1,530,000/mm ³

Examination of bone marrow shows normal cellularity, normal iron stores, and megakaryocytic hyperplasia. Which of the following is the most likely diagnosis?

- A. Chronic myelogenous leukemia
- B. Essential thrombocythemia
- C. Myeloid metaplasia
- D. Polycythemia vera
- E. Reactive thrombocytosis

▼ Explanation

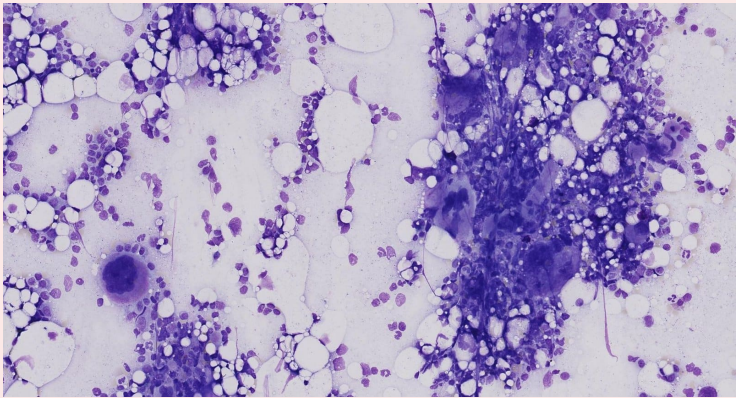
- **Answer is B (Essential Thrombocythemia)**
 - **IMP Clues:**
 - Left index finger is mottled blue & pale (ischemic)
 - PLT count 1,530,000 (wow, this is supppppper high & this confirms the dx)
 - BM examination shows normal cellularity, iron stores, and megakaryocytic hyperplasia (normal cellularity = not leukemia, Megakaryocyte hyperplasia = PLT production is increased)
- **Dx → Essential Thrombocythemia**
 - Basically, **JAK2 mutation** causes the **hematopoietic stem cells** to differentiate abnormally.
 - If it affects **Megakaryocytes → Essential Thrombocytosis**
 - **PLT count ≥ 1 million** (This is a keyword, over a million is Essential Thrombocythemia **NOT** Reactive Thrombocytosis)
 - The increased PLT load can lead to **Raynaud's phenomena** (present here), **pain in fingertips** (present here), and **headache (hyperviscosity syndrome)**
 - **THERE IS NO TRIGGERING EVENT** (unlike Reactive Thrombocytosis)


Chronic Myeloproliferative Disorders:

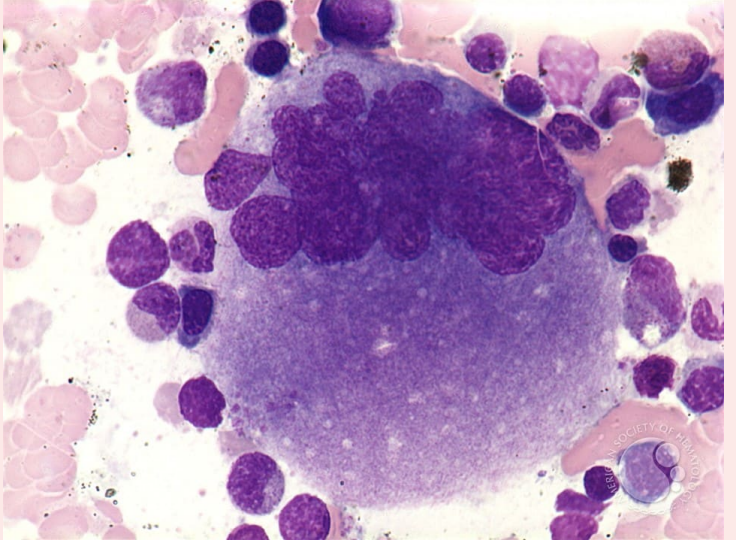
Feature	Polycythemia Vera (PV)	Essential Thrombocythemia (ET)	Primary Myelofibrosis (PMF)
Cell proliferation	RBCs + PLTs/WBCs or both	Platelets ONLY	Fibroblasts + Megakaryocytes
Etiology	JAK2 mutation	JAK2 mutation	JAK2 mutation
Blood smear	Increased RBCs +/- WBCs & platelets	Increased Platelets > 1 million	Teardrop RBCs cells (dacrocytes)
Bone marrow	Hypercellular, with increased hematopoietic precursors	Megakaryocytic hyperplasia	Fibrosis (dry tap)

USMLE can ask you what is seen on biopsy OR show you a bone marrow biopsy & ask for the diagnosis:

- Biopsy ⇒ **Megakaryocytic Hyperplasia** with NORMAL cellularity (excluding leukemia)
- **BM Aspirate:**



IF you don't know what a megakaryocyte looks like, then here is an isolated megakaryocyte below:



- ▼ Other Choices
- **Choice A** → CML would have an abnormally high Leukocyte count NOT isolated increase in PLTs.
 - **Choice C** → Myeloid Metaplasia (aka Myelofibrosis) would have Splenomegaly + “teardrop shaped” RBCs or a dry-tap bone marrow aspiration.
 - **Choice D** → Polycythemia Vera would have increased RBC count + increase in another line (PLTs or leukocytes)
 - **Choice E** → RT is triggered by a specific event (most commonly infection), which causes PLT to increase < 1 million. **OVER A MILLION IS ET EVEN IF THERE IS A TRIGGERING EVENT.**

Q14

A study is conducted to assess the extent of cardiac valvular abnormalities in patients receiving ergot dopamine agonists. Group X consists of 40 patients who have been treated with an ergot dopamine agonist for at least 1 year. Group Y consists of 54 age- and gender-matched controls. It is found that patients in Group X have significantly greater composite regurgitation scores (5 ± 2.1 [mean $\pm$ standard deviation {SD}]) than Group Y (3.3 ± 2 [mean $\pm$ SD]), $p < 0.05$. The

investigators decide to double the number of patients in each group, and keep the same criterion ($p < 0.05$) for statistical significance. This change will most likely have which of the following effects on probability of Type I and Type II error?

Choices	Type I Error	Type II Error
A	Increased	Increased
B	Increased	No change
C	Increased	Decreased
D	No change	Increased
E	No change	No change
F	No change	Decreased
G	Decreased	Increased
H	Decreased	No change
I	Decreased	Decreased

▼ Explanation

- Answer is F
 - Q keeps yapping but says that they decided to **double the number of participants and keep the same criteria ($p < 0.05$)**.
 - How does the sample size effect the study?
 - The **power of the study is equal to $1 - \text{Beta}$**
 - Power is **increased** by
 1. Increased Sample Size
 2. Increased Precision of measurements
 3. Increased expected effect size (alpha)
 - **The more you decrease Beta, the high the power.**
 - What we did here is **increase the sample size**, (this causes an increase in power) while **maintaining the same criteria ($p < 0.05$)**.
 - The increase in power = **decrease in Beta (Type 2 error)**
 - Keeping the same p = **same Alpha (Type 1 error)**
 - **So, answer is Same Type 1 error & decreased Type 2 error (Choice F)**

Q15

A previously healthy 26-year-old woman comes to the physician because of a 2-week history of fever, chills, malaise, rash, diarrhea, headache, and sore throat. Physical examination shows an erythematous throat, diffuse swelling of the lymph nodes, and an erythematous, maculopapular rash over the trunk and extremities. Laboratory studies show a leukocyte count of $10,000/\text{mm}^3$, CD4^+ T-lymphocyte count of $700/\text{mm}^3$ ($N > 500$), and plasma HIV viral load greater than 1 million copies/mL. Results of a serum HIV antibody test are negative. Which of the following best explains this patient's condition?

- A. Acute retroviral infection
- B. HIV-2 infection
- C. HTLV infection
- D. Late-stage AIDS

▼ Explanation

- Answer is A (Acute Retroviral Infection)
 - IMP Clues: (we're going to read / exclude as we go)
 - 2-week hx of fever, chills, malaise, rash, diarrhea, headache, sore throat, diffuse swelling of lymph nodes, erythematous maculopapular rash (This is the **prodromal stage of HIV** guys, remember sketchy? **Flu like symptoms + Diffuse lymphadenopathy**)
 - CD4^+ T-lymphocyte count of 700 (this excludes out Choice D, as AIDS is defined as less than 200)
 - Plasma HIV viral load greater than 1 million copies (this excludes B, as HIV-2 infection usually has a much lower viral load)
 - Serum HIV antibody test are negative (This is a trick, HIV ANTIBODY TESTING takes around 8-12 weeks to become positive)

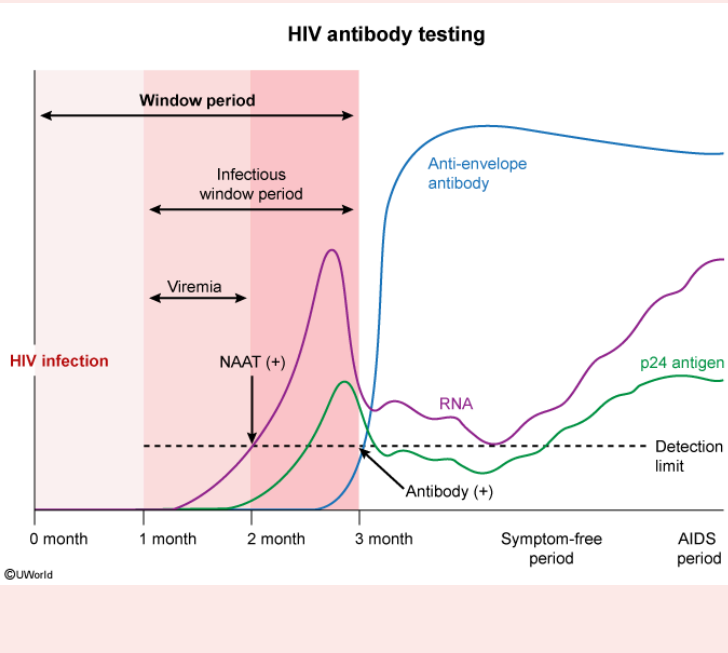


- **Negative HIV serology + low/maintained CD4 count + super high viral load → Early HIV infection (Choice A)**

Picture Below Shows Timing of detection of HIV testing (You don't need to memorize all of this):

Just know that:

- **First month** of HIV infection ⇒ Patients show **NEGATIVE** testing
- **2 months in** ⇒ Detectable by **RNA/PCR/NAAT**
- **3 months in** ⇒ **Antibodies** can be detected



Q16

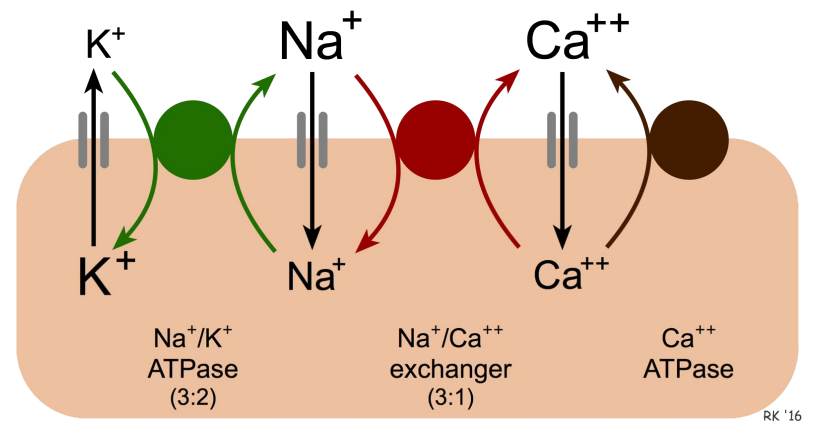
A 50-year-old man is admitted to the hospital because of severe chest pain for 30 minutes. An ECG shows ST-segment elevation in the anterior chest leads. Serum studies show increased creatine kinase activity and troponin I concentration. Compared with the electrolyte content of normal myocytes found in a healthy, asymptomatic 50-year-old man, which of the following best reflects the electrolyte content of the myocytes that produced the increased enzymes in this patient?

Choices	Intracellular [Na ⁺]	Intracellular [K ⁺]	Intracellular [Ca ²⁺]
A	Decreased	Decreased	Decreased
B	Decreased	Decreased	Increased
C	Decreased	Increased	Increased
D	Increased	Decreased	Decreased
E	Increased	Decreased	Increased
F	Increased	Increased	Increased

▼ **Explanation**

- **Answer is E**
 - Q asks how would the electrolytes in a myocyte of a person with an MI change in comparison to a myocyte in a healthy individual.
 - First, we need to understand the roles of Na, K, and Ca in a cardiac cell.
 - **Quick Basics Revision**
 - **Na** is *more outside* the cell (main extracellular ion)
 - **K** is *more inside* the cell (main intracellular ion)
 - Ions move **without** ATP from sites of **high concentration** → **low concentration**
 - For ions, to move in the **“opposite” direction (Low concentration → high concentration)**, they have to move through **ATP-using channels (e.g. Na/K ATPase)**
 - **The cardiac myocytes have these Na/K ATPase**
 - **AIM → Decrease intracellular Calcium so the heart can relax**
 - Calcium? We are talking about a Sodium & Potassium transporter. Let Explain. (Look at pic below while you read)
 - **Na/K ATPase**
 - **K is pulled into** the cell (*against concentration gradient*)
 - **Na is pushed out** of the cell (*against concentration gradient*)
 - **End Result is MORE K inside & LESS Na inside**

- **Na/Ca exchanger**
 - The cardiac cell wants to **get rid of calcium inside the cell**, so that it can relax
 - What is the most energy efficient way to get rid of calcium?
 - The **Na/K ATPase** resulted in **less Na inside the cell (and more Na outside the cell)**
 - **So, the Na wants to enter the cell (High conc outside → Low conc inside)**
 - The cell says okay, **let's exchange!**
 - **Calcium goes out**
 - **Sodium goes in**
 - **An ion for an ion.**
- Okay, with all these mechanisms in mind, how is the intracellular concentration of these molecules looking like?
 - **High Intracellular K**
 - **Low Intracellular Na**
 - **Low Intracellular Ca**



- **How does MI, affect these mechanisms?**
 - **MI = hypoxia = No ATP = dysfunction of ATP-using pumps = ATPase NOT working = Ca/Na exchanger NOT working**
 - End Result is opposite of what we have
 - **Decreased Intracellular K**
 - **Increased Intracellular Na**
 - **Increased Intracellular Ca**
 - **(Choice E)**

Q17

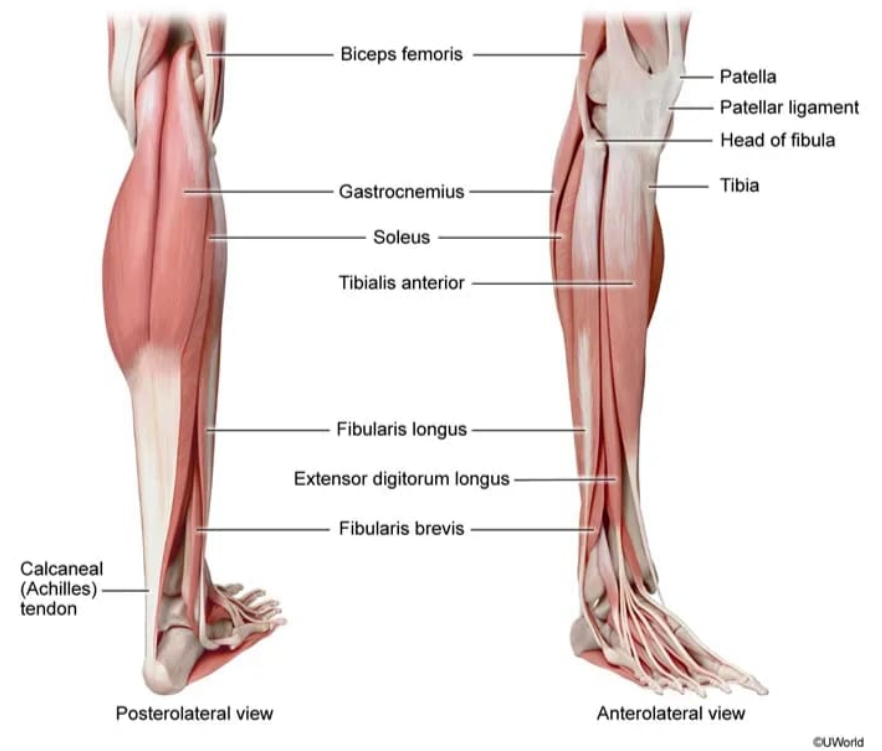
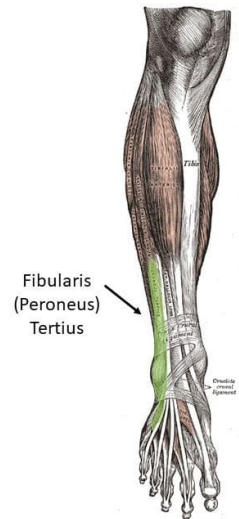
A 43-year-old man is brought to the emergency department 1 hour after forcible eversion of his left foot while jogging on uneven ground. Walking is limited by pain. He rates the pain as 7 on a 10-point scale. His vital signs are within normal limits. Physical examination shows tenderness and swelling over the lateral malleolus. An x-ray of the left lower extremity shows a fracture of the fibula above the distal tibiofibular articulation. Contraction of which of the following muscles most likely caused this patient's pain at the fracture?

- A. Extensor digitorum longus
- B. Fibularis (peroneus) brevis
- C. Fibularis (peroneus) tertius
- D. Flexor digitorum longus
- E. Tibialis anterior
- F. Tibialis posterior

▼ **Explanation**

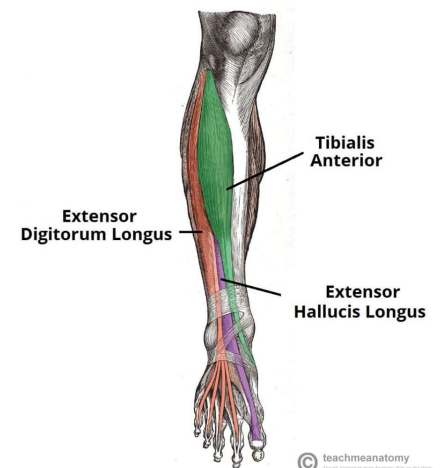
- **Answer is B (Fibularis (Peroneus) Brevis)**
 - **IMP Clues:**
 - Forcible Eversion of his foot (Ankle sprain / injury)
 - Tenderness & swelling over lateral malleolus (muscles around it will be irritated / contracted)
 - X-ray shows fracture of the fibula above distal tibiofibular articulation (fractured fibula)

- Q asks contraction of **which muscle causes this patient's pain?**
 - Okay so **lateral malleolus tenderness / swelling + fibular fracture** = almost definitely the affected muscle is in close proximity of these injuries (**Lateral aspect of the Leg**)
 - What are the 2 main muscles? **Fibularis Longus & Fibularis Brevis**
 - Of these two muscles, **only Fibularis Brevis is in the answer choices (Choice B)**
 - What about *Fibularis Tertius* (Choice C), it has fibularis in the name so it must be related to the above 2 right?
 - No, it's an anterior leg muscle that gets its origin from the fibula (anterior aspect of it)**

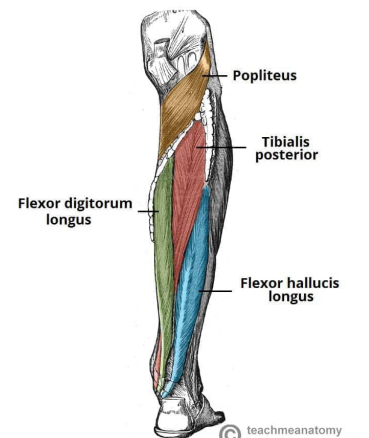


▼ Other Choices

- Choices A & C & E → Anterior aspect of the Leg



- Choice C & F → Posterior aspect of the Leg



Q18

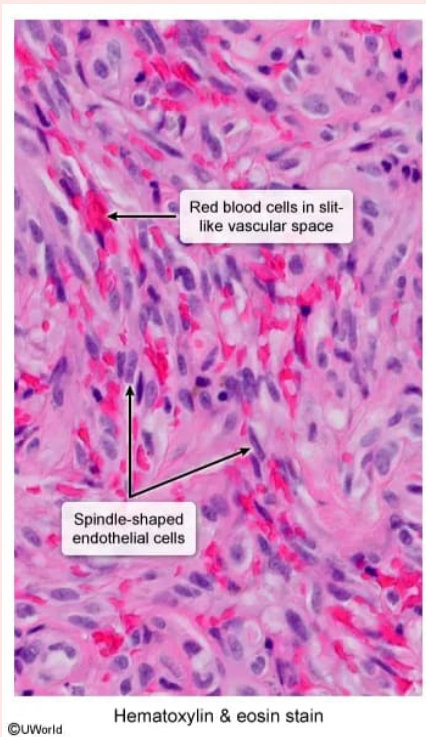
A 28-year-old man who is seropositive for HIV has numerous nonulcerated purple nodules on the skin. Examination of tissue obtained on biopsy of a lesion is most likely to show which of the following?

- A. Aggregates of large atypical lymphocytes
- B. Granulation tissue containing pseudohyphae and budding yeasts
- C. Intracellular yeasts in macrophages
- D. Macrophages containing acid-fast bacilli
- E. Multinuclear cells containing intranuclear inclusions
- F. Slit-like vascular spaces with plump spindle-shaped stromal cells

▼ Explanation

- Answer is F (Slit-like Vascular spaces with plump spindle-shaped stromal cells)
 - IMP Clues:
 - Seropositive for HIV (so it's probably an AIDS-associated disease)
 - Nonulcerated purple nodules (okay AIDS + purple nodules is either Kaposi Sarcoma (nonulcerated) or Bacillary angiomatosis (ulcerated usually))
- Dx → Kaposi Sarcoma
 - Common in AIDS patients & those on immunosuppressants
 - Caused by HHV-8
 - Presents as nontender nonulcerated purple nodules
 - Found on both skin & mucus membranes
 - Most common site is → Hard Palate
 - Biopsy shows slit like vascular spaces with spindle shaped stromal cells + lymphocytic infiltration (as it is a virus)

This spindle picture is super HY on the USMLE. The nodules picture is for demonstration purposes only:



USMLE loves to refer to these nodules/papules/plaques as "Painless Violaceous Lesions" that can be either MUCOSAL or CUTANEOUS.

- This differentiate it from bacillary angiomatosis's nodules that are:
 - PAINFUL
 - ONLY cutaneous

On the USMLE, AIDS Patient + Skin Nodules is one of two things:

Feature	Kaposi Sarcoma	Bacillary Angiomatosis
Etiology	HHV-8 (Human Herpesvirus 8)	Bartonella henselae (Gram-negative bacteria)
Appearance	Purple, red, or brown vascular plaques/nodules, nontender, nonulcerated	Red, friable papules or nodules, often tender or ulcerated
Site	Skin & Mucus membranes	Skin
Histology	Spindle cells, slit-like vascular spaces	Capillary proliferation with neutrophilic infiltrate
Organisms on biopsy	None - viruses are not stained	Bacteria visible with Warthin-Starry stain

▼ Other Choices

- Choice A → Refers to lymphoma.

? AIDS Patient with an enhancing brain lesion that was thought to be toxoplasmosis. They gave antibiotics, but the lesion got bigger + patient gets worse. What is Dx?

▼ Answer
Primary CNS Lymphoma

- Choice B → Refers to candida

- On the USMLE, HIV patients present was **esophageal candidiasis**
 - **HIV patient + odynophagia (pain during swallowing) is esophageal candidiasis until proven otherwise.**
 - Treated with **oral fluconazole** (not nystatin, this is for oropharyngeal candida)
- **Choice C** → Refers to **Histoplasmosis** (can also refer to **coccidiosis or blastomycosis**)
 - For Histoplasmosis, USMLE will give hx of cave exploration or close-proximity of bird droppings + TB-like lesions or erythema nodosum
 - For Coccidiosis, USMLE will give hx of earthquake + Larger than RBCs
 - For Blastomycosis, USMLE will give "broad-base budding yeast"
- **Choice D** → Refers to **TB**
- **Choice E** → Refers to **HSV or VZV**

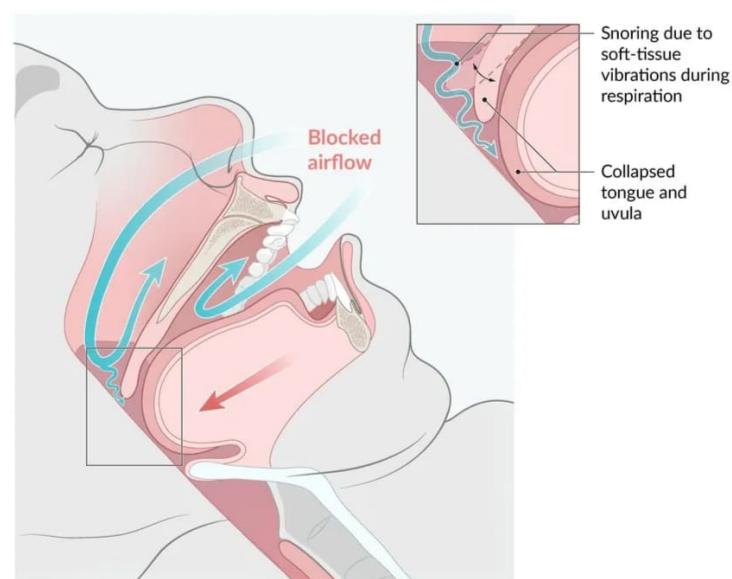
Q19

A 73-year-old man comes to the physician with his wife because of a 3-year history of daytime sleepiness. His wife says that he snores loudly. He is 183 cm (6 ft) tall and weighs 113 kg (250 lb); BMI is 34 kg/m². His pulse is 84/min, respirations are 18/min, and blood pressure is 175/105 mm Hg. Physical examination shows congested conjunctivae and centripetal obesity. Serum studies show a glucose concentration of 250 mg/dL, creatinine concentration of 2 mg/dL, and uric acid concentration of 10.1 mg/dL. Polysomnography confirms the diagnosis, and treatment with nasal continuous positive airway pressure at night is started. This therapy will most likely cause a decrease in which of the following?

- A. Blood pressure
- B. Pulse rate
- C. Serum creatinine concentration
- D. Serum glucose concentration
- E. Serum uric acid concentration

▼ **Explanation**

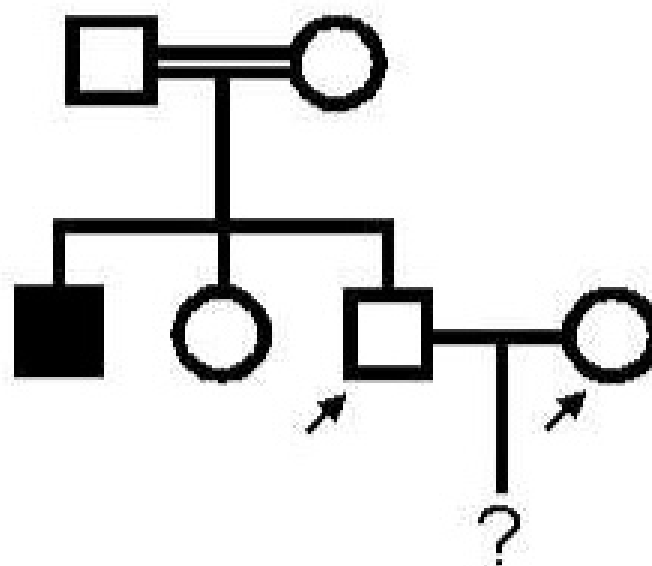
- **Answer is A (Blood Pressure)**
 - **IMP Clues:**
 - Daytime sleepiness + snores loudly (looks like a sleep apnea case)
 - BMI is 34 + centripetal obesity (he's obese, and this is an important risk factor for apnea)
 - Blood Pressure is 175/105 (Hypertensive, a complication of apnea)
 - Congested conjunctivae (prolonged hypoxia → polycythemia)
 - Glucose concentration of 250mg/dl (Insulin resistance)
 - Creatinine concentration of 2mg/dl (systemic hypoxia → VC → decreased renal flow)
 - Polysomnography confirms diagnosis (sleep study confirmed it) & treatment with nasal CPAP is started (the ttt)
 - **Dx → Obstructive Sleep Apnea**
 - Obesity causes **excess soft skin** at the level of the throat
 - Sleeping causes **relaxation of pharyngeal muscles**
 - **Excess soft skin + relaxed muscles = narrowed/collapsed airway**
 - Complications:
 - **Loud snoring, gasping, and choking** (affects quality of sleep → **daytime sleepiness & loss of concentration/fatigue**)
 - **Chronic hypoxia & decreased ventilation** causes:
 1. Pulmonary hypoxia → hypoxic VC → increased pulmonary arterial pressure & overtime pulmonary remodeling → **Pulmonary HTN**
 2. **Sympathetic overstimulation → catecholamines & stress hormones released**
 - a. Systemic VC → **Systemic resistant HTN & decreased renal flow**
 - b. Excessive catecholamines effect → **Arrhythmias & Sudden Death**
 - c. High stress & catecholamines levels → **Insulin resistance**



3. Increased EPO secretion → **Secondary Polycythemia** (conjunctival congestion & strokes)
- Treatment:
 - **Loss of Weight** (essential for tt)
 - **Night CPAP** (supports pharyngeal muscles + continuous O2 while asleep)
 - This reverses the effects.
 - Most importantly is the **Reversal of sympathetic stimulation, causing Blood Pressure to go down.**

Q20

A 30-year-old man and a 24-year-old woman (indicated by the arrows) request preconceptional counseling because the man's brother has type I oculocutaneous albinism. This is an autosomal recessive, single gene disorder thought to occur about once in every 40,000 persons in the general population. Assume that the alleles are in equilibrium in the population, that the woman's family history is negative for this disorder, and that the two probands have neither shared relatives nor common ethnicity. A pedigree is shown. Which of the following is the best estimate that their child will be affected with oculocutaneous albinism?



- A. 1 in 4
- B. 1 in 100
- C. 1 in 200
- D. 1 in 600
- E. 1 in 40,000

▼ **Explanation**

- **Answer is D (1 in 600)**
 - Okay Q asks what estimates the chance that the child will be affected with AR disease in the vignette.
 - **Formula is = "% of dad being a carrier" x "% of dad actually passing it" x "% of mom being a carrier" x "% of mom actually passing it"**
 - Let's do Dad first:
 - **% of dad being a carrier = 2/3.**
 - Disease is AR (so out of boxes on a Punnett square → One is not affected, One is affected, 2 carriers)
 - Brother is affected, so the chance of the dad being affected is 2/3
 - **% of dad actually passing it = 1/2**
 - Dad has 2 alleles, one affected and one is not, so 50%
 - Now, let's do Mom:
 - **% of mom being a carrier = 1/100**
 - Mom's history is nonsignificant, so how can we calculate the %? **Hardy-Weinberg Equation**
 - First what are the equations that we must know?
 - $p^2 + 2pq + q^2$
 - $p + q = 1$
 - p is normal people [always calculate it as 1, trust me]

- q is affected people
 - 2pq is carriers
 - Q tells us that $q^2 = 1/40,000$; so $q = 1/200$
 - $p + 1/200 = 1$, so $p = 199/200$
 - (basically 1, that's why I always say always calculate it as 1 directly, don't waste time)
 - carrier = $2pq = 2 \times 1 \times 1/200 = 1/100$
- % of mom actually passing it = 1/2
- Mom has 2 alleles, one may be affected, and one is not, so 50%
- Formula is = "% of dad being a carrier" x "% of dad actually passing it" x "% of mom being a carrier" x "% of mom actually passing it"
- $2/3 \times 1/2 \times 1/100 \times 1/2 = 2/1200 = 1/600$ (Choice D)

Q21

A 65-year-old man starts using topical fluorouracil for treatment of actinic keratoses on his scalp. Fluorouracil is most likely effective for this patient because it inhibits which of the following enzymes?

- A. Thymidine kinase
- B. Thymidine reductase
- C. Thymidylate synthase
- D. Uracil phosphoribosyltransferase
- E. Uracil reductase

▼ Explanation

- Answer is C (Thymidylate Synthase)
 - Straight up easy points pharma Q
 - MOA of Fluorouracil → Thymidine Synthase Inhibitor
 - Capecitabine is metabolized into 5-Fluorouracil, so also inhibits Thymidine Synthase

? How to overcome 5-FU toxicity?

▼ Answer

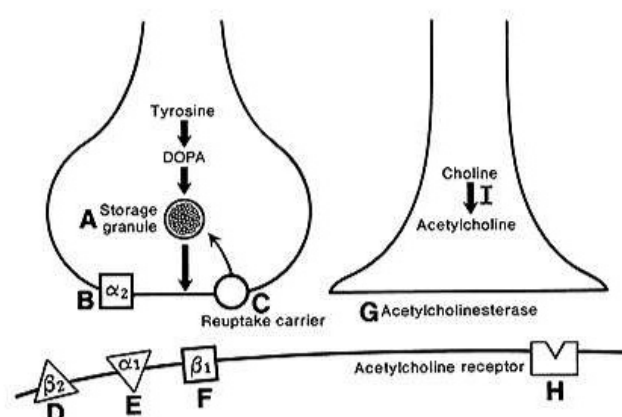
1. Oral Thymidine (just give the product)
2. Uridine (overwhelm the enzyme with the substrate)

▼ Other Choices

- Choice A → Choose altered / absent thymidine kinase when USMLE asks about the MOA of how HSV/VZV is resistant to Acyclovir or CMV is resistant to Ganciclovir
- Remaining Answer Choices are garbage. Don't bother.

Q22

A 73-year-old man has difficulty urinating and frequent urination. Improvement of these symptoms is most likely to result from treatment with a drug that blocks which of the following labeled sites?



A. A

- B. B
- C. C
- D. D
- E. E
- F. F
- G. G
- H. H
- I. I

▼ Explanation

- **Answer is E**

- 73-year-old man with urinary symptoms is BPH on the USMLE.

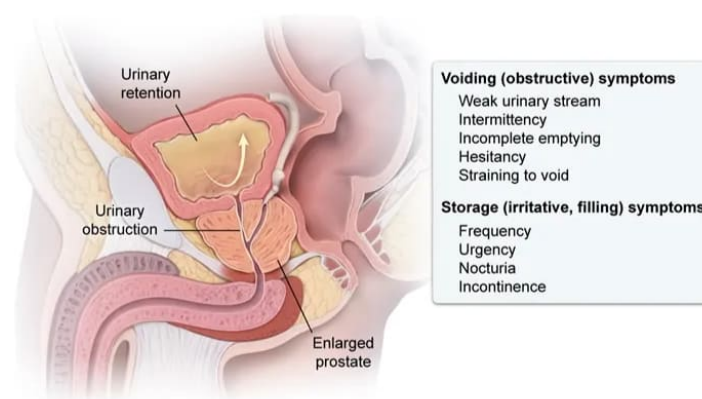
- BPH is treated by 2 regimens:

1. **Alpha-1 antagonists** (what we have here)

- Internal Sphincter is contracted when alpha-1 receptors are activated.
- **Inhibiting alpha-1 receptors relaxes the internal urinary sphincter → improvement of urinary symptoms**
- Examples of **alpha-1 antagonists** are *Prazosin*, *Tamsulosin*, *Terazosin*, and *Doxazosin*

2. **5-alpha reductase inhibitors**

- Glandular tissue enlarges in response to increased DHT.
- **Testosterone → DHT via 5-alpha reductase.**
- **5-alpha reductase inhibitor (Finasteride)** causes apoptosis of enlarged prostatic glandular tissue → **prostate shrinks in size.**



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Q23

A 32-year-old man comes to the physician because of a 2-week history of persistent thrush. He has been receiving a multidrug regimen including zidovudine (AZT) for 3 years, but he has had difficulty with compliance. Laboratory studies show a CD4+ T-lymphocyte count of $100/\text{mm}^3$ ($N \geq 500$) and plasma HIV viral load of 100,000 copies/mL. HIV genotyping shows a mutation consistent with zidovudine resistance. This mutation is most likely in which of the following viral genes?

- A. DNA polymerase
- B. Glycoprotein 41
- C. Glycoprotein 120
- D. Integrase
- E. Protease
- F. Reverse transcriptase
- G. Thymidine kinase

▼ Explanation

- **Answer is F (Reverse Transcriptase)**

- Another easy pharma Q.
- **Zidovudine** is an **NRTI**
 - **Zidovudine is the NRTI most notorious for Bone Marrow Suppression on the USMLE**
 - Zidovudine is the NRTI classically given **intrapartum to HIV positive pregnant women.**

▼ Other Choices

- **Choice A** → HIV is an RNA virus. So, no DNA polymerase inhibitor drug for it.
- **Choice B** → mutation in Glycoprotein 41 would cause resistance to **Enfuvirtide**
- **Choice C** → mutation in Glycoprotein 120 would probably cause resistance to **Maraviroc**

- **Choice D** → mutation in Integrase would cause resistance to **Raltegravir**.
- **Choice E** → mutations in Protease would cause resistance to **protease inhibitors ("-navir")**
- **Choice G** → mutation in thymidine kinase would cause **Acyclovir resistance in HSV/VZV or Ganciclovir resistance in CMV**

Q24

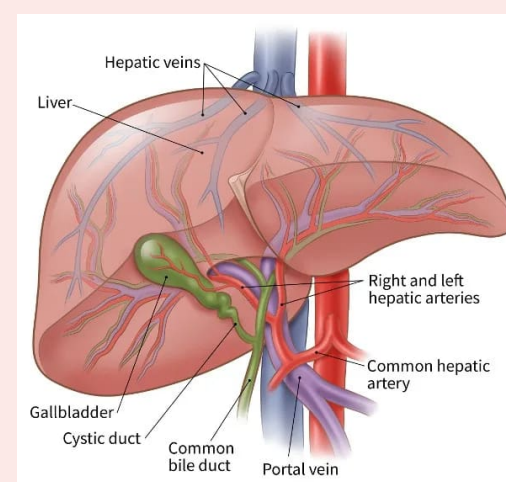
A 29-year-old woman is brought to the emergency department 1 hour after being injured in a motor vehicle collision. Abdominal examination shows tenderness with rebound. Vital signs are stable. A CT scan of the abdomen shows no abnormalities except for a small amount of intraperitoneal fluid. After 6 hours of observation, an exploratory laparotomy is done because of continuing severe abdominal pain. No abnormalities are seen until the surgeon gently slides his hand behind the liver; there is a sudden massive hemorrhage from the region of the hand, and the patient's blood pressure becomes undetectable within 1 minute. Which of the following underlying lesions is most likely associated with the hemorrhage?

- A. Avulsion of celiac trunk from the aorta
- B. Avulsion of hepatic veins from the inferior vena cava
- C. Traumatic transection of the aorta
- D. Traumatic transection of the hepatic artery
- E. Traumatic transection of the portal vein

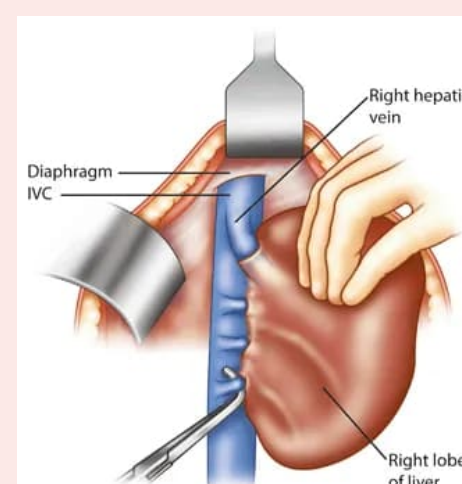
▼ **Explanation**

- **Answer is B (Avulsion of hepatic veins from the inferior vena cava)**
 - **IMP Clues:**
 - Tenderness with rebound (Acute abdomen)
 - Vitals are stable
 - No abnormalities on imaging except small intraperitoneal fluid + on laparotomy no abnormalities seen until surgeon slides his hands behind the liver (The Liver was putting pressure on the bleeder, hence no severe bleeding)
 - Sudden Massive hemorrhage from the region of the hand + BP becomes undetectable within 1 min (A LARGE VESSEL IS SEVERED)
 - Q asks about probable **source of bleeding**
 - The **source of the bleeding is behind the liver**, so let's exclude:
 - **Choice A** → Celiac trunk is an aortic branch. **Not really behind or close to the liver.**
 - **Choice C** → Aorta **not really related to the liver.**
 - **Choice D & E** → Portal vein & Hepatic artery are **below** the liver, and they divide into 2 before entering the liver. Not behind it.
 - This leaves out **Avulsion of the hepatic veins from the IVC** (Choice B)
 - As you can see, the Hepatic veins drain the liver, the **exit from the back of the liver & enter into the IVC** (which is related to the **backside** of the liver)
 - Avulsion of Hepatic veins from the IVC is one of the most lethal injuries.
 - **The bleeding is so severe & is associated with high mortality rate.**

Picture below shows how the Aorta, Celiac Trunk, Portal Vein, and Hepatic Artery all relate to the liver:



Picture below shows how the hepatic veins exit the backside of the liver and enter into the IVC:



Q25

A 26-year-old woman develops hypotension and hemoglobinuria after receiving 1 unit of packed red blood cells. Which of the following are most likely to be involved in her condition?

- A. Antibody, complement C5-9
- B. Circulating immune complexes, complement C5a, neutrophils
- C. Cytotoxic T lymphocytes
- D. IgE, mast cells, histamine, cytokines
- E. Lymphocytes, cytokines, macrophages

▼ Explanation

- Answer is A (Antibody, complement C5-C9)
 - IMP Clues:
 - Hypotension & Hemoglobinuria (Hemolysis causing anemic shock)
 - After receiving 1 unit of packed RBCs (Blood Transfusion Reaction)
 - Dx → Hemolytic ABO mismatch:
 - Hypotension, fever, chills +/- other symptoms of severe hemolysis (hemoglobinuria) within minutes of transfusion
 - MOA: **Preformed** IgM antibodies against donor's RBC (A/B) antigens [Coomb's/DAT positive]
 - For a reaction to happen that fast, this means we have *preformed* antibodies against the presented antigens:
 - **Type 2 Hypersensitivity Reaction**

? Fever + Chills post-transfusion. What are the possible causes if this happened after minutes VS hours VS days of the transfusion?

▼ Answer

- Do we have **Fever + chills post transfusion?**
 - Yes? look at time frame
 - Within **minutes** → **ABO mismatch** (present with signs of severe hemolysis + Coomb's *positive*)
 - Within **hours** → **FNHTR** (NO hemolysis, hence the name, + Coomb's *negative*)
 - Within **days to a week** → **Delayed Transfusion reaction** (present with signs of hemolysis + Coomb's *positive*)

▼ Other Choices

- **Choice B** → Type 3 HS like serum sickness (happens 2-4 days after injection)
- **Choice C** → Type 4 HS like contact dermatitis (commonly USMLE assesses it as Oak/Ivy poison or Necklace/Ring)
- **Choice D** → Type 1 HS like Anaphylaxis. Usually people get edema & urticaria.
- **Choice E** → It's just a generalized chronic inflammation.

Q26

A 74-year-old man with emphysema and lung cancer is brought to the clinic by a social worker because of his wasted appearance. His wife of 50 years died 8 months ago. He is impoverished, and his diet consists primarily of cereal and toast. He has lost 13.6 kg (30 lb) in the past 6 months. He has temporal muscle wasting, sunken eyes, loose skin, and edema of the lower extremities. He appears despondent and withdrawn. Serum albumin concentration is 2.5 g/dL. An x-ray of the chest shows a large mass in the hilum of the right lung. Which of the following best explains the edema?

- A. Anabolic state
- B. Glycogen depletion
- C. Lipolysis
- D. Negative nitrogen balance
- E. Starvation ketosis

▼ Explanation

- **Answer is D (Negative Nitrogen Balance)**
 - **IMP Clues:**
 - Lung-cancer (probably cachexic due to?? YES TNF-alpha [HY])
 - His diet consists of cereal & toast (No protein, No fats, No vitamins & minerals)
 - Wasted appearance + Lost 13.6 kg + Impoverished + Temporal muscle wasting (In a catabolic state due to his diet)
 - Edema of the lower limbs + Serum albumin concentration is 2.5 (Low albumin is due to low protein intake → low oncotic pressure → Edema)
 - **Dx → Severe malnutrition**
 - Patient's diet is **poor in protein** (and everything else, really)
 - **His intake is less than his expenditure, so he is in a "negative nitrogen/energy balance"**
 - Body needs energy, so it first goes to glycogen (depleted within 24 hours), then protein and fat, then protein as the last standing nutrient.
 - **Protein Breakdown = Catabolism (Wasted / Temporal muscle wasting)**
 - Decreased Protein intake = **decreased synthesis of protein products (albumin)** → less albumin causes **less oncotic pressure**, so fluids go into extravascular spaces → **EDEMA**.

▼ Other Choices

- **Choice A →** *He's catabolic, not anabolic.* He's breaking down his proteins and fats to maintain life. Anabolic is muscle building & fat/glycogen storage due to insulin. Bro's not eating, so there is no insulin
- **Choice B →** **Glycogen storages are depleted after fasting for 16-18 hours.** He's been like this for months. He's way past his glycogen storages.
- **Choices C & D →** Yes, he may be breaking down fat as well. Lipolysis causes ketones production. Not edema. **Edema is caused by less albumin due to either increased protein loss or decreased protein intake.**

Q27

A 22-year-old woman who is at 16 weeks' gestation has decreased serum concentrations of α -fetoprotein and unconjugated estriol and an increased serum concentration of human chorionic gonadotropin. Which of the following disorders affecting the fetus is most likely?

- A. Angelman syndrome
- B. Beckwith-Wiedemann syndrome
- C. Down syndrome
- D. Fragile X syndrome
- E. Myotonic dystrophy
- F. Prader-Willi syndrome

▼ Explanation

- **Answer is C (Down Syndrome)**
 - **IMP Clues:**
 - Decreased serum α -fetoprotein & unconjugated estriol & increased HCG (classic Triple Test for DS screening)
 - **Dx → Down Syndrome**

Any lab with the letter "**H**" choose **up** arrow for DS screening tests:

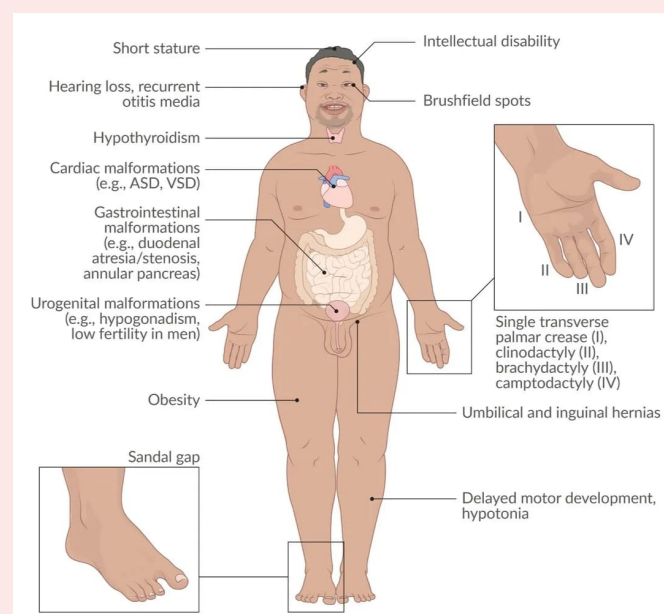
- **Triple Screening Test:**
 - **AFP → decreased**
 - **Unconjugated Estriol → decreased**

Picture below Shows Features of Down Syndrome (Trisomy 21):

- **HCG** → **increased**

◦ **Quad Screening Test:**

- **AFP** → **decreased**
- **Unconjugated Estriol** → **decreased**
- **HCG** → **increased**
- **InHibin A** → **increased**



HY Features USMLE likes:

- **VSD/ASD**
- **Duodenal Atresia & Annular Pancreas**
 - **DS + bilious emesis + double-bubble sign**
- **Hirschsprung Disease**
- **Early-onset Alzheimer Disease**
 - **APP gene on chromosome 21**
 - **DS has 3 chromosome 21, so increased expression of APP**
- **Increased risk of AML/ALL**
- **Increased risk of hypothyroidism**

▼ **Other Choices**

- **Choice A** → Angelman Syndrome is characterized by Maternal loss of chromosome 15
 - Maternal Deletion of chromosome 15
 - Paternal Uniparental Diosomy (The father gives both chromosomes 15, however they get silenced)
- **Choice F** → Prader-Willi Syndrome is characterized by Paternal loss of chromosome 15
 - Paternal Deletion of chromosome 15
 - Maternal Uniparental Diosomy (The mother gives both chromosomes 15, however they get silenced)
- **Choice B** → **Beckwith-Wiedemann Syndrome**
 - Wilms tumor + macrosomia (big baby >4,000g) + hemi-hypertrophy (half of the body is bigger than the other) + macroglossia + omphalocele + hypoglycemia
- **Choice D** → **Fragile X Syndrome**
 - TNR **CGG** [☞ "**C**ongenitally **G**iant **G**onads"]
 - Patients have long faces, long ears, large gonads, mental retardation
 - X-Linked Dominant Condition; **FMN1 gene mutation**
- **Choice E** → **Myotonic Dystrophy**
 - TNR **CTG** [☞ "**C**an't **T**erminate **G**rip"]
 - Presents as patient that cannot relax his muscles easily.
 - Patient opens door for someone & can't let go of doorknob
 - Patient shakes someone's hand & can't let go of the person's hand

Q28

A 50-year-old man comes to the physician 3 days after his first generalized tonic-clonic seizure. He has a 1-month history of frequent episodes of a pins-and-needles sensation around the mouth and in the hands and feet. He also has had occasional episodes of involuntary contraction of the muscles of the hands or feet leading to wrist flexion or foot plantar flexion. His pulse is 80/min, and blood pressure is 150/90 mm Hg. Neurologic examination shows mild, diffuse hyperreflexia. An abnormality of which of the following serum electrolyte concentrations is the most likely explanation for his symptoms?

- A. Bicarbonate
- B. Calcium
- C. Chloride
- D. Potassium
- E. Sodium

▼ Explanation

• Answer is B (Calcium)

◦ IMP Clues:

- Tonic-clonic seizure (seizures due to electrolyte imbalance is either hypocalcemia or hyponatremia)
- Pins-and-needles sensation around mouth & hands and feet (Peri-oral paresthesia + extremities too)
- Wrist Flexion or Foot planter Flexion (characteristic signs)
- Mild-diffuse hyperreflexia (another characteristic sign)

• Dx → Hypocalcemia

◦ Why does hypocalcemia cause neuronal hyperexcitability?

- **Calcium stabilizes Na voltage channels.** It increases the threshold needed to activate these channels.
- When calcium decreases, the threshold also decreases, causing Na to enter the cells → Neurons fire.

◦ Features of Hypocalcemia

- **Seizures**
- **Peri-oral numbness/tingling [peri-oral parathesis]**
- **Tingling & numbness of extremities**
- **Muscle cramps**
- **QT prolongation & arrhythmias**
- **Trousseau's sign** → Carpopedal spasm when BP is measured
- **Chvostek's sign** → Facial twitching on percussion of facial nerve



Q29

A 50-year-old man who has smoked 2 packs of cigarettes a day for 34 years has experienced gradually increasing shortness of breath on exertion, chronic cough productive of thick sputum, and frequent episodes of wheezing. The anteroposterior diameter of his chest is increased. Diminished breath sounds and scattered rhonchi are audible throughout the lung fields. Which of the following laboratory abnormalities is expected?

- A. Decreased blood Pco_2
- B. Increased blood HCO_3^-
- C. Increased blood pH
- D. Increased urinary excretion of HCO_3^-
- E. Increased urinary pH

▼ Explanation

• Answer is B (Increased Blood HCO_3^-)

◦ IMP Clues:

- Smoked 2 packs of cigarettes a day for 34 years (heavy smoker)
- Increasing SOB + chronic cough productive of thick sputum + wheezing + Increased AP diameter of chest (hyperinflated chest + plenty of secretions, this is classic COPD)

• Dx → COPD

◦ Smoking is the biggest risk factor for COPD

▪ why Smoking?

- **Smoking activates proteases → increased protease activity → elastic fibers breakdown → emphysema**
- Emphysema (Break down of elastic fibers) causes **decreased** alveolar recoil → **increases** lung compliance [asked on NBME]
- HY to know that **smoking** causes **Centrilobular/Centriacinar emphysema (Upper Lobes)**

• Another HY cause of COPD is **alpha-1 antitrypsin deficiency**

- **alpha-1 antitrypsin inhibits proteases**, so its deficiency causes **increased** protease activity → elastic fibers breakdown → emphysema
- Associated with **Liver Failure** (USMLE can give this as "parent died of a liver disease" or the patient himself is affected)
- HY to know that **alpha-1 antitrypsin deficiency** causes **Panacinar emphysema (Lower Lobes)**

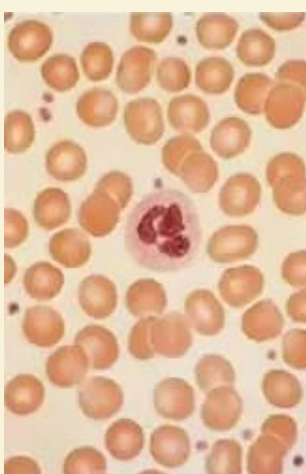
◦ Features of COPD:

- **Chest Hyperinflation** (air is trapped inside) & **Diminished air entry**
- **Chronic productive cough** (dysfunctional cilia + mucus gland hyperplasia/hypersecretion)
- **Wheezing & Exertional Dyspnea**
- **Chronic Hypoxia**
 - **Increased PCO₂**, so kidney stimulates HCO₃ reabsorption to balance the acidosis → **Increased blood HCO₃**

◦ HY Complications:

- Increased EPO → **Secondary Polycythemia**
- **Pulmonary HTN & Cor pulmonale**

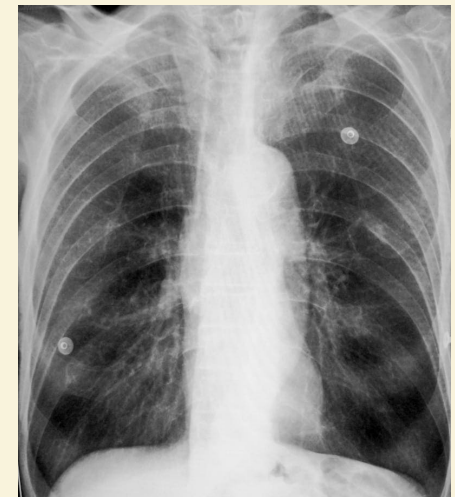
! These patients usually have **2ry polycythemia**, so USMLE might show you the **following smear with high hemoglobin & hematocrit** and ask for the cause; answer = **COPD**.



- Smear is **normal**. We just have **increased RBCs**.
- This is **reactive polycythemia**, secondary to chronic hypoxia → **Kidneys** increases **EPO** production → EPO goes to **bone marrow** → binds to **EPO Receptors** on **erythroid progenitor cells** → **JAK-STAT2** pathway → increased proliferation & differentiation → **increased RBCs**

! Ways the USMLE hint that this person has COPD:

- History of heaving **SMOKING FOR YEARS**
- Examination Findings of COPD: **decreased** TVF & breath sounds + **hyperresonance**
- Physical Findings: **Increased AP diameter**, Parallel Ribs, Accessory muscles usage
- **Obstructive PFTs pattern**
- CXR: showing **narrowing** of cardiac silhouette + flat diaphragm + hyperinflated lungs + **increased** bronchial markings (CXR shown below)



USMLE Asks about management of COPD:

B2 agonist (Albuterol) + Muscarinic Antagonist (Ipratropium)

- **B2 Agonists** → stimulates **B2 receptors** in the lungs → **bronchodilation**
- **Muscarinic Antagonists** → **Block M receptors** in the lungs → **inhibit** bronchoconstriction

! **Albuterol** is a **SHORT-ACTING** beta 2 agonist [asked on NBME]

? What is a HY side effect of B2 agonists USMLE wants you to know?

▼ Answer

Tremors - B2 agonists cause tremors (USMLE likes hand tremors)

! Obstructive VS Restrictive Lung Diseases PFTs:

PFTs	Obstructive Lung Disease	Restrictive Lung Disease
Residual Volume (RV)	↑	↓
Functional Residual Capacity (FRC)	↑	↓
Total Lung Capacity (TLC)	↑	↓
FEV1	↓↓	↓
FVC	↓	↓
FEV1/FVC	↓	normal/↑↑↑

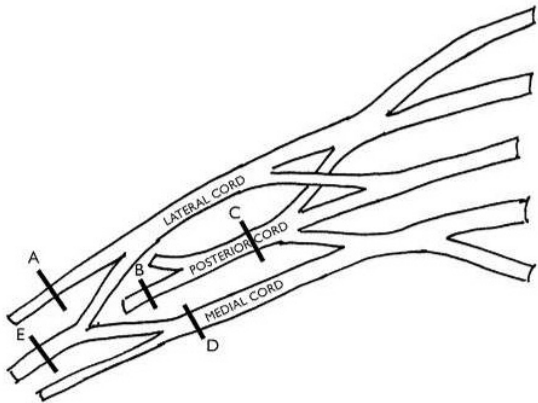
▼ Other Choices

- **Choice A** → COPD causes chronic hypoxia, which means **increased blood PCO₂**. **Not decreased**.

- **Choice C** → Chronic Hypoxia & High PCO₂ would cause Respiratory Acidosis, which is **low blood pH**
- **Choices D & E** → Kidney increases reabsorption of HCO₃ to *neutralize some of the respiratory acidosis*. **This causes higher blood HCO₃, less HCO₃ excretion in urine, and a decreased urine pH**

Q30

A 20-year-old man comes to the physician because of tingling and numbness of the dorsum of his right hand for 3 weeks. He has been using crutches for 1 month following a severe ankle injury. Physical examination shows weak extension of the right hand at the wrist and difficulty raising the right arm above the shoulder. This patient most likely has a nerve injury at which of the following labeled locations in the diagram?

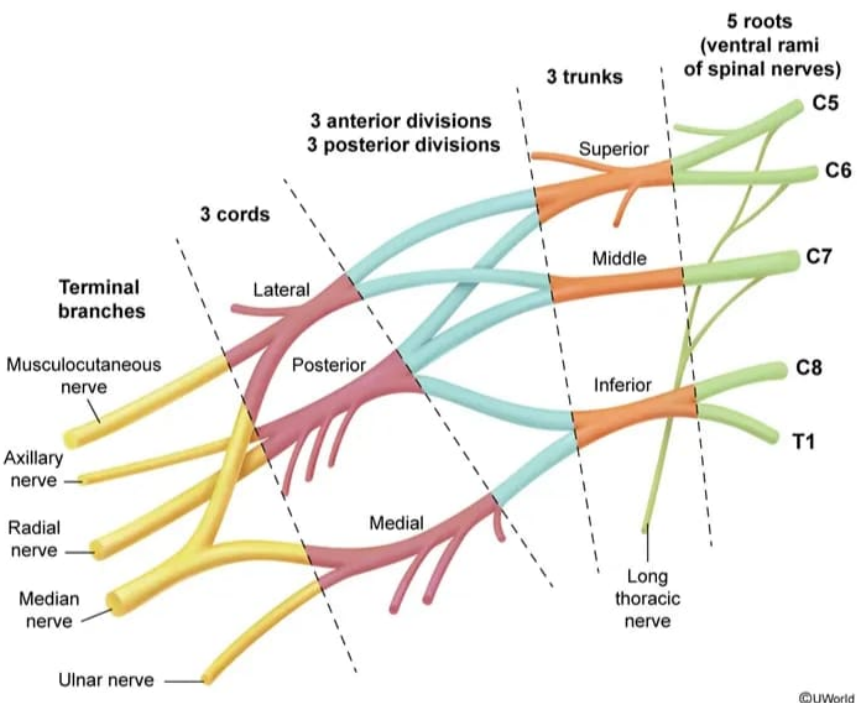
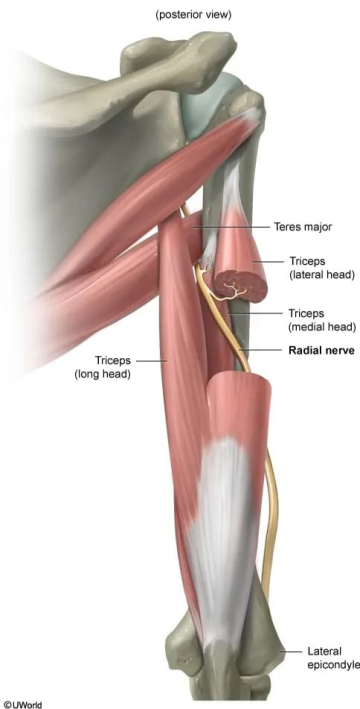
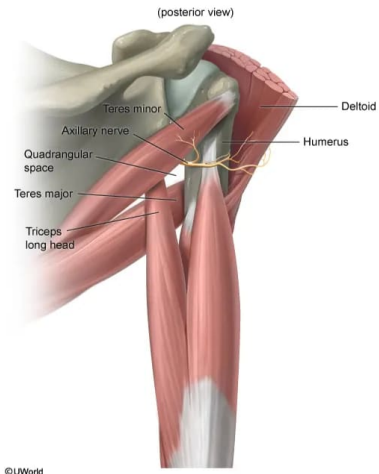


- A. A
- B. B
- C. C
- D. D
- E. E

▼ Explanation

- **Answer is C**
 - **IMP Clues:**
 - Has been using crutches (crutches compress the axilla, which have the brachial plexus)
 - Weak extension of the right hand at wrist (Extension is affected = radial nerve)
 - Difficulty raising the right arm above the shoulder (Raising arm = Axillary nerve)

- **Dx → Posterior Cord Injury**
 - Posterior Cord divides to give **axillary nerve & radial nerve**
 - Axillary Nerve innervates the **shoulder** muscle (+ others, but this is what we need now) → **Inability to raise arms**
 - Radial Nerve which innervates the **extensors** of the upper limb → **Inability to extend wrist**



▼ Other Choices

- **Choice A → Musculocutaneous nerve** which innervates the biceps.
 - Injury = inability to flex or supinate arms
- **Choice B → Radial nerve** which innervates the arm extensors.
 - Injury = inability to extend arm or wrist.
 - Shoulder would still be intact though, so incorrect.
- **Choice D → Ulnar nerve** injury + mild affection of median nerve.
 - Injury of ulnar nerve = Claw hand + atrophy of hypothenar eminence + loss of ulnar flexion + loss of adduction & abduction of fingers + loss of thumb adduction
- **Choice E → Median Nerve** injury
 - Injury would cause symptoms similar to carpal tunnel syndrome
 - Atrophy of thenar eminence + loss of sensation of lateral three & half fingers + ape hand deformity.

Q31

An unimmunized 1-year-old boy is admitted to the hospital because of fever, irritability, and a stiff neck. Cultures of the nasopharynx and cerebrospinal fluid grow gram-negative coccobacilli. Electron microscopic examination shows the presence of pili on the bacteria recovered from the nasopharynx, but absence of pili on the bacteria of the same species recovered from the cerebrospinal fluid. Which of the following processes shuts off expression of pili in this bacterium following invasion?

- A. Horizontal gene transfer
- B. Phase variation
- C. Plasmid acquisition
- D. Point mutation
- E. Transposon mutagenesis

▼ Explanation

- **Answer is B (Phase Variation)**
 - Q says culture of both nasopharynx & CSF grow gram negative coccobacilli; however, the bacteria in the nasopharynx have pili, while those in the CSF have no pili. Q asks what process shuts off expression of pili.
 - **Choice A → Horizontal Gene Transfer**
 - This is how bacteria **exchange genes** with each other & has 3 types
 1. *Conjugation* (direct contact with the other bacteria)
 2. *Transduction* (viruses "bacteriophages" carry the DNA from one bacteria to another)
 3. *Transformation* (bacteria takes up free DNA from surroundings)
 - **This usually involves gaining / losing features not just "shutting off expression"**
 - **Choice B → Phase Variation**
 - This is how bacteria **"shuts off/on expression of genes"** depending in **environment** & to **evade host immunity**.
 - Bacteria can turn of genes of "components" they have like pili in this example, flagella, or LPS surface antigens.
 - It is **reversible**, meaning it is literally an **on/off switch, which changes based on environment & host immunity**
 - **Choice C → Plasmid Acquisition**
 - On the USMLE, Plasmid Acquisition will be the answer when they ask you about how the bacteria gained *antibiotic resistance (there are other ways)* or how did they produce that new toxin.
 - These changes are however irreversible; this is new DNA acquired by the bacteria
 - **Choice D → Point mutation**
 - Is when a single nucleotide changes in the DNA
 - It can in fact cause gene turn off but having the same bacteria in 2 different locations (different environments) with the bacteria in the CSF "turning off" its pili to evade the immune system points more to phase variation.

- Point mutation is a “mutation”. It is random & irreversible. What happened in the vignette seems calculated & controlled.
- **Change in environment → Change in features SCREAMS Phase variation**
- **Choice E → Transposon mutagenesis**
 - Like Point mutation, it is random & irreversible. Not “calculated” & controlled.
 - Transposons are “moving” DNA sequences within the genome that inserts itself into the DNA & causes disruption.

Q32

A previously healthy 7-year-old girl is brought to the physician by her parents because of a 1-month history of excessive urination; she also has had a 2.3-kg (5-lb) weight loss during this period. Her pulse is 110/min, and blood pressure is 92/58 mm Hg. Physical examination shows poor skin turgor and a fruity odor on her breath. Her blood glucose concentration is 612 mg/dL. Laboratory studies are most likely to show an increase in which of the following?

- A. Arterial pH
- B. Serum bicarbonate concentration
- C. Serum chloride concentration
- D. Serum potassium concentration
- E. Serum sodium concentration

▼ **Explanation**

- **Answer is D (Serum Potassium Concentration)**
 - **IMP Clues:**
 - Excessive urination & weight loss (buzzy for DM)
 - Pulse 110/min & BP is 92/58mmHg (she's shocked)
 - Poor skin turgor (dehydrated, probably hypovolemic shock)
 - Fruity odor & Blood glucose is 612mg/dl (that's DKA)
- **Dx → Diabetic Ketoacidosis**
 - “*Diabetic*” = affects diabetics (Type 1 DM) & may be in fact the first presentation of DM
 - “*Keto*” = Starvation & no insulin causes production of ketones
 - “*acidosis*” = ketones are acidic & cause metabolic acidosis
 - Let's go through the pathophysiology of DKA
 - **Diabetic patient undergoes fasting** (no insulin + increased glucagon, catecholamines, cortisol)
 - 1. **Increased gluconeogenesis**
 - Increase blood glucose
 - Glucose concentration bypasses renal reabsorption capacity → glucosuria.
 - Glucose is *hyperosmolar*, pulls more water into urine (**Osmotic diuresis**)
 - Where water goes, **solute (K, Cl, Na)** follow (**Electrolyte Disturbance**)
 - 2. **Increased Lipolysis**
 - Increased Free Fatty acids → Ketones production
 - Metabolic Acidosis (decreased HCO₃, decreased pH, decreased CO₂)
 - Kussmaul Breathing (compensatory mechanism to blow off CO₂ to decrease acidity)
 - Fruity / acetone Odor
 - 3. **Hyperkalemia**
 - **Dysfunction of Na/K ATPase**
 - 3Na stays in and 2K stays out ⇒ hyperkalemia

? How are the serum & total Potassium concentrations affected in DKA?

▼ **Answer**

Decreased Total Potassium & Increased Serum Potassium

- K pulled out of the cells → High serum K
- Osmotic diuresis pulls K into urine & out → Low total K

- **Potassium-Proton Shift**
 - Acidosis causes H/K exchanger to take H into the cell & kicks K out (as a trial to decreases acidity) ⇒ hyperkalemia



What Normally Happens?

- **Insulin upregulates Na/K ATPase** → 3Na out for 2K in ⇒ *decreases* serum potassium
- **Insulin upregulates H/K exchanger** → H out for K in ⇒ *decreases* serum potassium

▼ Other Choices

- **Choices A & B** → pH & **Bicarb** decreases since we have metabolic acidosis
- **Choice C & E** → Both **Na** & **Cl** are pulled out into the urine (Osmotic diuresis) & peed out, so decreased Na & Cl.

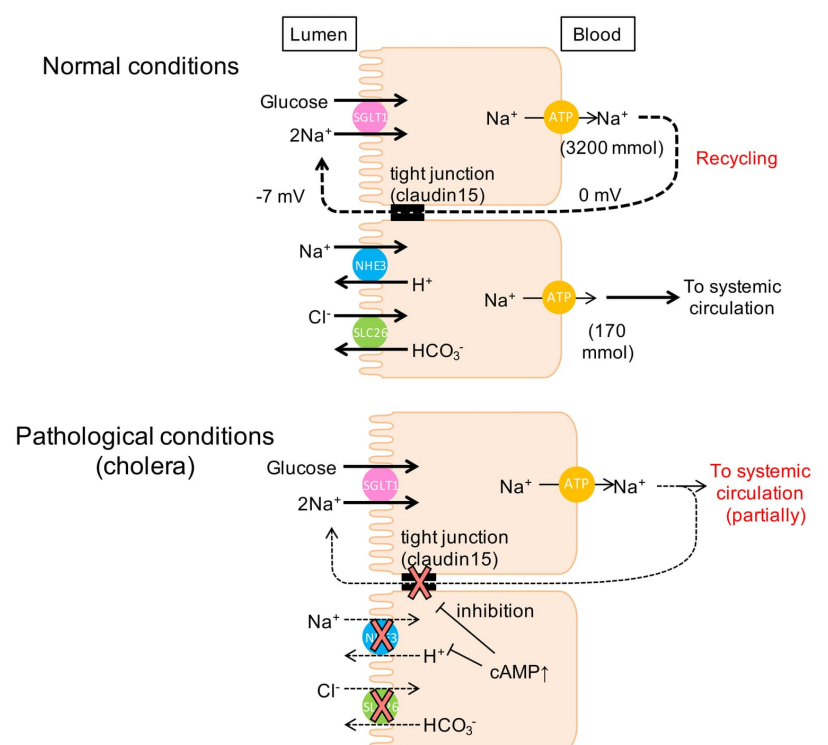
Q33

A previously healthy 12-year-old boy is brought to the emergency department because of a 6-hour history of severe diarrhea. His temperature is 37.0°C (98.6°F), pulse is 100/min, respirations are 16/min, and blood pressure is 110/70 mm Hg. He appears markedly dehydrated. Physical examination shows no other abnormalities. The most appropriate treatment for this patient is an oral rehydration solution containing which of the following sets of ingredients?

- A. Bicarbonate and potassium
- B. Bicarbonate and sodium
- C. Glucose and insulin
- D. Glucose and sodium
- E. Lactate and bicarbonate
- F. Lactate and potassium

▼ Explanation

- **Answer is D (Glucose and Sodium)**
 - **IMP Clues:**
 - 6-hour history of severe diarrhea (probably super dehydrated & electrolytes all over the place)
 - Appears markedly dehydrated (yep)
 - Q asks what should the ORS contain?
 - This Q test the concept of **SGLT-1 Co-transport**.
 - Basically, our intestines have this super potent SGLT-1 co-transported that **absorbs both sodium & glucose**.
 - When glucose & Sodium is given together, water & other electrolytes also follow. So, it's the perfect ORS in cases of severe diarrhea.
 - **Sometimes, in patients with severe diarrhea or even cholera, most of the intestinal transporters are messed up. SGLT-1 STILL WORKS IN THESE PEOPLE & IT IS SUPER EFFICIENT.** (Look at pic below)



Q34

A 4-month-old boy is brought to the office by his parents because of his small size, and difficulty feeding from a bottle. His mother states that he was recently adopted from a developing country, and his medical history is unknown. His vital signs are within normal limits. He is at the 10th percentile for weight and 40th percentile for length. Physical examination shows the findings in the photograph. The most likely cause of the facial finding involving the lip in this patient is a failure of normal fusion of which of the following pairs of structures?



- A. Lateral nasal and mandibular prominences
- B. Lateral nasal and maxillary prominences
- C. Lateral nasal and medial nasal prominences
- D. Mandibular and maxillary prominences
- E. Mandibular and medial nasal prominences
- F. Maxillary and medial nasal prominences

▼ Explanation

• Answer is F (Maxillary & Medial Nasal Prominences)

- Picture shows a cleft lip + palate. Let's review the embryological origins (ik man, i hate it too 🙄)

- Look at the picture below while you read the following:

◦ How do lips form?

- **Fusion of Medial nasal prominences to form Intermaxillary Segment, which fuses with Maxillary Prominences on either side.**
- So, **failure of fusion of intermaxillary segment (of medial nasal prominences) ⇒ Cleft Lip**

◦ How does the palate form?

- **Fusion of Maxillary prominences** (Palatine part of maxillary & intermaxillary segment)
- So, **failure of fusion of maxillary prominences/palatine shelves ⇒ Cleft Palate**

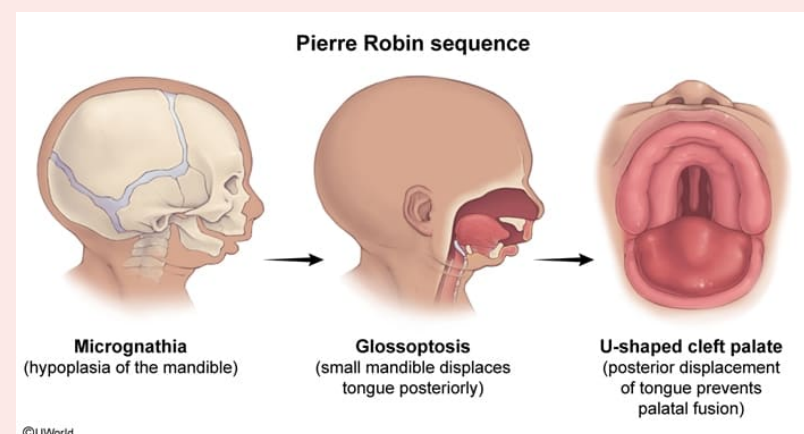
◦ How do you get Cleft lip + Palate?

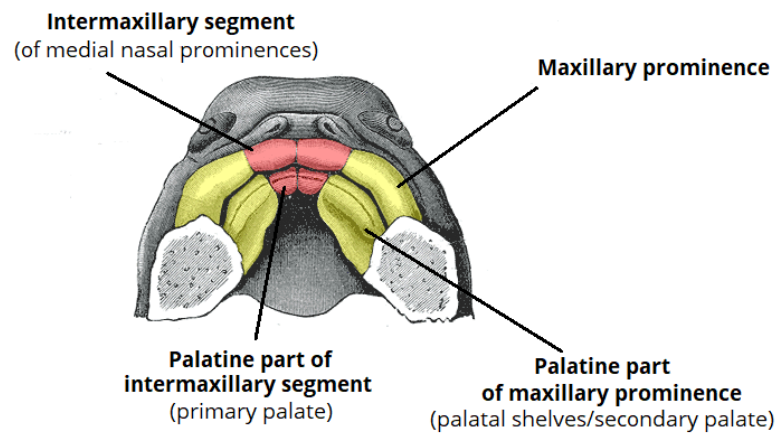
- **Failure of Fusion of Maxillary prominences & Medial nasal prominences**

What's a HY Related Condition?

Pierre Robin Sequence

- Named a "**Sequence**" as a primary defect causes in multiple second defects:
- **Micrognathia/Mandibular Retrognathia ⇒ Glossoptosis ⇒ U-shaped Cleft Palate**





▼ Other Choices

Remaining Choices not really assessed on the USMLE, but let's go through them via common sense.

- **Choice A → Mandibular prominence** makes up the mandible, so failure causes mandible hypoplasia or even absence (agnathia). Lateral nasal prominences form the ala of the nose, so failure to fusion would cause cleft ala.
- **Choice B → Lateral nasal prominences** form the ala of the nose, so failure to fusion would cause cleft ala.
- **Choice C → Lateral nasal prominences** form the ala of the nose, so failure to fusion would cause cleft ala
- **Choice D → Mandibular prominence** makes up the mandible, so failure causes mandible hypoplasia or even absence (agnathia).
- **Choice E → Mandibular prominence** makes up the mandible, so failure causes mandible hypoplasia or even absence (agnathia).

Q35

A 24-year-old woman, gravida 1, para 1, comes to the physician because of nervousness and tremor since delivering a healthy female newborn 6 weeks ago. She also has had a 5-kg (11-lb) weight loss during this period. She has a history of panic disorder and carpal tunnel syndrome. Her temperature is 37°C (98.6°F), pulse is 100/min, and blood pressure is 140/80 mm Hg. Physical examination shows a firm thyroid gland that is twice the normal size. Serum studies show a free thyroxine (FT₄) concentration of 2.4 ng/dL (N=0.8-2.4), thyroid-stimulating hormone concentration of less than 0.03 µU/mL, and 24-hour thyroid radioactive iodine uptake of 1% (N=8-25%). Which of the following is the most likely explanation for this patient's symptoms?

- Anaplastic thyroid carcinoma
- Hypothyroidism
- Release of stored thyroid hormone from a thyroid gland infiltrated by lymphocytes
- Release of thyroid hormone from a lymphomatous thyroid gland
- Release of thyroid hormone from a thyroid gland stimulated by antibodies

▼ Explanation

- **Answer is C**
 - **IMP Clues:**
 - Symptoms since delivering a healthy female newborn 6 weeks ago (key hx)
 - Nervousness & Tremor + Weight loss (Sounds like hyperthyroidism)
 - Firm thyroid gland that is twice the normal size (Some sort of thyroid pathology)
 - Free T4 of 2.4ng/dl (at upper limit) + TSH < 0.03 (Low) + Radioactive iodine uptake 1% (Low)
 - **Dx → Postpartum Thyroiditis**
 - Patient had low TSH & normal/high Free T4 → **Hyperthyroidism**
 - So, you think this is either *Grave's disease or something else that destroys thyroid follicular cells which causes hyperthyroidism.*
 - To differentiate we look at **Radioactive Iodine uptake**
 - If increased (increased Thyroid hormone synthesis) = Grave's
 - If normal/decreased = NOT graves (what we have here)
 - [🧠] **On the USMLE, Increased Radioactive Iodine uptake is Grave's. Nothing else. If not increased, it can be anything but Grave's.**
 - **History of delivery is the key → Postpartum Thyroiditis**
 - A *self-limiting* subtype of Hashimoto Thyroiditis that arises **< 1 year after delivery**

- Has 3 Stages
 1. **Hyperthyroidism** - due to destruction of follicular cells so thyroid hormone is released
 2. **Hypothyroidism** - depletion of preformed thyroid hormone + no cells to form new hormones
 3. **Euthyroidism** - cells start to regenerate so thyroid levels get back to normal

- Histology would be the same as Hashimoto → **Lymphocyte infiltration**

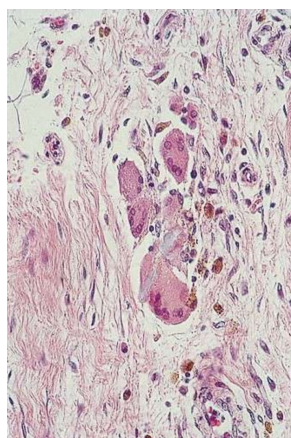
- **So all-in-all, what we have is hyperthyroidism due to release of stored thyroid hormone from a thyroid gland infiltrated by lymphocytes (Choice C)**

▼ Other Choices

- **Choice A → Anaplastic Thyroid Carcinoma**
 - Affects **older patients**
 - Presents with a **rapidly growing neck mass that causes compression symptoms (dyspnea, dysphagia, hoarseness)**
 - Associated with a **TP53 mutation** → Poor prognosis
- **Choice B** → Patient is clearly thyrotoxic not hypo. Will be hypo after though.
- **Choice D → Refers to Hashimoto Thyroiditis**
 - Yes, Postpartum thyroiditis is a subtype of Hashimoto's, but for Hashimoto's (the REAL ONE), you'd need antibodies to confirm.
 - Hashimoto can have a brief "thyrotoxic" phase before the classic hypothyroidism, so he's trying to trick use here.
 - Histology of Hashimoto → Hurthle cells + **lymphoid aggregates with germinal centers (so looks like lymph nodes), hence the "lymphomatous" thyroid gland**
- **Choice E → Grave's.** Will have High Radioactive Iodine uptake.

Q36

A 10-year-old girl has a slightly painful 2-mm subcutaneous nodule on her chin. Ten weeks ago, she required sutures after she lacerated her chin playing basketball. A photomicrograph of tissue obtained on biopsy of the nodule is shown. Which of the following best describes the pathologic features?



- A. Amyloid
- B. Granulation tissue
- C. Granuloma
- D. Lymphocytic infiltrate
- E. Neutrophilic infiltrate

▼ Explanation

- **Answer is C (Granuloma)**
 - Picture shows **multinucleated giant cells + epithelioid cells + some foreign object in the middle.**
 - What probably happened was that some foreign object was not debrided out as needed, so macrophages came & detected that foreign object, which was too large, so they decided they will just block it off the body → Make a granuloma.
 - Okay so what cytokine forms these granulomas?
 - **Interferon-gamma**

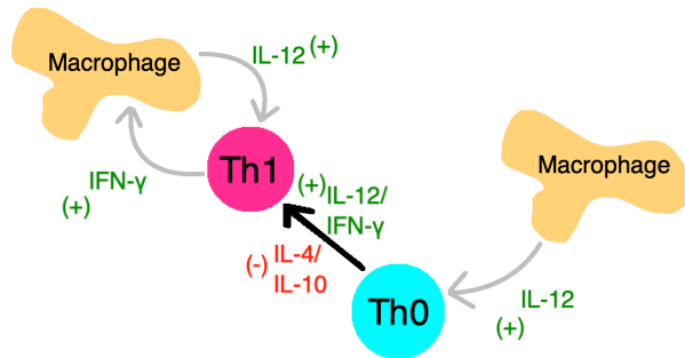


HY Related Concepts:

- **Cytokine** responsible for the **formation** of granulomas → **INF-gamma**
- **Cell** responsible for the **formation** of granulomas → **Macrophages**
- **Cytokine** responsible for the **maintenance** of granulomas → **TNF-alpha**

- Let's recap as this cycle is so HY:

1. **Th1** is stimulated to release **INF-gamma**.
2. **INF-gamma** activates **macrophages**.
3. **Macrophages** form the **granulomas**.
4. Both **IL-12** & **INF-gamma** further stimulate conversion of **Th0** to **Th1**.



? Patient started Infliximab + develops fever, night sweats, and a productive cough. What cytokine dysfunction caused the above C/P??

▼ Answer

- TNF-alpha** - Infliximab is TNF-alpha monoclonal antibody
- TNF-alpha maintains granulomas.
 - Infliximab inhibits TNF-alpha → reactivation of TB

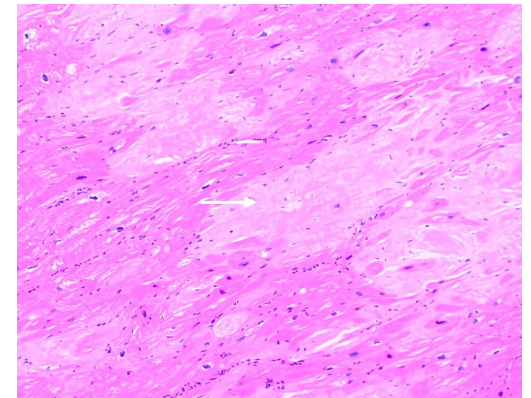
? Patient works in glass-making for 30 years. What drugs shouldn't be given to him without prior testing?

▼ Answer

TNF-alpha blockers - Patients with silicosis are at increased risk of TB as silica causes macrophage dysfunction. TNF-alpha blockers cause granuloma dysfunction. So, a patient with silicosis (glass making is HY risk factor), should get tested for TB before initiating TNF-alpha blockers

▼ Other Choices

- Choice A** → **Amyloidosis** is irrelevant here. This is a case of retained suture/foreign body forming a granuloma. There are no features of amyloidosis, No organ failure, no restrictive cardiomyopathy, no carpal tunnel syndrome. The histology is also not what you would see in an amyloidosis biopsy



- Choice B** → Remember the Wound Healing Diagram?
 - Granulation tissue formation** was between 3 days & 3 weeks. Here the Q says 10 weeks, which is way beyond when you'd expect granulation tissue.

▼ Review Wound Healing

1. **3 mins - 3 hours**
 - Homeostasis** (Vasoconstriction & Fibrin clot formation)
2. **3 hours - 3 days**
 - Inflammation** (Vasodilation, increased vascular permeability, neutrophils chemotaxis, macrophages influx)
3. **3 days - 3 weeks**
 - Proliferation** (Angiogenesis, Formation of Type 3 collagen granulation tissue, Re-epithelization)
4. **3 weeks - 3 months**
 - Remodeling** (Type 3 collagen is converted to Type 1 collagen which increases tensile strength of wound)

- Choice D** → The picture attached shows multinucleated giant cells & epithelioid cells. They're activated macrophages. **No lymphocytes seen here.**
- Choice E** → **Neutrophils infiltration** would happen in the first 2-3 days of wound healing. You'd already know that because you reviewed the Wound Healing that I placed above, right?

Q37

A 5-year-old boy with mental retardation is grossly obese and has facial features of Prader-Willi syndrome (PWS). Karyotyping and fluorescent in situ hybridization studies do not show deletion in the usual site on chromosome 15. Which of the following findings is most likely to confirm PWS in this child?

- Deletion in the short arm of chromosome 15
- Duplication within chromosome 15

- C. Large trinucleotide repeat expansion in the PWS area of chromosome 15
- D. Maternal origin of both chromosomes 15
- E. Translocation in the short arm of chromosome 15

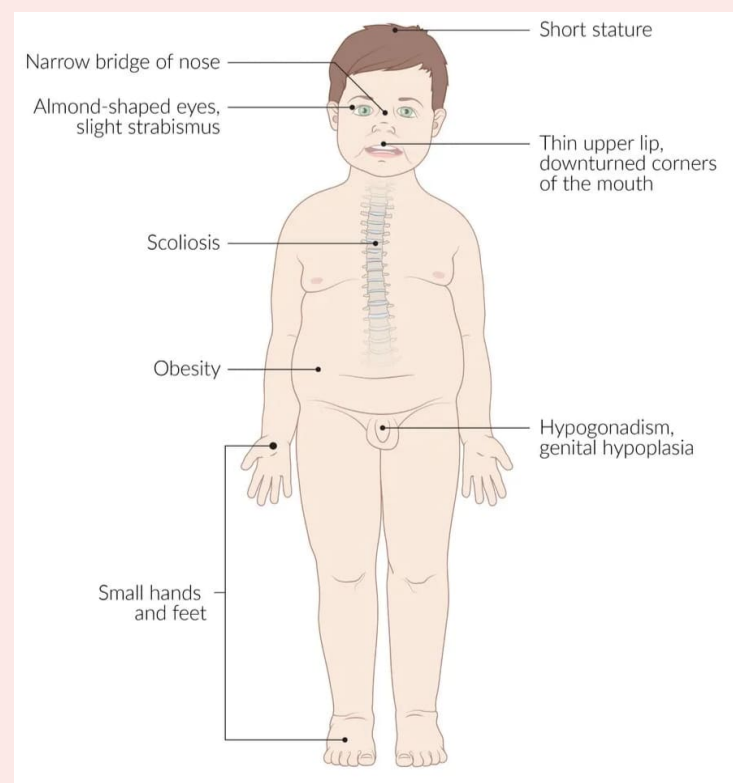
▼ Explanation

- Answer is D (Maternal Origin of Both Chromosomes 15)
 - Prader-Willi Syndrome
 - Presents as: **Mentally retarded Obese** kid with **hyperphagia**
 - Caused by either:
 1. Deletion of paternal chromosome 15 copy
 2. **Maternal uniparental disomy, where both maternal genes are received but both get silenced**
 - End Result → **Child with mental retardation + inability to regulate satiety → Hyperphagia → Obesity.**

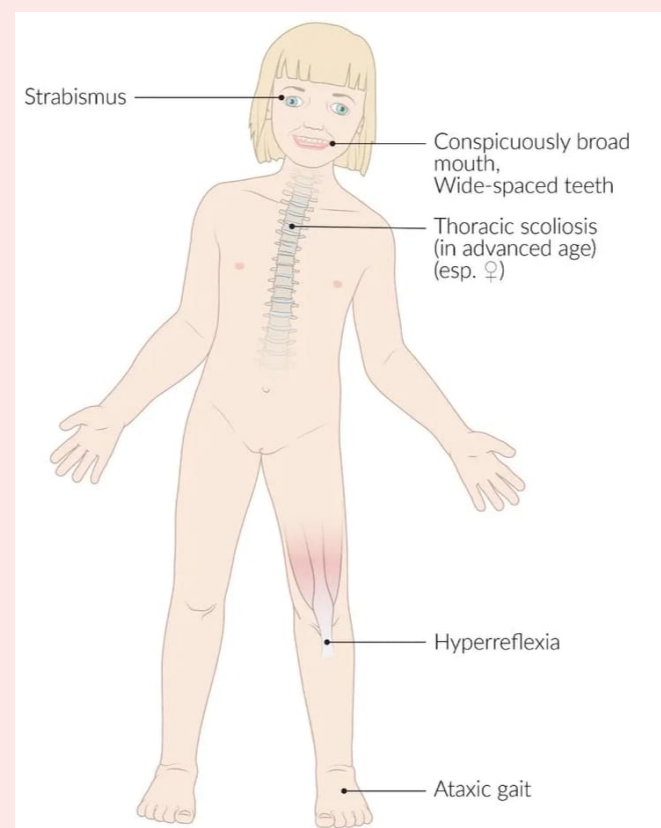
 **Compare between Prader-Willi Syndrome & Angelman Syndrome**

Feature	Prader-Willi Syndrome	Angelman Syndrome
Chromosome	15	15
Genetic mechanism	Loss of paternal allele function: - Paternal deletion OR - Maternal uniparental disomy	Loss of maternal allele function: - Maternal deletion OR - Paternal uniparental disomy
Normal imprinting	Maternal allele is normally imprinted (silenced), so you need the paternal copy to work	Paternal allele is normally imprinted (silenced), so you need the maternal copy to work
Key gene lost [asked on NBME]	Multiple genes	UBE3A gene (important for brain development)
Main features	- Hyperphagia & obesity - Hypotonia (infant) - Short stature - Hypogonadism - Mild intellectual disability	- Severe intellectual disability - Seizures - Ataxia - Inappropriate laughter ("happy puppet")
 Mnemonics	P rader-Willi = P aternal loss	Angel M an = M aternal loss

Shown below are Prader-Willi Syndrome Features:



Shown below are Angelman Syndrome Features:



Q38

A 45-year-old man who is HIV positive comes to the physician because of a 1-week history of headaches and blurred vision. A lumbar puncture is done. Laboratory studies show:

Serum glucose	95 mg/dL
Cerebrospinal fluid	
Appearance	cloudy, straw-colored
Leukocyte count	400/mm ³ (100% lymphocytes)
Erythrocyte count	50/mm ³
Glucose concentration	30 mg/dL

Total protein concentration	68 mg/dL
Fungal stain	positive for yeast

The most appropriate treatment for this patient is a drug with which of the following mechanisms of action?

- A. Antagonism of murein hydrolase
- B. Blockade of microtubule polymerization
- C. Disruption of the pathogene cell membrane
- D. Induction of cytochrome P450 enzymes
- E. Inhibition of pathogen cell wall synthesis

▼ Explanation

- **Answer is C (Disruption of the pathogen cell membrane)**
 - **IMP Clues:**
 - HIV positive (Now we have special disease in mind)
 - Headache & Blurred vision (probably due to high intracranial pressure, so maybe meningitis?)
 - Lumbar puncture shows cloudy-straw-colored fluid (has increased cells, usually infection), 100% lymphocytes (TB, fungus, or viral), Fungal stain positive for yeast (confirmed fungal etiology)
- **Dx → Cryptococcus meningitis**

⚠ HIV patient + meningitis → Always check for **Cryptococcus Neoformans** First

- What is the treatment of Cryptococcus Meningitis?
 - **Amphotericin B + Flucytosine THEN Fluconazole for 1 year.**
 - Amphotericin B MOA
 - **Ionophore - forms pores in cell membrane (Choice C)**
 - Flucytosine MOA
 - **metabolized to 5-Flurouracil which inhibits thymidylate synthase** (inhibits DNA & RNA formation)
 - Fluconazole MOA
 - **-azole; inhibits ergosterol synthesis via inhibition of 14-demethylase**



The 3 stains used to diagnose Cryptococcus Neoformans:

1. **Methenamine Stain**
2. **Mucicarmine Stain**
3. **India Ink**

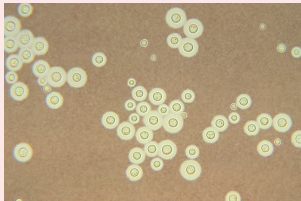


Cryptococcus Neoformans Microbiology Quiz!

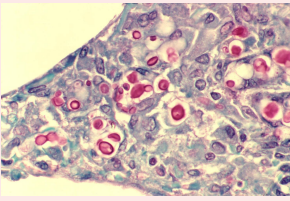
- ▼ What is the composition of Cryptococcus Neoformans capsule?
Repeating Polysaccharides
- ▼ How does patients get Cryptococcus Neoformans?
Inhalation near pigeon droppings
- ▼ What's another way to diagnose Cryptococcus Neoformans by its capsule?
Latex Agglutination

Below are the stains that can be used for Cryptococcus Neoformans:

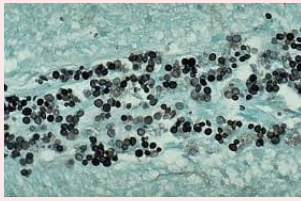
India Ink Stain:



Mucicarmine Red Stain:



Methenamine Silver Stain:



▼ Other Choices

- **Choice A** → Garbage. Not sure something like that exists. Anyways, you will not get assessed / nor see this again
- **Choice B** → Microtubule Inhibitors.

? What are the microtubule-related drugs on the USMLE?

▼ Answer

1. Microtubule Inhibitors

- Vincristine
- Vinblastine
- Colchicine
- Griseofulvin
- -bendazoles (albendazole & Mebendazole)

2. Microtubule Stabilizers

- Taxanes (Paclitaxel & Docetaxel)

- **Choice D** → A million different drug does that. It is not the main mechanism of action of any anti-fungal drug.
- **Choice E** → Echinocandins inhibits fungal cell wall synthesis by inhibiting 1,3, B-D-Glucan Synthase.

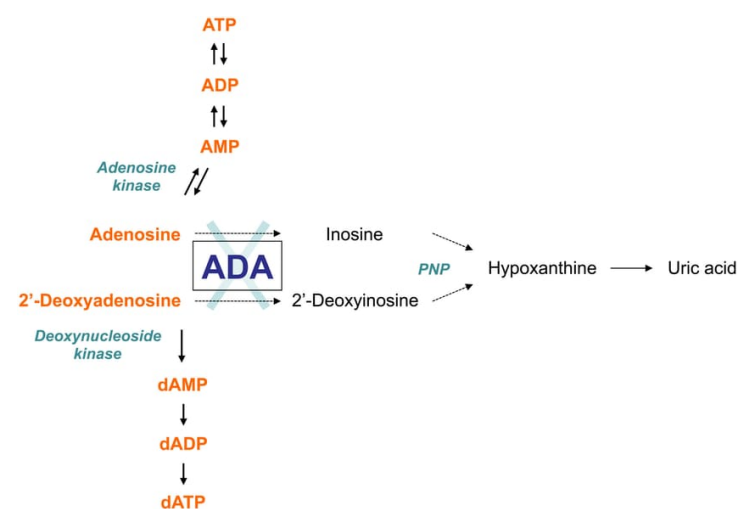
Q39

In patients with adenosine deaminase deficiency, there is a 50- to 100-fold increase in dATP concentration in T lymphocytes. This increase in dATP inhibits which of the following enzymes, thus compromising DNA synthesis?

- A. DNA ligase
- B. DNA polymerase I
- C. Nucleoside monophosphate kinase
- D. Ribonucleotide reductase
- E. Thymidylate synthase

▼ Explanation

- **Answer is D (Ribonucleotide reductase)**
 - **Garbage Biochemistry;** Let's go through what happens:
 - **Adenosine deaminase (ADA) deficiency** leads to a buildup of adenosine, which is then converted into deoxyadenosine and eventually to **dATP**
 - This massive increase in dATP concentration acts as a **strong allosteric inhibitor** of the enzyme **ribonucleotide reductase**.
 - This enzyme is crucial for **synthesizing the building blocks of DNA** (dATP, dGTP, dCTP, and dTTP) from their RNA precursors (ATP, GTP, CTP, and UTP).
 - **Inhibition of ribonucleotide reductase = inhibition of synthesis of all other deoxyribonucleotides = inhibition of DNA synthesis = inhibition of lymphocytes production (and other cells)**



? Patient has ADA. What would be the expected arrows of IL-2, NK cells, B-cells, T-cells?

▼ Answer

Decreased IL-2

Decreased NK cells

Decreased B-cells

Decreased T-cells

Q40

Patients with mucopolidosis II (I-cell disease) lack the phosphotransferase required for the formation of mannose 6-phosphate residues that are normally attached to enzymes destined for the lysosome. The mannose 6-phosphate sorting signal is normally added to proteins in the cis-Golgi. Which of the following most likely occurs to the lysosomal enzymes in these patients?

- A. Degraded in the lysosome
- B. Imported into the nucleus
- C. Retained in the rough endoplasmic reticulum
- D. Secreted from the cells
- E. Sorted into the mitochondria

▼ Explanation

- Answer is D (Secreted from the cells)

- I-Cell Disease

- Enzyme deficiency = **acetylglucosamine-1-phosphotransferase**
- Buildup = Many lysosomal enzymes
- Pathophysiology
 - **Cannot synthesize mannose-6-phosphate at the Golgi**
 - M6P needed to *target lysosomal enzymes to the lysosomes*
 - **Missing M6P = lysosomal enzymes are secreted into cytosol + serum**
- Clinical Features
 - **Course facial features**
 - **Joint contractures**
 - Hepatomegaly
 - Recurrent ear infections



I-CELL DISEASE HACKS

- If USMLE asks for the location of the error/problem → **Golgi**
- If USMLE asks for where the enzymes can't go → **lysosome**
- If USMLE asks for where the enzymes do go → **cytosol/plasma/serum**

Q41

A 37-year-old man comes to the physician for a follow-up examination. He has a 1-year history of hypertension. Despite aggressive pharmacotherapy, his blood pressure has averaged 188/131 mm Hg. His blood pressure today is 190/135 mm Hg. Funduscopic examination shows multiple flame hemorrhages with severe arteriolar narrowing. Which of the following disorders of blood vessels is most likely to be caused by this condition?

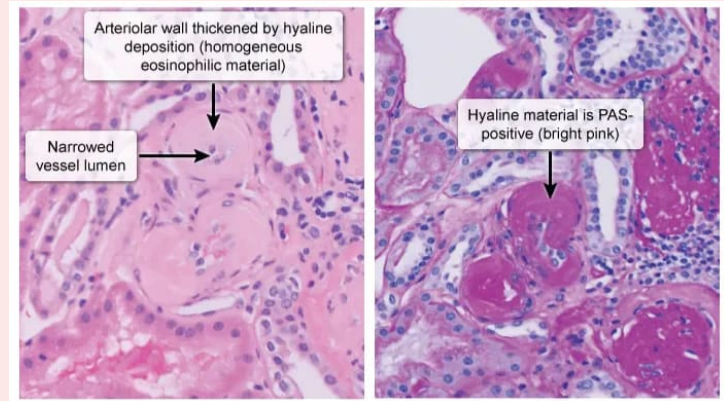
- A. Berry aneurysm
- B. Fusiform aneurysm
- C. Hyperplastic arteriolosclerosis
- D. Medial arterial calcification (Monckeberg arteriosclerosis)
- E. Temporal arteritis

▼ Explanation

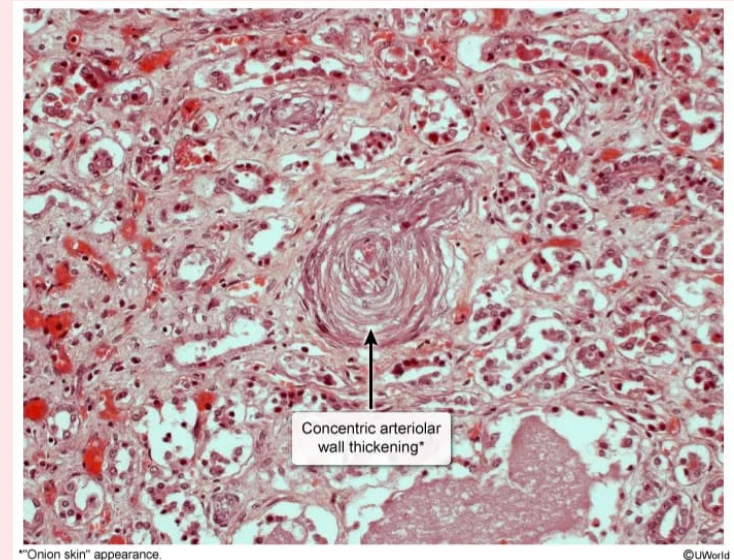
- Answer is C (Hyperplastic Arteriosclerosis)

- **IMP Clues:**
 - Despite aggressive therapy, blood pressure averaged 188/131 (chronic HTN)
 - BP today is 190/135 mmHg + Multiple flame hemorrhages with arteriolar narrowing (Hypertensive Emergency = Malignant HTN + End-organ damage)
- **Vascular Changes in HTN**
 - **Chronic HTN & DM → Hyaline Arteriosclerosis**
 - Chronic injury → **Plasma protein leakage** & Extracellular matrix deposition
 - Histology: **homogeneous, pink, glassy (hyaline) thickening** of the arteriolar wall
 - **Malignant HTN → Hyperplastic Arteriosclerosis +/- Fibrinoid Necrosis**
 - Acute injury → **smooth muscle proliferation** in *concentric* manner
 - Histology: **"Onion Skin"** appearance (*proliferation of smooth muscle in concentric / laminated manner*)

Picture below shows Hyaline Arteriosclerosis:



Picture below shows Hyperplastic Arteriosclerosis:



▼ Other Choices

- **Choice A → Berry aneurysms** commonly affect Circle of Willis. Their rupture cause Subarachnoid hemorrhage.
 - Chronic HTN is a very important risk factor
 - Other HY risk factors are ADPKD
- **Choice B → Fusiform Aneurysms** usually affect the aorta. They cause a pulsatile abdominal mass.

? Hypertensive smoker with vague abdominal pain + history of mother dying suddenly with no issue in her "heart". What is the diagnosis?

▼ Answer

Abdominal Aortic Aneurysm - Yes, they can be this vague.

- **Choice D → Medial Arterial Calcification**
 - Medial = Tunica Media
 - Arterial = Arteries
 - Calcification = Calcification (duh)
 - So, it is calcification in tunica media of arteries **with no narrowing of lumen**. It is a benign age-related disorder that is mostly discovered incidentally.
 - **Not associated with HTN**
- **Choice E → Temporal Arteritis** presents as **temporal headache + intermittent jaw pain +/- proximal muscle pain (NOT WEAKNESS)**.
 - How to confirm diagnosis → **ESR** (should be elevated)
 - **FIRST INTERVENTION → STEROIDS** (to prevent blindness)
 - **THEN → Biopsy**

A case-control study is conducted to assess the relationship between exposure to environmental tobacco smoke and sinusitis. The table shows the results of the study.

	Cases	Controls
Exposed to smoke	20	25
Not exposed to smoke	5	100

Which of the following is the prevalence of sinusitis in the general population?

- A. 16%
- B. 40%
- C. 50%
- D. 80%
- E. Cannot be determined from the data given

▼ Explanation

- Answer is E (Cannot be determined from the data given)
 - This is a **case-control study**.
 - In **case-control studies we measure the Odds Ratio**, not prevalence or incidence.
 - **Prevalence & Incidence are measured in cross-sectional Studies**
 - In **Cohort studies**, we measure **Relative Risk**.

Q43

A 52-year-old man with metastatic oat cell carcinoma begins to receive hospice care. Treatment with narcotic medication is initiated for severe bone pain. Which of the following actions by the physician regarding this treatment is most appropriate?

- A. Begin with minimal amounts of pain medication to monitor any adverse effects
- B. Carefully monitor the administration of this pain medication to avoid patient addiction
- C. Ensure that the patient receives enough medication to control his pain
- D. Make sure that the patient does not have direct access to the pain medication to avoid intentional overdose
- E. Regularly assess the patient for respiratory depression due to the pain medication

▼ Explanation

- Answer is C
 - The man has metastatic oat cell carcinoma & is in hospice care (His carcinoma is untreatable, so he's **receiving palliative treatment**). He is getting narcotic meds for the pain (this is part of palliative ttt).
 - You will get these Qs a lot on the USMLE, **Patient with end-stage cancer / Babies born with conditions that will kill them, and you will have to provide for them the most comfortable circumstances for them to die peacefully. (Choice C)**
 - **Choice A** → Minimal is not enough. Start with whatever dose makes him comfortable.
 - **Choice B** → Screw patient addiction, the patient has end-stage cancer.
 - **Choice D** → Again, the morphine overdose will do less harm than the cancer
 - **Choice E** → This is true & should be done; however, control the pain first & make the patient comfortable then you can assess & follow-up the complications.

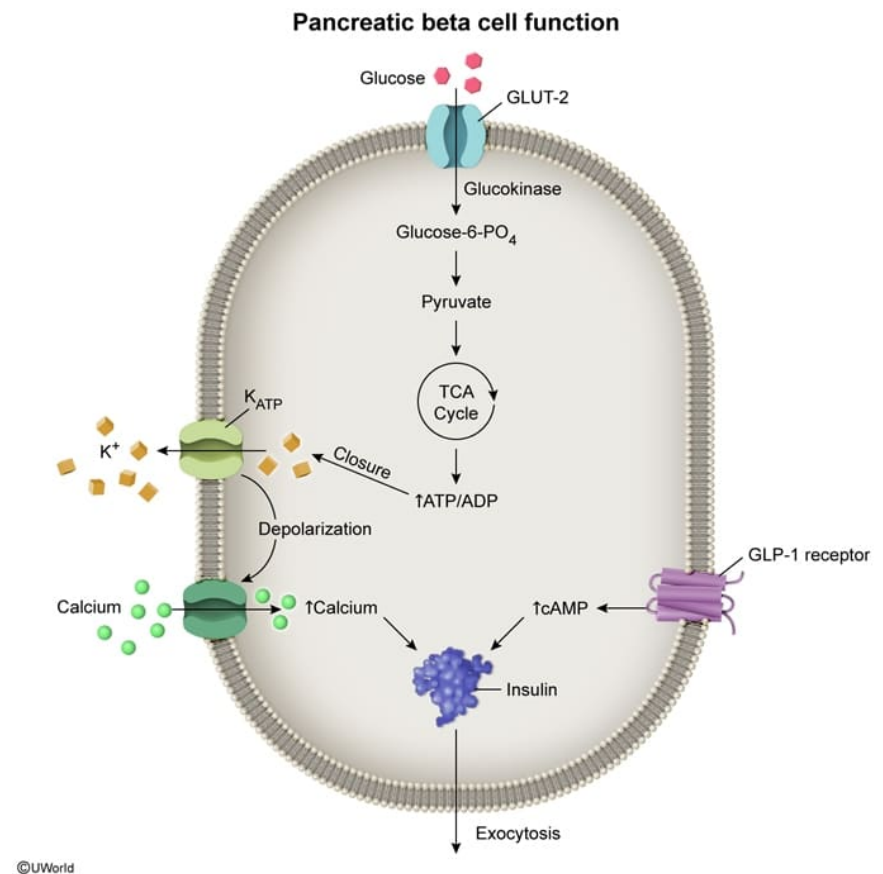
Q44

A healthy 25-year-old man eats a meal consisting of 60% carbohydrates, 30% fat, and 10% protein. His serum insulin concentration is increased after the meal. Which of the following is the most likely mechanism of pancreatic secretion of insulin in this man?

- A. Diffusion of insulin across the plasma membrane by an increase in intracellular bicarbonate concentration
- B. Diffusion of insulin across the plasma membrane through a glucose transporter
- C. Diffusion of insulin across the plasma membrane through a protein transporter
- D. Enzymatic hydrolysis of the plasma membrane
- E. Fusion of an intracellular vesicle with the plasma membrane

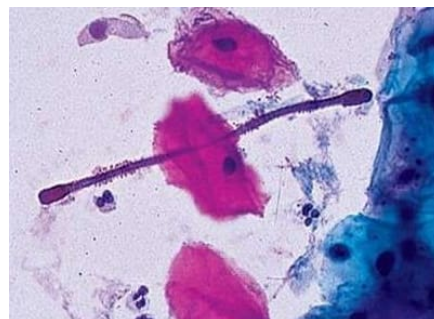
▼ Explanation

- **Answer is E (Fusion of an intracellular vesicle with the plasma membrane)**
 - Q asks about the mechanism of pancreatic secretion of insulin
 - Let's go through the Mechanism (we're nearly over with this block :P)
 1. You eat some carbs & the glucose get absorbed into the blood stream
 2. Glucose enters the Pancreatic beta cells via the **GLUT2 transporter**
 3. Glucose is metabolized (TCA → oxidative phosphorylation) and **ATP is produced.**
 4. **ATP-gated K channels close** → less K goes out → Depolarization
 5. **Voltage-gated Calcium channels open** → more Ca goes in
 6. **Calcium triggers the fusion of insulin-containing vesicles with plasma membrane**
 7. Insulin is secreted (finally)



Q45

A 60-year-old man comes to the physician because of progressive shortness of breath during the past 3 months. He states that for many years he has worked in a shipyard. His respirations are 25/min. Bilateral basilar crepitant crackles are heard. An x-ray of the chest shows reticulonodular pulmonary infiltrates consistent with interstitial fibrosis. Microscopic examination of sputum shows occasional elongate structures as shown. The fibrosis was most likely initiated by interaction of these structures with which of the following cell types?



- Alveolar capillary endothelial cell
- Alveolar macrophage
- Chondrocyte
- Ciliated columnar epithelial cell
- Clara cell
- Goblet cell
- Kulchitsky cell
- Squamous epithelial cell
- Type I pneumocyte
- Type II pneumocyte

▼ Explanation

- **Answer is B (Alveolar Macrophages)**
 - **IMP Clues:**
 - Progressive SOB + Bilateral basilar crepitant crackles (Lung Pathology)
 - Worked in a shipyard (massive keyword, ships on USMLE = asbestosis)
 - CXR shows reticulonodular infiltrates (buzzy for fibrosis)
 - Sputum Microscopy pics shown (Ferruginous Bodies)

- **Dx → Asbestosis**

- A type of **pneumoconiosis** (Restrictive Lung Disease) that affects **Lower Lobes**
- **Associated with Shipbuilding, roofing, and plumbing**

- HY Complications:

1. **Pulmonary Fibrosis**

- **Macrophages try & engulf the asbestos fibers**, but they are too large. This triggers the macrophages to **produce ROS, proteolytic enzymes, and cytokines to break down these fibers**.
 - ROS & Proteolytic enzymes → **Lung endothelial damage**
 - Cytokines → increase **Fibroblast activation** → **Collagen deposition**
 - **Endothelial Damage + Collagen Deposition = Fibrosis (Reticulonodular pattern / honeycombing)**

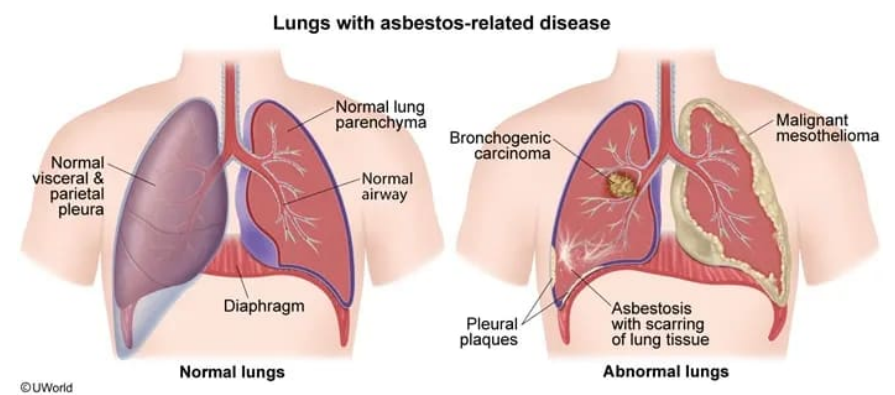
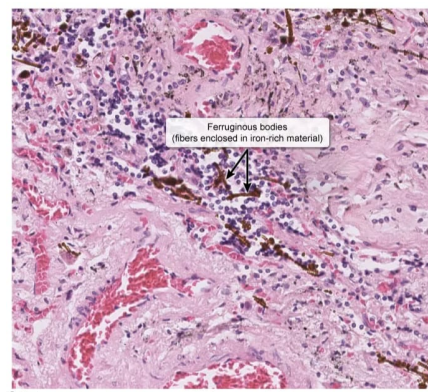
2. **Pleural Effusion & Disease**

3. **Malignancy** (Bronchogenic carcinoma > Mesothelioma)

- Most Common malignancy caused by asbestos exposure → **Bronchogenic Carcinoma**
- Most Common cause of Mesothelioma → **Asbestosis**

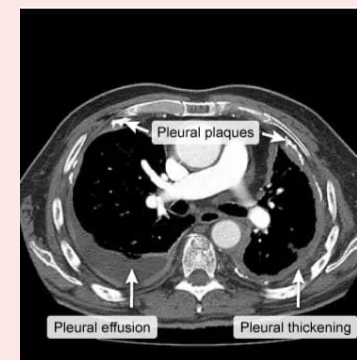
- Features:

- **Calcified Pleural Plaques**
- **Asbestos (Ferruginous) bodies**

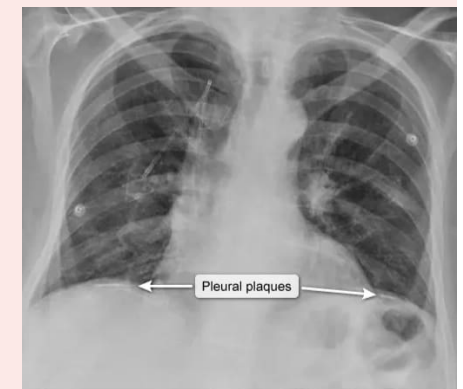


Shown below are imaging findings of Asbestos-Related Diseases:

Mesothelioma:



Asbestosis:



▼ **Other Choices**

- **Choices A & H & I** → Alveolar capillary endothelial cells + Type 1 pneumocytes (Squamous Epithelial cells) form the Alveolar-Arterial "exchange barrier". Their sole function is diffusion of air in & out.
- **Choice C** → Chondrocytes are cells that make up cartilage
- **Choice D & F** → Respiratory Epithelium (Ciliated columnar epithelium with goblet cells)
- **Choice E** → Clara cells (Club cells) are non-ciliated low columnar / cuboid cells with secretory granules. They degrade toxins via cytochrome P450. They also act as progenitor cells for other club cells & ciliated cells
- **Choice G** → Neuroendocrinal cells of the Lungs. Origin of Small Cell lung cancer.
- **Choice J** → Type 2 pneumocytes produce surfactant & responsible for lung regeneration.

Q46

A 65-year-old woman with a 20-year history of osteoarthritis of the hands now has pain radiating down the distal anterior thigh, knee, medial leg, and foot. Bony outgrowth of vertebrae compressing one of the spinal nerves is suspected. Compression of a nerve root in which of the following intervertebral foramina is the most likely cause of her symptoms?

A. T-10 to 11

- B. L-1 to 2
- C. L-3 to 4
- D. S-1 to 2
- E. S-4 to 5

▼ Explanation

- **Answer is C (L3 to L4)**

- Patient has a nerve root compression, which causes pain radiating down the distal anterior thigh, medial leg, and foot.

- **Dx → L3-L4 Radiculopathy**

- First, you must know the HY Dermatomes

- **C8-T1 → Hand**
- **T4 → Nipple Line**
- **T10 → Umbilicus**
- **L1 → Inguinal Ligament**
- **Lower Limb Dermatomes are HY so know them**

- Then, let's go through the HY Radiculopathies

- **C8-T1 → Hand muscles** weakness, numbness, atrophy
- **L3-L4 → Pain in distribution + Leg Extension** weakness + loss of **Patellar reflex**
- **L5-S1 → Pain in distribution + Planter Flexion** weakness + loss of **Achillis reflex**



Rapid Case Scenarios:

▼ Female Patient has weakness, atrophy, tingling & numbness in her hands. What is level of nerve compression?

C8-T1

▼ Female patient has Multiple Sclerosis; she reports pain & tingling on her chest at the level of her nipples. What is dermatome affected?

T4

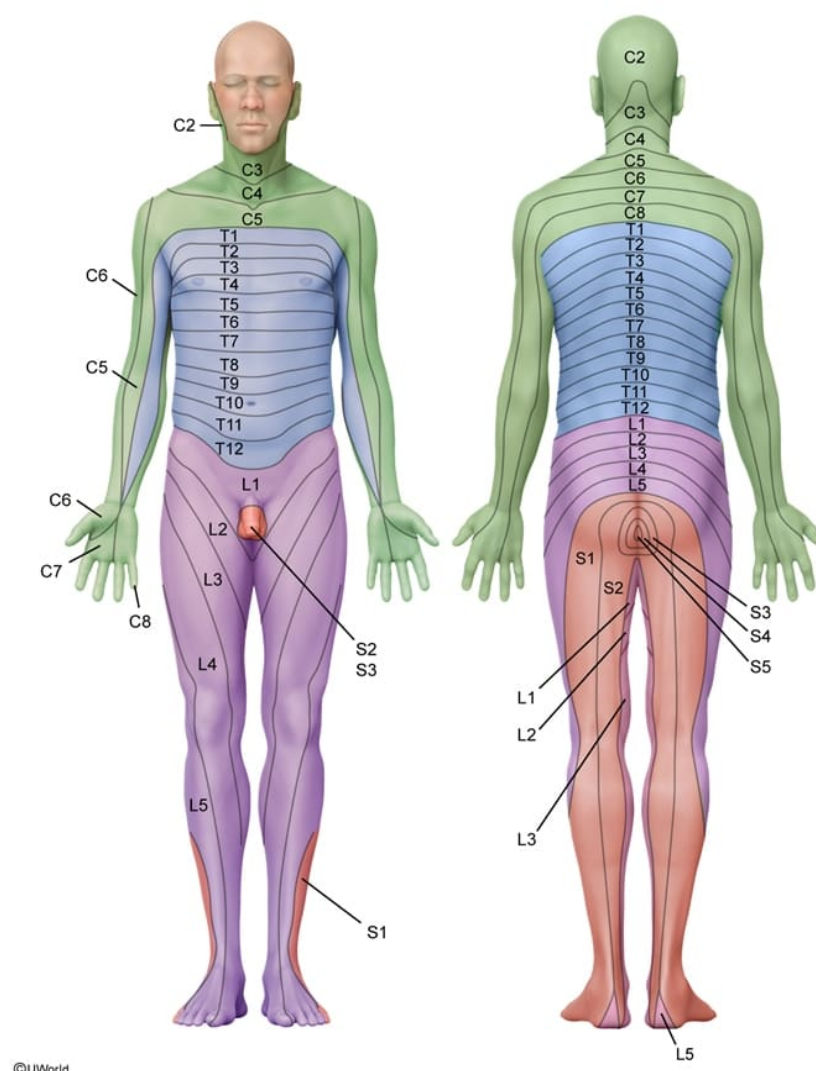
▼ Patient has LL weakness + loss of leg extension / patellar reflex. What is affected root?

L4

▼ Patient has LL weakness + loss of planter flexion / Achillis reflex. What is affected root?

S1

Dermatomes



▼ Other Choices

- **Choice A** → Would cause pain at umbilicus & region directly below it
- **Choice B** → Would cause upper & medial thigh pain
- **Choice D** → We talked about it
- **Choice E** → Would cause loss of sensation to the saddle area, loss of bladder & rectal control (pudendal nerve affection) + sexual dysfunction.

A 15-year-old girl is brought to the physician by her mother because of a 1-day history of redness and painful skin following sunbathing. She reports that she used sunblock every few hours. She takes no medications. Physical examination shows severe erythema of the back and extremities. There are no blisters. Which of the following best describes her condition?

- A. Allergic reaction to the sun
- B. First-degree burn
- C. Rhus dermatitis
- D. Second-degree burn
- E. Third-degree burn

▼ Explanation

- Answer is B (First-degree burn)

- IMP Clues:

- 1-day history of redness & painful skin following sunbathing
 - Takes no medications
 - No blisters

- Dx → 1st Degree Sun Burn

- Painful erythema with **NO Blisters** (only the epidermis is affected)
 - Excessive UVB radiation → DNA breaks → Keratinocytes apoptosis → Inflammatory reaction.
 - Increases risk of Skin Cancer (The whiter you are, the higher the risk as melatonin is protective)



Don't Get it Mixed Up!

- UVB → SunBurns
- UVA → TAnning & photoAging

▼ Other Choices

- Choice A → Allergic reaction to the sun would probably be due to medications. Tetracycline is the most notorious for photosensitivity. Patients with PCT + carbamazepine (or CYP inducers) can also get attacks of photosensitivity



14-year-old boy had an infection & the doctor prescribed some drugs. 2 days later, boy was playing in the park & developed severe sunburns. What is MOA of drug causing this reaction?

▼ Answer

Inhibits 30S ribosomal subunit - Tetracyclines

- Choice C → Ivy/Oak contain *urushiol*, which causes Type 4 Delayed HS reaction.
 - Presents as pruritic painful vesicles in a linear streak along site of contact with the plant
- Choice D → Involves the dermis, which would cause blisters
 - Painful erythema + Blisters = Type 2 Sunburn
- Choice E → Involves subcutaneous tissue, so PAINLESS.

Q48

A 48-year-old man begins furosemide therapy for pedal edema associated with biventricular failure and hypertension. Five days later, the edema is not fully resolved, and his serum potassium concentration has decreased from 4.2 mEq/L to 3 mEq/L. A drug with which of the following actions should be added to this patient's medication regimen?

- A. Blocks basolateral K⁺ channels in the collecting duct
- B. Decreases the luminal permeability to Na⁺ in the collecting duct
- C. Increases the delivery of Na⁺ and K⁺ to the collecting duct
- D. Increases the negative charge of the luminal tubule fluid
- E. Stimulates Na⁺-K⁺ATPase in the collecting duct

▼ Explanation

- Answer is B (Decrease the luminal permeability to Na in the CD)

- IMP Clues:

- Furosemide therapy for pedal edema (He's on a diuretic so expect MOA/SE Qs)
- Edema is not full resolved & serum K decreased to 3mEq/L. (There's the SE)
- Q asks what drug should be added?
 - Loop Diuretics are called "Loop," because they act in the *ascending loop of Henle* on the **Na/K/2Cl channels**.
 - They inhibit these channels, so
 - Na & Cl are excreted → **Water follow** (diuresis)
 - K is also excreted, causing the notorious SE → **hypokalemia** (what we have here)
- Sometimes the effect of the Loops are not enough, so *we need to add another diuretic*. Problem is, **most of them also cause hypokalemia**, so we are risking severe side effects.
- We need a **Potassium-Sparing Diuretic**.
 1. **Aldosterone Receptor Antagonists** in CD (*Spironolactone, Eplerenone*)
 2. **ENaC Inhibitors** in CD (*Amiloride, Triamterene*)
 - **They inhibit Na reabsorption in late-DCT & CD.**
 - This is the same as "Decrease luminal permeability to Na in CD". Easy.

Q49

A 10-month-old girl is brought to the emergency department because she is pale and unresponsive. Her mother has given her 3 adult doses of loperamide over the past 6 hours for diarrhea. Her pulse is 120/min and respirations are 10/min. Examination shows marked abdominal distention. If medication is required, which of the following is the most appropriate therapy?

- A. Bethenchol
- B. Diphenhydramine
- C. Epinephrine
- D. Naloxone
- E. Physostigmine

▼ **Explanation**

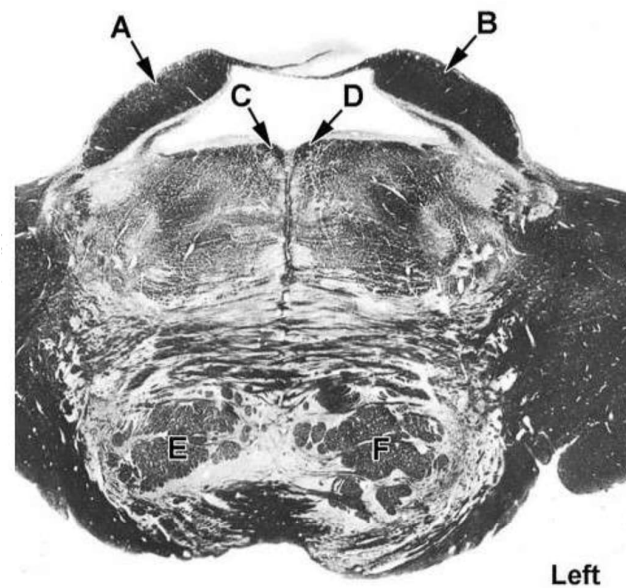
- **Answer is D (Naloxone)**
 - **IMP Clues:**
 - 3 adult doses of loperamide in past 6 hours (She's definitely ODeD)
 - Marked abdominal distention (Loperamide stimulates constipation → OD = no GI motility = Distention)
 - Q asks what should I give her?
 - **Loperamide**
 - **Mu-opioid receptor agonist** with **LOW** addictive potential. Like really low. This is because it **doesn't pass the BBB**. Only works peripherally.
 - Used as an **anti-diarrheal**.
 - Overdose = decreased GI motility to the point that it causes intestinal ileus.
 - In opioid overdose, **Naloxone is given (Opioid Receptor Antagonist)**.
 - Kicks Loperamide off the receptor & inhibits it → Symptoms Resolve

▼ **Other Choices**

- **Choice A** → Bethanechol is a *muscarinic receptor agonist* used for **flaccid/neurogenic bladder**
- **Choice B** → Antihistamine which has *anti-cholinergic side effects*. This would cause a worse outcome. Anti-cholinergic drugs also slow down GI motility, a big no no.
- **Choice C** → Epinephrine *stimulates adrenergic receptors*. This would further slow down GI motility, also another big no no.
- **Choice E** → Physostigmine is a *cholinesterase inhibitor*. It is used for **Myasthenia Gravis & Atropine Toxicity**.

Q50

A 28-year-old woman is brought to the physician because of a 3-week history of double vision. One year ago, she had an episode of blurry vision in her left eye that gradually improved during the next 2 months without treatment. Neurologic examination shows that the right eye does not adduct past the midline on horizontal gaze when looking to the left. When convergence is tested, the right eye is able to adduct past the midline. Rightward horizontal gaze is normal. This patient most likely has a lesion involving which of the following labeled structures in the photograph of the brain stem shown?



- A. A
- B. B
- C. C
- D. D
- E. E
- F. F

▼ Explanation

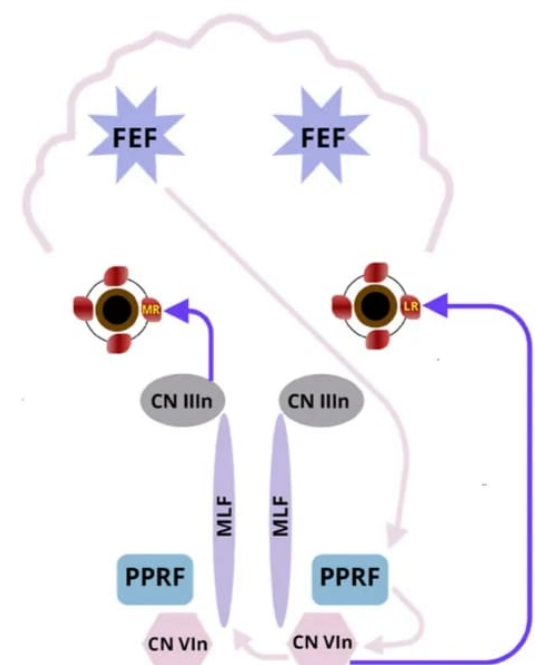
• Answer is C

◦ IMP Clues:

- 28-year-old woman (autoimmune disease more common in women)
- Double vision + hx of left eye blurriness (Sounds like MS, on the USMLE Middle aged woman + eye symptoms, think of MS)
- Right eye doesn't adduct when looking to the left but can adduct when convergence is tested (this tells us that CN 3 is intact, the problem is in the "connection" between the 2 eyes)
- Rightwards horizontal gaze is normal (both left & right eyes can look to the right together)

• Dx → Internuclear Ophthalmoplegia (INO)

- On the USMLE, INO = MS. Period.
- INO is caused by a lesion of the MLF (Medial Longitudinal Fasciculus) (Choices C&D)
- Basically, how the eye works is:
 - You decide to look to the **left**.
 - This is how the impulses go: (look at below pic as you read)
 1. **Right Frontal Eye Field on the cerebral cortex Activates**
 2. **Left PPRF is activated**
 3. **Left PPRF activates Left Abducens Nerve (Left eye abducts)**
 4. **LEFT PPRF activates Right MLF to activate right CN 3 (Right eye adducts)**
- Now Let's review the vignette.
 - "Right eye doesn't adduct when looking to the left" → **Connection to right PPRF to Right MLF is dysfunctional**
 - "Rightwards horizontal gaze is normal" → **Connection of Right PPRF to Left MLF is intact**



▼ **Other Choices**

- **Choices A & B** → Inferior Colliculus
- **Choice D** → Would present as left eye not adducting when looking to the right
- **Choices E & F** → Pyramids



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