



NBME EXPLANATIONS

NBME 23 Block 1

from CrackNBME

23-Block 1

Q1

A 75-year-old man with prostate cancer has metastases to the spine near L-2. Which of the following is the most likely route of metastatic spread?

- A. Inferior vesicle artery to a lumbar artery
- B. Lymphatic drainage to the iliac nodes
- C. Lymphatic drainage to the sacral nodes
- D. Prostatic venous plexus to the internal iliac veins
- E. Prostatic venous plexus to the vertebral venous plexus

▼ Explanation

- **Answer is E (Prostatic venous plexus to the vertebral venous plexus)**
 - Q asks for route of metastasis of prostate cancer to spine.
 - HY to know the significance of the **Batson's (vertebral) venous plexus**.
 - It's a **valveless** venous system that connects the pelvis and thoracic veins with the spine & brain.
 - **HY Cancers YOU MUST KNOW: [asked on NBMEs]**
 - **Prostate Cancer:** Prostatic Venous Plexus → Vertebral Venous Plexus
 - **Breast Cancer:** Intercostal Vein → Azygous Vein → Vertebral Venous Plexus.

Q2

A 2-year-old girl is brought to the physician because she is "cross-eyed." Physical examination shows moderate strabismus. If not treated, she will most likely have deficits in depth perception due to lack of appropriate competitive interactions in the visual cortex. Calcium entry through which of the following receptors mediates the outcome of this competitive process?

- A. γ-Aminobutyric acid A (GABA)
- B. Glycine
- C. Metabotropic glutamate
- D. N-methyl-D-aspartate (NMDA)
- E. Serotonin (5-HT₃)

▼ Explanation

- **Answer is D (NMDA)**
 - Q asks calcium entry through which receptor mediates the outcome of "this competitive process"
 - You probably (me included) have no idea what this competitive process is about or its steps. All you need is the word **"Calcium entry"**. So we know that our receptor has calcium involved somehow.
 - **NMDA receptors are the only receptors here that use Calcium.**
 - On the USMLE, if Qs are this vague/stupid, chances are they're just garbage/trick Qs.

Q3

A 45-year-old woman is brought to the emergency department because of a 1-day history of fever and constant, right-sided abdominal pain. She has had previous episodes of similar pain after high-fat meals, but they have always resolved in the past. Her temperature is 38.3°C (101°F), pulse is 102/min, and blood pressure is 100/60 mm Hg. Which of the following findings is most likely on abdominal examination in this patient?

- A. Inspiratory pause on right upper quadrant palpation
- B. Palpable gallbladder
- C. Periumbilical ecchymoses
- D. Rebound tenderness and guarding in the right lower quadrant

E. Tenderness of the epigastrium on palpation

▼ **Explanation**

- **Answer is A (Inspiratory pause on right upper quadrant palpation)**

- **IMP Clues**

- 45-year-old woman (remember the Fatty Forty Female phrase, yah this is it)
- Fever (some sort of -itis) + right sided abdominal pain after fatty meals (sounds like biliary)
- Q asks what is most likely to be found on abdominal examination of this patient?

- **Dx → Acute cholecystitis**

- **Inflammation of the Gallbladder**, most likely caused by a **gallstone**.

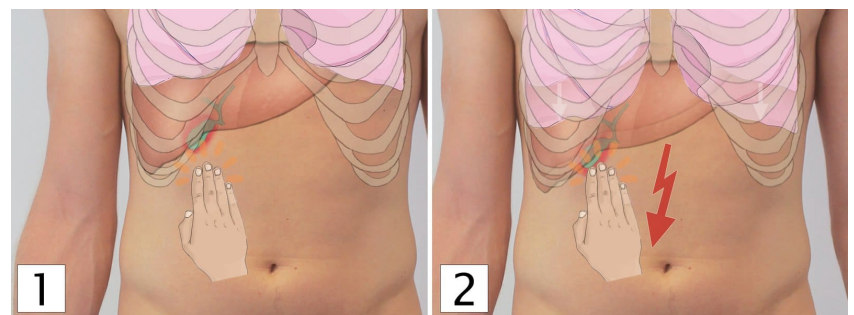
- **Estrogen** (causes upregulation of cholesterol synthesis) → Higher incidence of cholesterol stones formation.

- Stones sometimes get infected → Cholecystitis

- **RUQ Pain, fever, and Murphy's sign** (what the Q is assessing)

- **Murphy's sign** is a **pause in inspiration** caused by **deep RUQ palpation** of the **inflamed gallbladder**.
- Basically when you inspire, the inflamed GB is pushed out + you try to palpate it deeply, if it touches your hand → pain → stops inspiration. Easy.

Picture below shows Murphy's Sign:



▼ **Other Choices**

- **Choice B → Palpable GB** could mean a few things

- **MOST IMP: A painless palpable GB + jaundice is pancreatic head cancer** until proven otherwise → **Obstructive jaundice**

- **Choice C → Actually HY and I want you to know this. So, pay attention. Retroperitoneal/Intraperitoneal organ bleeding (Most HY on the USMLE → spleen & pancreas) causes 2 important findings you need to know:**

1. **Grey Turner's Sign:** Flank discoloration
2. **Cullen's Sign:** Periumbilical ecchymoses

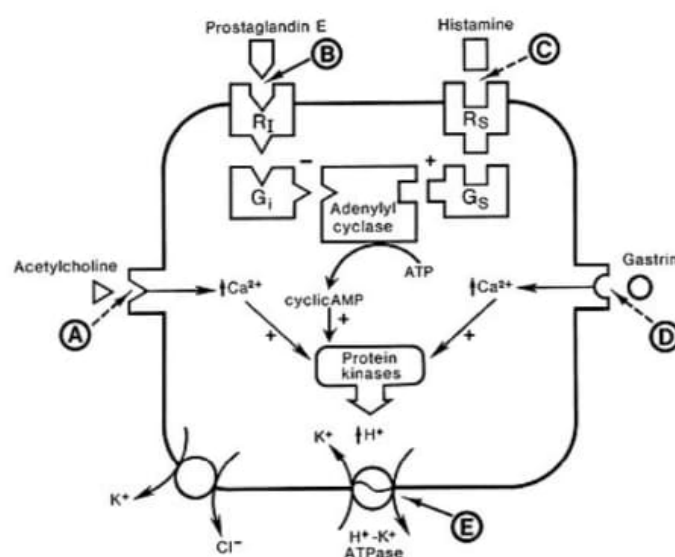


- **Choice D → Refers to a perforated appendix.**

- **Choice E → Usually refers to Peptic Ulcer on the USMLE.**

Q4

A 68-year-old man who has been treated for the past 4 weeks with a new nonsteroidal anti-inflammatory drug for rheumatoid arthritis has severe gastric burning and discomfort. A second drug decreases these adverse effects, but the patient develops severe diarrhea. The second drug most likely acts at which of the following sites?

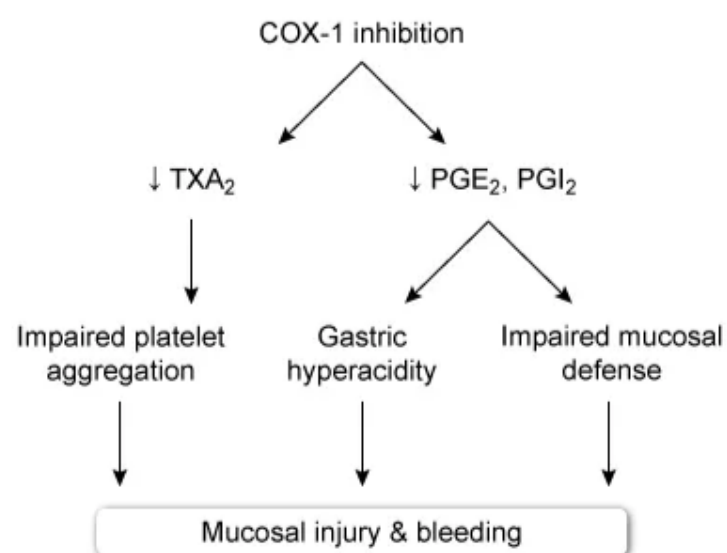


- A. A
- B. B
- C. C
- D. D
- E. E

▼ Explanation

• Answer is B

- Okay, appears confusing at first I know, but let's approach it together.
- Patient has RA + managed with NSAIDs, which on the long run caused gastritis/GU due to decreased PG synthesis.
 - PG are produced by COX, which is inhibited by NSAIDs
 - PG protect the gastric mucosa. No PG = No gastric mucosa protection = Gastritis/GU
- A second drug is added to decrease these side effects but causes diarrhea.
 - No drugs affect Choices A & D
 - All remaining choices technically "decreases these adverse effects", but the keyword is diarrhea
- Choice C → H2-Blockers decrease acid production
 - HY Side effects: Cimetidine → CYP450 inhibitor & gynecomastia
- Choice E → PPIs also decrease acid production
 - HY Side effects: Osteoporosis, rebound hypersecretion, increases risk of acid labile infections
- Choice B → Misoprostol (PG analogue) would restore the normal protective layer → gastric mucosa
 - Actually First line for NSAID-induced gastritis/gastric ulcers
 - HY Side effects: Diarrhea, abdominal cramping, and uterine contractions (contraindicated in pregnancy, unless of course for the use in abortion)



? What are the drugs used in medical abortion?

▼ Answer

- First → Mifepristone (Progesterone Receptor Antagonist)
- 24-48hrs after → Misoprostol (PGE1 analogue)

[Order is asked on NBME] Mifepristone THEN Misoprostol.

Q5

A 65-year-old man recovering from a cerebral infarction due to atherosclerotic vascular disease begins treatment with warfarin. Clopidogrel is added to the medication regimen because of his intolerance to aspirin. Which of the following is the most likely mechanism of decreased platelet aggregation due to clopidogrel in this patient?

- A. Changing the tertiary structure of fibrinogen

- B. Enhancing cAMP-mediated inhibition of platelet thromboxane A₂ synthesis
- C. Increasing prostacyclin (PGI₂) biosynthesis in vascular endothelium
- D. Preventing ADP-stimulated platelet activation
- E. Stimulating biosynthesis of cell adhesion molecules

▼ Explanation

- **Answer is D (Preventing ADP-stimulated platelet activation)**
 - Q asks what is the mechanism of decreased PLT aggregation due to Clopidogrel?
 - Simple pharma. **Clopidogrel is an anti-platelet medication (ADP2Y12 Blocker)**. So, choice D makes the most sense.
 - HY ADP blockers are: **Prasugrel, Clopidogrel, Ticlopidine, and Ticagrelor**
 - **How do they work?**
 - **Inhibition of ADP2Y12 Receptors on platelets → decreased expression of Glycoprotein IIb/IIIa Receptors on platelets → Inhibition of platelet aggregation**



Remember that!

Glycoprotein **Ib** activation ⇒ Platelet **Adhesion**
 Glycoprotein **IIb/IIIa** activation ⇒ Platelet **Aggregation**



What are the HY side effects of ADP2Y12 Blockers?

▼ Answer

1. **Thrombotic Thrombocytopenic Purpura** (especially **Prasugrel and Clopidogrel**)
2. **Hemorrhagic Stroke** (**Prasugrel > Clopidogrel**)
3. **Neutropenia** (**Ticlopidine**)

Let's Review Platelet Hemostasis:

***vWF was already released by endothelial cells in response to endothelial injury, causing its binding to exposed collagen

1. **Platelet Adhesion:** Platelets bind to vWF via **Glycoprotein Ib** Receptor
2. **Platelet Activation:** Change of platelet shape & release of **cytokines** (ADP, TXA₂, Calcium, and PAF)
3. **Platelet Aggregation:** Expression of **Glycoprotein IIb/IIIa Receptors & Fibrinogen**, resulting in the formation of white thrombus

▼ Other Choices

- **Choice A → Refers to Glycoprotein 2b/3a inhibitors (Abciximab, Eptifibatide, and Tirofiban)**, which **prevent PLT aggregation** (fibrinogen crosslinking is a step in PLT aggregation)
 - USMLE assess these as **"Fibrinogen antagonists"** sometimes
- **Choice B → Refers to Phosphodiesterase inhibitors (Dipyridamole & Cilostazol)**, which **inhibit PDE → increases cAMP in platelets → less PLT aggregation**
 - Also causes vasodilation of **arteries** (used in chronic limb ischemia, patient that gets claudication/leg pain/cramping after walking)
 - *USMLE might show you a stupid sketch and ask you to point out where Cilostazol acts, choose the arteries.*
- **Choices C & E → No drug does this. Garbage.**

Q6

A 65-year-old woman with diabetic ketoacidosis has had a fever and proptosis of the left eye over the past 3 days. She is unable to move the left eye. A black eschar is present on the nasal mucosa. Which of the following is the most likely diagnosis?

- A. Aspergillosis
- B. Candidiasis
- C. Coccidioidomycosis
- D. Cryptococcosis
- E. Histoplasmosis
- F. Mucormycosis

▼ Explanation

- **Answer is F (Mucormycosis)**
 - **IMP Clues**
 - Woman with diabetic ketoacidosis (major risk factor for mucormycosis, remember sketchy?)
 - Fever and proptosis of the left eye + unable to move the eye (sounds like cavernous sinus thrombosis)
 - Black eschar is present on the nasal mucosa (characteristic for Mucor & Rhizopus infections)

- Dx → Mucormycosis
 - An **opportunistic fungi** that affects **immunocompromised patients**
 - **Diabetics or DKA is a buzzy major risk factor**

- Transmission via **spore inhalation** → spores **proliferate in blood vessels of nasal mucosa** → **necrosis (the black eschar)**

- Can spread to the **cavernous system** → **Cavernous sinus thrombosis** (Swelling, Fever, Proptosis, Ophthalmoplegia)
- Can invade through the **cribriform plate** into the skull → **Frontal Lobe Abscess**



- Treatment → **Amphotericin B**

? What is the MOA of Amphotericin B?

- ▼ Answer
Ionophore - causes holes in cell membrane of fungus



? Differentiate between the morphology of Mucormycosis & Aspergillus.

▼ Answer

- **Mucormycosis** → **90 degree** branching with **NO** septations
- **Aspergillus** → **Acute angle** branching with **septations**

Q7

A 42-year-old man comes to the physician because of a 1-month history of intermittent high-grade fever, dizziness, diarrhea, and fatigue; he also has had a 5-kg (11-lb) weight loss during this period. During a trip to India 3 months ago, he was bitten by an insect, and he says that a sore developed at the site of the bite. His temperature is 38°C (100.4°F). Physical examination shows splenomegaly and muscle wasting. Laboratory studies show pancytopenia. Which of the following is the most likely vector of this patient's infection?

- A. Black fly
- B. Deer fly
- C. Ghat
- D. Sand fly
- E. Tsetse fly

▼ Explanation

- Answer is D (Sand fly)

◦ IMP Clues

- He was bitten by an insect (probably an arthropod-borne disease)
- Fever + Splenomegaly + labs show pancytopenia (splenomegaly + pancytopenia from an insect bite, that's leishmaniasis)

- Dx → **Visceral Leishmaniasis (Kala Azar Fever)**

- Transmitted by **Sand Fly**, on the USMLE it is classically found in **"hot areas" (Middle East, Africa, South America)**

- Causes Leishmaniasis, which has 2 HY presentations:

1. Visceral Leishmaniasis (Kala Azar Fever)

"Remember that visceral leishmaniasis is caused by **Leishmania donovani**."

- Presents as a classic triad of **hepatosplenomegaly, pancytopenia, and fever** +/- weight loss & hyperpigmented skin lesions
 - Promastigotes (inactive in female sandfly) → blood → **phagocytosed by macrophages** → transforms into **amastigotes** → multiply → spread via reticuloendothelial system
 - **Liver & Spleen** ⇒ **Hepatosplenomegaly**
 - **Lymph Nodes** ⇒ **Generalized Lymphadenopathy**
 - **Bone Marrow** ⇒ **Pancytopenia**



- Diagnosis → seeing the *amastigotes in macrophages*

2. Cutaneous Leishmaniasis

- Presents as a **treatment-resistant *ULCER***
 - Qs could be so vague and is usually "*a military personal that is sent to the Middle East, who slept in a hot area + got bitten and the bite then ulcerated/became ttt-resistant.*"

? How is Visceral Leishmaniasis vs Cutaneous Leishmaniasis treated on the USMLE?

▼ Answer

- Cutaneous Leishmaniasis ⇒ **Sodium Stibogluconate**
- Visceral Leishmaniasis ⇒ **Amphotericin B**

? What type of immunity is essential for disease control?

▼ Answer

Th1 (Cell Mediated Immunity) as it is intracellular.

▼ Other Choices

- **Choice A** → Transmits Onchocerca Volvulus
- **Choice B** → Transmits Loa Loa infection
- **Choice C** → Garbage and not on USMLE anywhere.
- **Choice D** → Causes African Sleeping Sickness (Trypanosomiasis)

Q8

A 62-year-old woman is brought to the physician because her left foot has become cool and discolored, and she has begun to have difficulty walking. Her symptoms began 4 hours ago with several acute episodes of palpitations followed by tingling and numbness of the left foot several hours later. She was not too concerned until the current symptoms occurred. Which of the following is the most likely explanation for these findings?

- A. Early signs of an intracranial tumor
- B. Embolus to the femoral artery with left leg ischemia
- C. Peripheral neuropathy caused by lumbar nerve root compression
- D. Small cerebral hemorrhage due to a sudden episode of hypertension
- E. Small cerebral infarction due to regional ischemia

▼ Explanation

- **Answer is B (Embolus to the femoral artery with left leg ischemia)**
 - **IMP Clues**
 - Left foot became cool and discolored + difficulty walking (Cool & discolored leg, probably dusky purple or blue, sounds like limb ischemia)
 - Symptoms began 4 hours after severe acute episodes of palpitations (sounds like AF, which would cause a mural thrombus formation, which can get launched off anywhere. In this case it seems like the left leg was the target)
 - Followed by numbness of the left foot (nonspecific, could be neuro, stroke, or due to ischemia. But leg numbness + local manifestations like color change and cold limb = Acute Limb Ischemia)
- **Dx → Acute Limb Ischemia secondary to AF**
 - **Basically, AF causes no "efficient" atrial contractions → blood stagnates → a thrombus forms (called mural thrombus) → Can get launched off anywhere as an embolism:**
 - Cerebral Arteries: **Stroke**
 - Retinal artery: **Central Retinal Artery Occlusion (CRAO)** → **painless** loss of vision + cherry-red macula
 - SMA/IMA: **Acute Mesenteric Ischemia** → severe GI pain + bleeding
 - Limb arteries: **Acute Limb Ischemia** → **Loss of pulse, Color changes, Cold limb, Limb pain**

The Classic Presentation of Acute Limb Ischemia is the "6 Ps":

- Pain in the distal extremity.
- Pallor of the skin and delayed capillary refill.
- Paresthesia, including tingling, numbness, and loss of sensation often starts in the dorsum of the foot.
- Pulselessness is expected in the affected extremity (lack of a palpable arterial pulse).
- Poikilothermia (coldness to touch) is typically present.
- Paralysis is a late finding in acute limb ischemia.

- This patient got the latter presentation → **Acute Limb Ischemia**
 - Out of these, **Choice B** makes the most sense. AF caused an embolus that got launched into the leg arterial supply, the femoral artery.

? What are the Differential Diagnoses of Cherry-Red Macula?

▼ Answer

1. **CRAO**
2. **Tay-Sachs Disease**
3. **Niemann-Pick Disease**

▼ Other Choices

- **Choice A** → Early signs of ICP is like headache, blurry vision, early morning projectile vomiting. None of these signs of brain tumors. No seizures too. Unlikely.
- **Choice C** → Would cause sciatica pain, which would present as acute pain that “shoots down the leg”. This wouldn’t cause color changes or temperature changes.
- **Choice D** → Nothing here says HTN. We have AF, which causes occluding embolism → Ischemic stroke, not hemorrhagic strokes
- **Choice E** → Cerebral infarction would cause numbness & tingling if the medial post-central gyrus is affected yes. However, the limb won’t be cool or discolored.

Q9

A 4-year-old boy is brought to the physician by his parents because of marked yellowing of the skin. He and his family do not eat meat, milk, eggs, or other foods derived from animal products. There have not been any changes in stool or urine color. He has not traveled, and no members of his family have been ill. His temperature is 37°C (98.6°F), pulse is 80/min, respirations are 12/min, and blood pressure is 100/60 mm Hg. Examination shows yellow-tinged skin, but his sclerae are nonicteric. Which of the following interventions is most likely to improve this child's appearance?

- A. Ascorbic acid
- B. Dietary change
- C. Folic acid
- D. Interferon alfa plus ribavirin
- E. Vitamin B₁ (thiamine)
- F. Vitamin B₆ (pyridoxine)

▼ Explanation

- **Answer is B (Dietary change)**
 - **IMP Clues**
 - Marked yellowing of the skin (You read this and think haaaa jaundice, so you start thinking of the DDs. This is why you always start with the last few sentences.)
 - Examination shows yellow-tinged skin, but his sclerae are non-icteric (this excludes jaundice, as jaundice appears first in the eyes THEN skin. So, if eyes are not affected, but skin is then chances are that this is NOT jaundice)
 - He & his family do not eat meat... (okay so a vegan)
 - No changes in stool or urine color (excludes hyperbilirubinemia too)
 - **Dx → Carotenemia**
 - This kid is vegan, so probably eats shit tone of carrots which contain **beta-carotene → causes orange discoloration of skin. SKIN. Just stop eating carrots. (Choice B)**
 - Jaundice causes discoloration of eyes THEN skin. Eyes here are non-icteric.

Q10

A 56-year-old man comes to the physician because of severe pain in the great toe of his right foot. He says that he is allergic to aspirin and many similar drugs. He has had four surgical procedures to remove nasal polyps. Physical examination shows swelling and marked tenderness of the first metatarsophalangeal

joint of the right foot. Microscopic examination of joint fluid obtained by arthrocentesis shows negatively birefringent crystals. Which of the following is the most appropriate acute treatment?

- A. Acetaminophen
- B. Allopurinol
- C. Colchicine
- D. Indomethacin
- E. Sulfipyrazone

▼ Explanation

• Answer is C (Colchicine)

◦ IMP Clues

- Severe pain in the great toe of his right foot + Swelling and tenderness of 1st MTP (Classical gout site)
- Allergic to Aspirin and many similar drugs (This is important, but answer choices not really tricky but other Q are tricky)
- Arthrocentesis shows negatively birefringent crystals (confirms the dx, this is gout)
- Q asks for acute ttt

• Dx → Gout

- Treatment of gout is very HY, so let's do it:
- Treatment is divided into **2 arms: Acute Gout (during attack) & Chronic Gout (in between attacks)**:
 - **Acute Gout (During Attacks)**
 1. **1st Line** → **NSAIDs** (Indomethacin preferably)
 2. **2nd Line** → **Corticosteroids**
 - **Used if: hx of renal failure, renal transplant, peptic ulcer, or NSAIDs are contraindicated**
 3. **3rd Line** → **Colchicine** (if neither NSAIDs or Corticosteroids are in answer choices)
 - **MOA of Colchicine** ⇒ **Microtubule inhibitor**
 - **Chronic Gout (In-between Attacks)**
 1. **1st Line** → **Xanthine Oxidase inhibitors** (Allopurinol & Febuxostat)
 2. **2nd Line** → **Uricosuric drugs** (Probenecid & Sulfipyrazone)
 - a. **Contraindicated in: hx of renal / uric stones or uric acid production (Lesch-Nyhan Syndrome or Tumor Lysis Syndrome)**
 3. **3rd Line** → **Urate Oxidase analogues** (Rasburicase & Pegloticase)
 - a. **Used in: Uric acid overproduction (Lesch-Nyhan Syndrome or Tumor Lysis Syndrome)**

This picture of Tophi was also used on NBME 19:



? What is the cause of swelling of the patient's toe?

▼ Answer

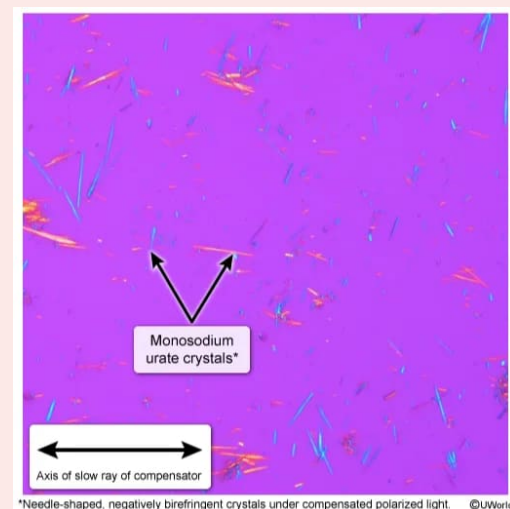
Vasodilation - **Crystals deposition & mobilization** from joints cause the release of inflammatory mediators. They cause:

- **Vasodilation** (cause of swelling)
- **Neutrophils migration** (due to chemotactic molecules)

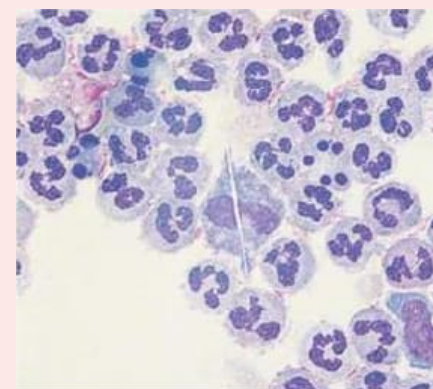
NBME asks this Q and the answer was **"increased vascular permeability"**

How does the Crystals look like?

They are **Monosodium Urate Crystals**, needle-like in shape, and **"Negatively Birefringent"**



The below picture was on NBME 18, answer was Gout (due to presence of that singular needle-shaped crystal:



*** Tophi are chalky-white extraarticular urate crystal deposits that may form under the skin. They are **PAINLESS**.

Q11

A 42-year-old man with a history of recurrent pyelonephritis comes to the office because of a 2-day history of left flank pain, fever, and chills. His temperature is 38.8°C (101.8°F). He appears anxious and is in moderate distress. Physical examination shows left costovertebral angle tenderness exacerbated by percussion. His urine is cloudy and has a pH of 7.3. A CT scan of the abdomen shows a large renal calculus. Extracorporeal shock wave lithotripsy is done for fragmentation and removal. A photograph of a resected calculus from a patient with a similar condition is shown. Based on these findings, this patient most likely has a calculus composed of which of the following substances?



- A. Calcium oxalate
- B. Calcium oxalate and phosphate
- C. Calcium phosphate
- D. Magnesium ammonium phosphate
- E. Uric acid

▼ **Explanation**

- **Answer is D (Magnesium ammonium phosphate)**
 - **IMP Clues**
 - Urine has a pH of 7.3 (alkaline, pH >7 start thinking urease+ organisms)
 - Photograph of resected calculus is shown (looks like a staghorn stone)
 - Q asks what is this stone made of?
 - **Dx → Struvite Stone**
 - Struvite stones are made up of **Magnesium ammonium phosphate**.
- On the USMLE, you will find these Qs all the time.
 - They present you a patient with **alkaline urine + stone**. They then ask:
 1. **What is stone made up of → Magnesium ammonium phosphate**
 2. **What organism is highly associated with it → Proteus mirabilis**
 - Other HY causes are **Klebsiella & Serratia**, but if you find all of them as choices, choose Proteus
 3. **What kind of organisms can cause these stones → Urease positive**
 4. They might show you a **picture like the above stone** & ask for diagnosis → **Struvite stone**
 5. They might show you **radiology pic** and ask for diagnosis → **Struvite stone**

Below Pictures are super HY:

Struvite Kidney Stone on CT:



Struvite Kidney Stone on X-Ray:

? How would Struvite Stones appear in a uranalysis?

▼ Answer

Coffin Lid-shaped Stones



Q12

Which of the following pairs of drugs interferes with DNA synthesis by crosslinking?

- A. Colchicine and lomustine
- B. Colchicine and vinblastine
- C. Cytosine arabinoside and cyclophosphamide
- D. Fluorouracil and methotrexate
- E. Lomustine and cyclophosphamide

▼ Explanation

- **Answer is E (Lomustine and cyclophosphamide)**
 - Q asks which drugs **interferes with DNA synthesis by crosslinking?**
 - Let's go through the answer choices
 - **Choice A** → Colchicine is a *microtubules inhibitor*, while **Lomustine inhibits crosslinking**. Nope.
 - **Choice B** → Both colchicine and vinblastine are *microtubules inhibitors*. Nope.
 - **Choice C** → **Cyclophosphamide inhibits crosslinking**, and I'm not familiar with Cytosine arabinoside (it is not assessed anywhere on the USMLE, so probably garbage). Maybe.
 - **Choice D** → MTX is a *DHFR inhibitor*, while 5-FU inhibits *Thymidylate Synthase*. Nope.
 - **Choice E** → **Both Lomustine & Cyclophosphamide inhibit DNA crosslinking. YESS.**
 - Lomustine (and Carmustine) → Nitrosourea drugs that cross BBB, so used for brain tumors

? Patient has leukemia & is receiving ttt. 2 weeks after starting ttt, he develops red urine. Doctors suspect that this is a drug side effect. What is the site of the cause of the red urine?

▼ Answer

Bladder - Patient has **Hemorrhagic Cystitis**, which is a **very HY side effect of Cyclophosphamide**.

Treatment → **Mesna (or NAC if mesna not listed)**

Other HY causes of Hemorrhagic Cystitis on the USMLE → **Adenovirus & BK virus**

Q13

A 55-year-old man comes to the physician because of a 1-year history of progressive shortness of breath. He recently retired after 30 years as a construction worker. He does not smoke. Bilateral basilar, fine, end-inspiratory crackles are heard over the lung fields. A chest x-ray shows diffuse, bilateral parenchymal opacities with a reticular pattern and bilateral diaphragmatic pleural plaques. Microscopic examination of a sputum sample shows no atypical cells. Pulmonary function testing is likely to show which of the following sets of results in this patient?

Choice	FEV ₁ /FVC	FVC	Diffusing Capacity of the Lung for Carbon Monoxide
A	Decreased	decreased	decreased
B	Decreased	decreased	normal
C	Decreased	normal	normal
D	Normal	decreased	decreased
E	Normal	decreased	normal
F	Normal	normal	normal

▼ Explanation

• Answer is D

◦ IMP Clues

- Construction worker (Pulmonology Q + construction worker = expect some sort of pneumoconiosis)
- Does not smoke (Okay this decreases the probability of COPD)
- CXR shows diffuse bilateral opacities with reticular pattern (Reticular pattern = Fibrosis)
- Bilateral diaphragmatic pleural plaques (buzzy keyword for asbestosis)
- Sputum samples shows no atypical cells (excludes tumors)
- Q asks about expect pulmonary functions?

◦ Dx → Asbestosis

- Asbestos is a HY pneumoconiosis** (chances are if you're asked about a type of pneumoconiosis it's going to be asbestosis or silicosis) that affects the **Lower Lobes**
 - Associated with **shipbuilding, roofing, and plumbing**
 - HY Complications: **Pulmonary Fibrosis, Pleural effusion, and malignancy**
- Pneumoconiosis are **restrictive lung disease**.
- For restrictive patterns choose:**
 - Increased/normal FEV1/FVC ratio**
 - Decreased everything else**
- On the USMLE, **DCLO is always decreased, except in asthma → Increases**
 - Asthma is obstructive, but just saying

? What is the most common tumor caused by asbestos exposure?

▼ Answer

Bronchogenic Carcinoma - yes, this is not a mistake. Most **common** tumor caused by asbestos exposure → **Bronchogenic Carcinoma**
Most **specific** tumor caused by asbestos exposure → **Mesothelioma**

In other words, **Mesothelioma is most commonly caused by asbestos exposure**, but **asbestos exposure causes bronchogenic carcinoma > Mesothelioma**. Get it?

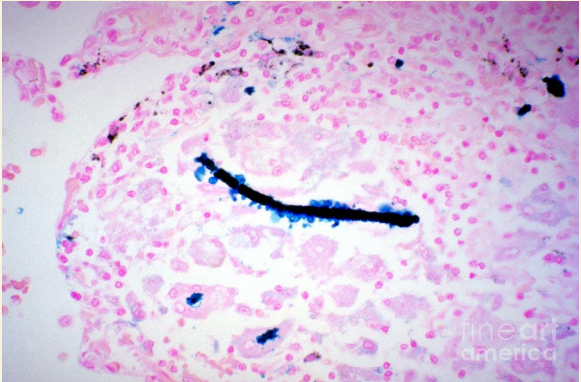
? What is the cause of lung fibrosis in asbestosis?

▼ Answer

Macrophages - 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:**

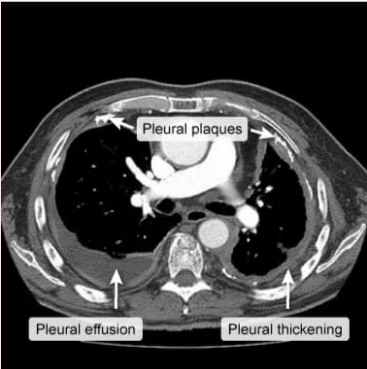
- ROS & Proteolytic enzymes → **Lung endothelial damage**
- Cytokines → **increase Fibroblast activation → Collagen deposition**
 - Endothelial Damage + Collagen Deposition = Fibrosis (Reticulonodular pattern / honeycombing)**

Ferruginous Bodies are what is seen in sputum microscopy in asbestosis, they are **macrophages which contain the asbestos fibers + iron deposition around it**

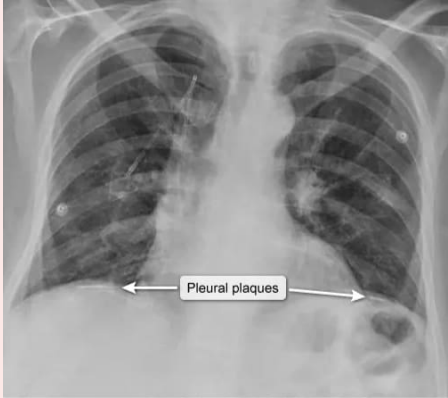


Shown below are imaging findings of Asbestos-Related Diseases:

Mesothelioma:



Asbestosis:



Q14

A 47-year-old woman has had a goiter for 10 months. She has adequate iodine in her diet and there is no family history of any thyroid disorder. Antithyroid peroxidase antibodies are identified in her serum. Serum concentrations of triiodothyronine (T_3) and thyroxine (T_4) are decreased, and serum thyroid-stimulating hormone concentration is increased. Which of the following is most likely to be involved in the pathogenesis of this disorder?

- A. Diffuse fibrosis of the thyroid parenchyma
- B. Hyalinization and scarring of the thyroid parenchyma
- C. Multiple giant cell granulomata throughout the thyroid parenchyma
- D. Patchy areas of liquefaction necrosis in the thyroid parenchyma
- E. Replacement of thyroid parenchyma by lymphoid cells

▼ Explanation

- Answer is E (Replacement of thyroid parenchyma by lymphoid cells)

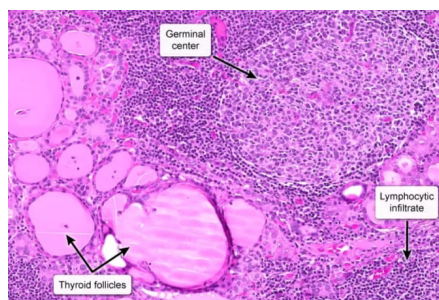
- IMP Clues

- Woman has had a goiter (okay so thyroid stuff, free points)
- She has adequate iodine in her diet (So not iodine deficiency, which is rare anyways in the US)
- Antithyroid peroxidase antibodies are identified in her serum (Hashimoto Thyroiditis)
- Serum concentrations of T_3 and T_4 are decreased, and serum TSH concentration is increased (so Primary Hypothyroidism, consistent with Hashimoto)
- Q asks for the involved pathogenesis

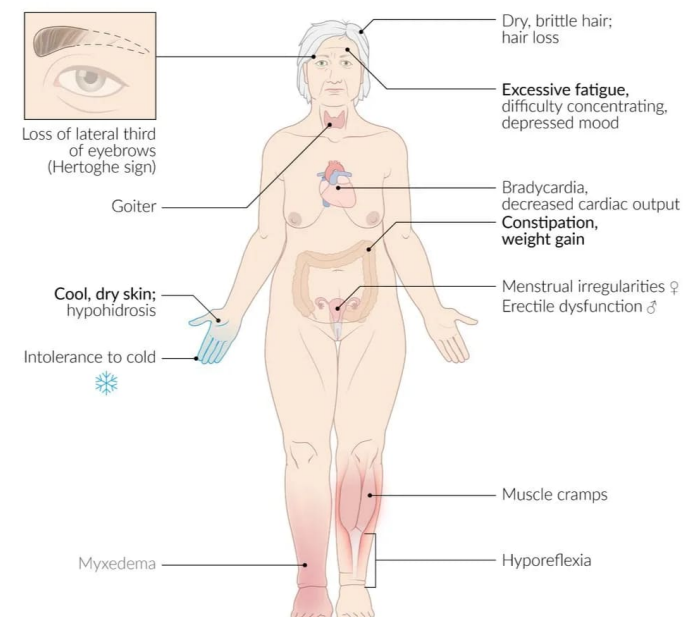
- Dx → Hashimoto Thyroiditis

- Biopsy findings are classically →
Hurthle cells, and lymphoid aggregates with germinal centers

- However, most of the time, the Hurthle cells are not assessed or mentioned. So know **"Lymphoid aggregates with germinal centers"**



- Q can also call Hashimoto as **"chronic autoimmune thyroiditis"**
- Presents as a **painless goiter + primary hypothyroidism**
- HY antibodies are: **Antithyroid peroxidase** and **Antithyroglobulin antibodies**



? What is the patient at risk of developing if she is not treated? If the patient got pregnant, what is the child at risk of if not treated adequately?

▼ Answer

Patient → **Thyroid Lymphoma** (B-cell lymphoma)

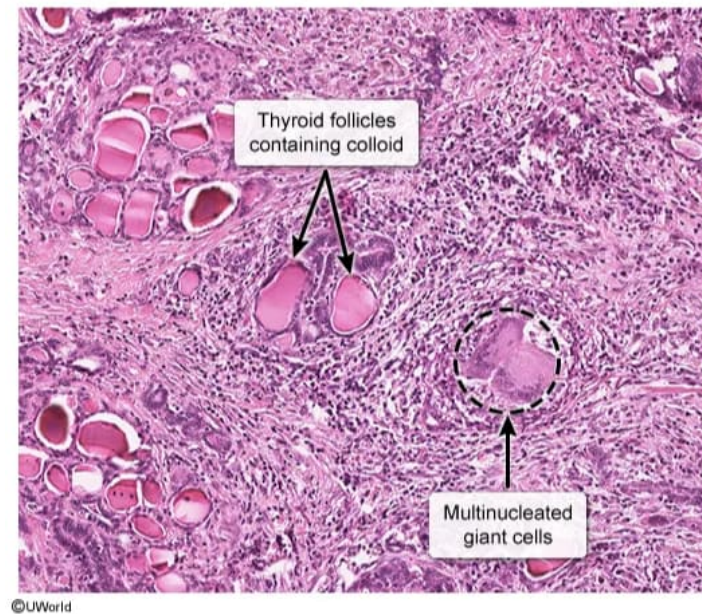
Baby → **Cretinism**

- USMLE assess this by asking if mother has Hashimoto's and what would happen to the baby if TSH increases?
 - If TSH increases, then this would mean **that T_3/T_4 has decreased** → **Hypothyroidism**, so the baby would be **at risk of cretinism**
 - **HY Presentation is a baby with abnormal brain development, umbilical hernia, and a protruded tongue**

▼ Other Choices

- **Choice A** → Refers to **Riedel Thyroiditis**, which is **characterized by fibrosis formation**
 - Presents as a **HARD fixed goiter + compression symptoms**
 - Can be associated with fibrosis of other areas (pancreatic duct → pancreatitis, retroperitoneal fibrosis, Aortitis)

- **Choice B** → A little vague to be honest, but hyalinization and scarring is nonspecific, but anyways there are more correct answer choices.
- **Choice C** → Refers to **Subacute granulomatous thyroiditis (de Quervian Thyroiditis)**
 - Usually **preceded by a viral infection**
 - Presents as **PAINFUL thyroid (HY) + high ESR +/- jaw pain**
 - Biopsy: Shows Multinucleated Giant Cells



- **Choice D** → Sounds like a thyroid abscess of some sort?

Q15

A 36-year-old woman comes to the physician for a follow-up examination 1 week after being diagnosed with severe hypertension. Her blood pressure is 180/120 mm Hg. Physical examination shows no other abnormalities. A CT scan of the abdomen shows a renal artery aneurysm. A renal angiogram obtained from a femoral approach is shown. Which of the following is the most likely cause of these findings?



- A. Atherosclerotic renal artery disease
- B. Calcific nephrosclerosis
- C. Fibromuscular dysplasia
- D. Polyarteritis nodosa
- E. Polycystic kidney disease

▼ **Explanation**

- **Answer is C (Fibromuscular Dysplasia)**

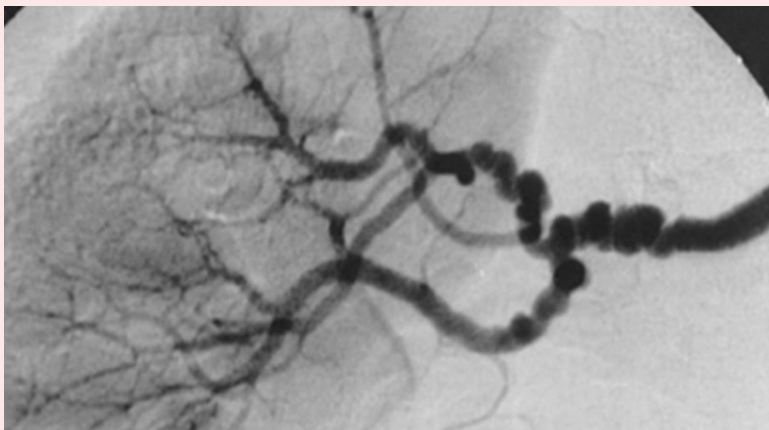
- **IMP Clues**

- 36-year-old woman with severe HTN + BP is 180/120mmHg (very unusual for a young woman to present with HTN, especially severe. So you must think of 2ry HTN)
- CT scan shows a renal artery aneurysm + renal angiogram is shown (So the kidney is the cause of the 2ry HTN)
- Q asks for the Dx

- **Dx → Fibromuscular Dysplasia (FMD)**

- Can sometimes be referred to as **"Renal Artery Dysplasia"** on NBMEs
- It is not a dysplasia really, it is **hyperplasia of the tunica media**
- It is an **autoimmune disease that affects middle-aged women with NO hx of cardiovascular disease**
- Causes the **"string of beads"** appearance on CT angiography
 - My opinion, knowing the CT scans will not help you as much as looking for risk factors like Age, hx of CVD, or other HY findings (listed below)

Picture below shows String of Beads appearance seen on CT Angiography of Renal Artery:



You will get this type of Q on every NBME, so let's run through what you need to know

- **50-60y Male OR Female + hx of cardiovascular disease / atherosclerosis / smoking?**
 - **Dx → Atherosclerosis**
 - Vignettes can be tricky by saying **"BMI is 35"** or **"a carotid bruit is heard on examination"** instead of atherosclerosis.
 - BMI is high usually means he's atherosclerotic especially in this age group
 - If a patient has a carotid bruit, which is due to atherosclerosis, chances are he also has atherosclerotic arteries in other sites (Renal Artery)
- **20-40y F + NO hx of cardiovascular disease / atherosclerosis / smoking?**
 - **Dx → FMD**
- **20-40y F + was given ACEi/ARBs + Creatinine levels have risen. What is diagnosis?**
 - **FMD**
- **64M + was given ACEi/ARBs + Creatinine levels have risen. What is diagnosis?**
 - **Atherosclerotic Renal Artery**
- **55F + was given ACEi/ARBs + Creatinine levels have risen. What is diagnosis?**
 - **Atherosclerotic Renal Artery**

Reason is in **FMD or Atherosclerosis**, the renal blood supply is **decreased**, but the body adapts by **producing renin & AT-2**, which causes **vasoconstriction** of the **efferent renal arterioles** → **maintains GFR**

If **ACEi/ARBs** are administered, **efferent arterioles dilate** → **decreased GFR** → **creatinine rises**.

▼ **Other Choices**

- **Choice A** → Discussed above
- **Choice B** → Deposition of calcium in the kidneys. **Can be caused by disease that cause high serum calcium.**
 - CT scan would show white spots in the kidney (the deposited calcium)
- **Choice D** → **Presents as HTN + red urine + abdominal pain + muscle aches.** A type of vasculitis, which is **associated with HBV affection.**
 - CT scan shows **"String of pearls"** appearance.
 - Biopsy shows **Fibrinoid necrosis**
- **Choice E** → **ADPKD** would present as an **adult patient with family hx of HTN, kidney disease, or SAH.**
 - Cysts in the kidney compressed the renal vasculature → decreased blood flow → increased renin & AT-2 → high blood pressure
 - CT scan would show **cystic large kidneys**
 - **Associated with hepatic cysts & Circle of Willis Berry aneurysms → Subarachnoid hemorrhage**

Cyclophosphamide and some other chemotherapeutic agents kill mitotic cells. Which of the following cellular compartments is most rapidly depleted during cyclophosphamide therapy?

- A. B lymphocytes
- B. Granulocytes
- C. Hepatocytes
- D. Sensory neurons
- E. T lymphocytes
- F. Vascular endothelium

▼ Explanation

- Answer is B (Granulocytes)

- This Q tests the **difference between labile cells, stable cells, and permanent cells.**
- You need to know that **chemo and anti-cancer drugs in general kill highly active replicating (labile) cells more than the kill/affect stable & permanent cells.**

- What are Labile Cells?

- **Labile Cells are cells that have the *highest* regenerative capacity.**
 - **Remains in G1 forever & NEVER enters G0**
 - HY Examples of Labile cells are **Skin epithelium, GI epithelium, Hair follicles, Bone marrow, and Germ cells.**
- What are the other types of cells?
 - **Stable Cells go from G0 → G1 when stimulated** (so **moderate** regenerative capacity)
 - HY Examples are **Hepatocytes, Lymphocytes, Renal Tubular Cells, and Smooth muscle.**
 - Regenerates **if the structural framework is preserved:**
 - If the reticulin structure is preserved, Liver regenerates with **NO FIBROSIS**
 - If destroyed → **Fibrosis**
 - **Permanent Cells have NO regenerative capacity** (may regenerate from stem cells, but limited)
 - **Remains in G0 forever**
 - HY Examples are **RBCs, Neurons, and Skeletal & Cardiac muscles.**
 - Dead **Neurons** (Pos-Stroke) in CNS are replaced by **gliosis**.
 - Dead **Cardiocytes** (Post-MI) are replaced by **scar tissue**



Labile Cells are the most affected by chemo/anti-cancer drugs due to their **rapid turnover**.

- This is why patients on chemo/anti-cancer drugs develop **sores, infertility, neutropenia, and hair fall.**



Patient takes chemo for cancer. Hair starts falling out, why?

▼ Answer

Hair Follicles have high turnover rates.

▼ Other Choices

- **Choices A, C, E, F → Stable Cells**
- **Choice D → Permanent Cells**

Q17

A newborn has external genitalia that appear to be male. Chromosomal analysis shows a 46,XX karyotype. Which of the following is the most likely explanation for the physical findings?

- A. Abnormal androgen receptors
- B. Gonadal dysgenesis
- C. Hyperplastic fetal adrenal glands
- D. Testicular tissue in the gonads
- E. Unilateral testis and ovary

▼ Explanation

- Answer is C (Hyperplastic fetal adrenal glands)

- IMP Clues

- Newborn has external genitalia appears to be male + chromosomal analysis shows a 46XX (genitalia appears male but chromosomes are female, this means something is producing androgen, which is causing virilization)

- Let's go through the answer choices & look for source of androgen secretion

- Choice A → Abnormal Androgen Receptors (Androgen Insensitivity Syndrome) presents as a 46XY genotype with a female phenotype.

- No androgen receptors so Wolffian duct doesn't develop.
- Testicles are present but undescended.
- As there is no androgen receptors, there will be scant or absent axillary/pubic hair.
- They usually have well developed breasts due to aromatization of androgen into estrogen.

- Choice B → Gonadal Dysgenesis presents as a 46XX female with streak gonads

- Choice C → Hyperplastic Fetal Adrenal Glands (The Answer)

- If the adrenal glands are hyperplastic then they are hypersecreting.
- The Zona Reticularis secretes androgens which would be the cause of virilization

- Choice D & E → What? Garbage.

Q18

An 8-year-old boy is brought to the physician by his mother 6 days after she noticed a lump on the left side of his neck. He is at the 75th percentile for height and weight. Physical examination shows pectus excavatum. There are two 2-mm, subcutaneous nodules on the lips, an irregular 2 × 2.5-cm mass on the left side of the neck, and anterior cervical lymphadenopathy. His 14-year-old sister had similar findings at the age of 10 years. Which of the following studies is most likely to support the diagnosis?

- A. Antithyroglobulin antibodies titer
- B. Dexamethasone suppression test
- C. Serum calcitonin concentration
- D. Serum thyroid-stimulating hormone concentration
- E. Thyroid-stimulating hormone receptor antibodies titer

▼ Explanation

- Answer is C (Serum calcitonin concentration)

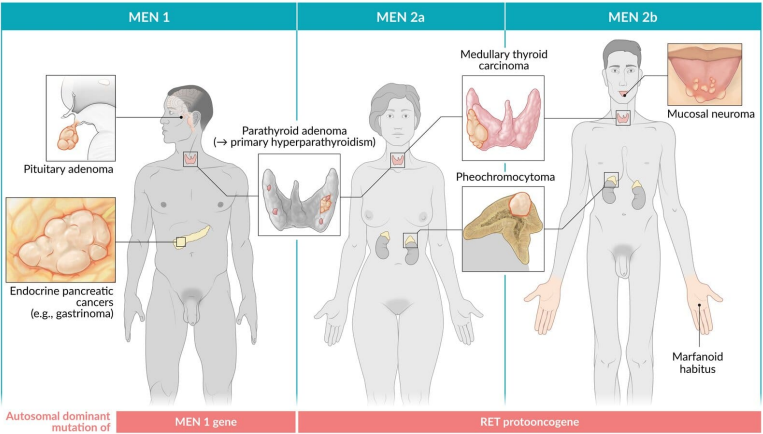
- IMP Clues

- Pectus excavatum
- Two 2mm subcutaneous nodules on the lips
- Irregular 2×2.5cm mass on the left side of his neck + anterior cervical lymphadenopathy
- 25-year-old sister had similar findings

- Dx → MEN 2B

USMLE usually does this. They don't give you the full triad, they only give you a feature or two. They sometimes also give a feature in the child + another feature in the sister/mother/father + asks for diagnosis or genetic mutation.

- "The neck mass + cervical lymphadenopathy" is cancer, side of the neck hints to cancer ⇒ Medullary Thyroid Carcinoma, which causes increased calcitonin concentration (Choice C)
 - Medullary Thyroid Carcinoma
 - Tumor of the C-cells, which produce calcitonin.
 - Q asks us which markers should be monitored for the recurrence, so Calcitonin (which is released by the tumor) is the answer.
 - Biopsy Findings: spindle-shaped cells/polygonal cells in sheets with amyloid stroma (Congo red positive)



- “Two 2mm subcutaneous nodules on the lips” ⇒ **Mucosal Neuromas**
- The “*pectus excavatum*” is the associated **marfanoid habitus** features in **MEN2B**



SUPER FUCKING HY TO KNOW:
MEN 1 ⇒ Autosomal Dominant Mutation of **MEN 1 Gene** (encodes for **Menin** protein), which is a **Tumor Suppressor gene** on Chromosome 11

MEN 2A/B ⇒ Autosomal Dominant Mutation of **RET** (mutation causes **increased tyrosine kinase activity**), which is a **Proto-Oncogene** on Chromosome 10

? Compare between the genetic mutation, features, and associations of MEN Syndromes.

▼ Answer

Feature	MEN1	MEN2A	MEN2B
Genetic Mutation	Menin (tumor suppressor gene) on chromosome 11	RET (proto-oncogene) on chromosome 10	RET (proto-oncogene) on chromosome 10
Triad	1. Pituitary Adenoma 2. Pancreatic Tumor 3. Parathyroid Adenoma	1.. Medullary Thyroid Carcinoma 2. Parathyroid Adenoma 3. Pheochromocytoma	1. Mucosal Neuroma 2. Medullary Thyroid Carcinoma 3. Pheochromocytoma
Associations	Meningioma, Lipoma, Collagenoma, Angiofibroma	None	Marfanoid Habitus

Q19

A 2-week-old girl is brought to the physician by her parents for a well-child examination. Physical examination shows an asymmetric left pupil. Ophthalmologic examination shows a coloboma of the left eye. Incomplete closure of the embryonic fissure that is limited to which of the following structures of the left eye is most likely to spare this patient's vision?

- A. Choroid
- B. Iris
- C. Lens
- D. Macula
- E. Optic nerve
- F. Retina

▼ Explanation

- Answer is B (Iris)
 - IMP Clues
 - Asymmetric left pupil + Coloboma of the eye
 - Q asks “incomplete closure of the embryonic fissure” if limited to a structure that would likely to spare the patient’s vision, then what is that structure?
- To understand the Q, you need to understand that a **coloboma is incomplete closure/formation of the iris, retina, choroid, lens, or optic disc**.
 - Q asks having a coloboma of which of the following structures would **spare the vision**?
 - If you have a “hole” in the **retina, macula, choroid, or optic disc** → **YOU LOSE VISION IN THAT AREA**
 - If you have a “coloboma of the lens,” that a little different → **Defective zonules “the fibers that hold the lens in place” → Blurry Vision & higher incidence of cataract → Vision affected**

Picture below shows how an Iris Coloboma looks like:

- If you have a “hole” in your iris → **You can still see fine.** So this is the answer.

? Newborn baby is found to have a heart defect on ECHO. He also turns blue when breastfed and returns to normal color when he cries. What is associated finding expected to be seen in his eyes?

▼ **Answer**

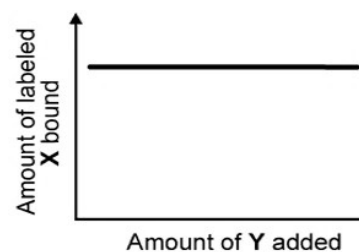
Coloboma - This is CHARGE Syndrome

- **C = Coloboma**
- **H = Heart Defect**
- **A = Atresia of Choanae**
 - If bilateral causes baby to turn blue when breast feeding as his choanae are closed, and when he cries he opens his mouth so can breath and return to normal color
- **R = Retardation** in physical and mental development
- **G = Genital** abnormalities
- **E = Ear** malformations



Q20

An antiserum is elicited by immunization with protein X, and the anti-X antibodies are adsorbed to microtiter wells. The graph shows the amount of radiolabeled protein X bound by the antiserum in the presence of varying concentrations of protein Y. With respect to the anti-X serum, which of the following interpretations of the epitopes expressed by proteins X and Y is correct?



- A. Proteins X and Y express the same epitopes
- B. Proteins X and Y have no epitopes in common
- C. Protein X expresses all of the epitopes expressed by protein Y, but protein Y does not express all of the epitopes expressed by protein X
- D. Protein Y expresses all of the epitopes expressed by protein X, but protein X does not express all of the epitopes expressed by protein Y

▼ **Explanation**

- **Answer is B (Proteins X and Y have no epitopes in common)**
 - Looks hard, but I promise you this is easy.
 - Graph shows **The X is at specific value which DOESN'T increase as Y is increasing. So, there is no relation between X & Y** → **Choice B (No epitopes in common)**

▼ **Other Choices**

- **Choice A** → If they share the same epitopes, the curve would start at the top, and the more you add Y, the curve would drop.
- **Choice C** → Again, starts at the top and then drops as you add Y, until some value above 0, then plateaus.
- **Choice D** → like choice A, starts at the top and drops as you add Y.

Q21

A 46-year-old woman has a 1-day history of high-grade fever, productive cough, and pleuritic chest pain. Laboratory studies show:

Leukocyte count	35,000/mm ³
Neutrophils	70%
Bands	10%
Lymphocytes	12%
Monocytes	5%
Metamyelocytes	3%
Leukocyte alkaline phosphatase	300 U/L (N=20–100)

Which of the following findings most reliably distinguishes a leukemoid reaction from chronic myelogenous leukemia in this patient?

- A. Leukocyte count greater than 25,000/mm³
- B. Leukocyte alkaline phosphatase activity greater than 250 U/L
- C. 0% Basophils on the peripheral smear
- D. 0% Blasts on the peripheral smear
- E. More than 60% mature neutrophils on the peripheral smear

▼ Explanation

- Answer is B (Leukocyte alkaline phosphate activity greater than 250 U/L)
 - IMP Clues
 - Easy Q. I talked about this in the previous NBMEs. The way to differentiate between Leukemia & Leukemoid reaction is by Leukocyte ALP.
 - Leukocyte ALP reflects functional leukocytes.
 - Increased Leukocyte ALP ⇒ **Increased** number of functional leukocytes
 - This is what is happening in **Leukemoid Reaction**, *Leukocytes are functioning normally, but they’re just MORE.*
 - Decreased Leukocyte ALP ⇒ **Decreased** number of functional leukocytes
 - This is what is happening in Leukemia, we have **abnormal proliferation of ABNORMAL leukocytes**. Yes they’re many, but they’re dysfunctional
 - This is why patients is **leukemia** are immunocompromised despite the massive number of leukocytes

Q22

A cohort study is conducted to examine the association between cigarette smoking and lung cancer in a sample of 4000 people. One thousand participants smoke cigarettes, and 3000 participants do not smoke. After 10 years of follow-up, there are 30 cases of lung cancer among the smokers and 30 cases of lung cancer among the nonsmokers. According to these results, how many lung cancer cases attributable to smoking would be expected to occur in a group of 10,000 smokers over the same period of time?

- A. 30
- B. 100
- C. 150
- D. 200
- E. 300

▼ Explanation

- Answer is D (200)
 - Q asks for **Attributable Risk**.
 - **1000 smokers → 30 cases** of lung cancer. So, **30/1000 = 3%**
 - **3000 nonsmokers → 30 cases** of lung cancer. So, **30/3000 = 1%**
 - Attributable Risk (the risk of developing lung cancer due to smoking is 2% more than nonsmokers)
 - **3%-1% = 2%**
 - Q asks what is expected AR of lung cancer in a group of 10,000 smokers.
 - **2% of 10,000 is 200 (Choice D)**

Q23

An 18-year-old woman comes to the physician because of a 6-month history of progressive muscle weakness, poor exercise tolerance, and shortness of breath with exertion. She also has had difficulty following moving objects with her eyes, especially when she is tired. Her pulse is 110/min, respirations are 22/min, and blood pressure is 105/85 mm Hg. Physical examination shows bilateral ptosis. Muscle strength is 3/5 to 4/5 in all extremities. Examination of a muscle biopsy specimen shows abnormal accumulations of mitochondria in the subscarcolemmal regions. Which of the following additional sets of findings is most likely in this patient?

Choice	Maximum Oxygen Consumption (VO ₂ max)	Venous Blood Lactate	Energy Production by Glycolysis
A	↑	↑	↑
B	↑	↑	↓
C	↑	↓	↑
D	↑	↓	↓
E	↓	↑	↑
F	↓	↑	↓
G	↓	↓	↑
H	↓	↓	↓

▼ Explanation

• Answer E

- Q says that we have a tired patient with weakness + muscle biopsy shows abnormal accumulation of mitochondria in the subsarcolemmal regions

- This is a mitochondria disease called **MERRF Syndrome**, which is characterized by the **Ragged Red Fibers**:

- **Ragged Red Fibers = Gomori trichome stain showing abnormal accumulation of mitochondria in the subsarcolemmal regions**

- So, mitochondria not working, so no aerobic respiration, just anaerobic.

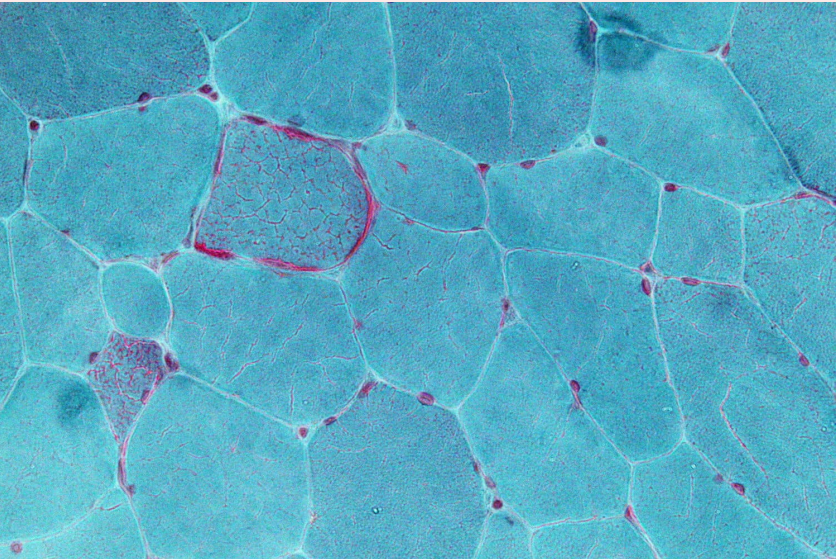
▪ Anaerobic Respiration:

- **Less Oxygen consumption**
- **Increased Glycolysis → Pyruvate → Lactate (Increased Lactic acid production)**
 - Pyruvate can't be shunted to TCA as the mitochondria are dysfunctional.
 - Glycolysis occurs in the **cytosol** not mitochondria so not affected.

• **MERRF Syndrome:**

- "ME" = **Myoclonic Epilepsy**
- "RRF" = **Ragged Red Fibers**
- Other possible presentations include **Generalized Seizures**, **Cerebellar Ataxia**, and **Dementia**

Picture below shows Ragged Red Fibers with Gomori Trichome Stain:



Q24

Which of the following types of vaccine is most appropriate to prevent mumps?

- A. Bacterial by-products
- B. Bacterial polysaccharides
- C. Inactivated bacteria
- D. Inactivated virus
- E. Inactive viral antigen
- F. Live attenuated bacteria
- G. Live attenuated virus

▼ Explanation

- **Answer is G (Live attenuated virus)**

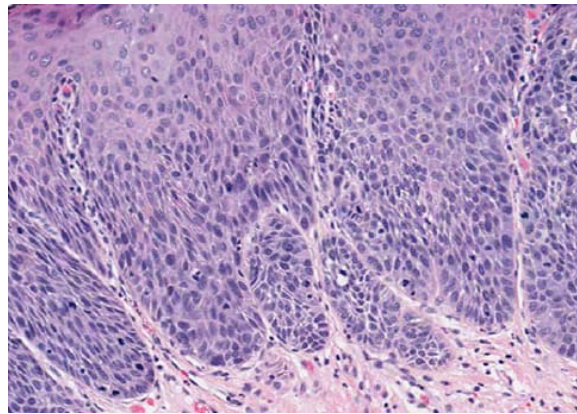
- Q asks for appropriate vaccination of mumps
 - I think it is common knowledge that mumps is one of the **MMR vaccine constituents**.
 - **MMR vaccine is a live attenuated vaccine** against **Measles, Mumps, and Rubella**.
 - They are **all viruses** so answer is **Choice G (Live attenuated Virus)**

? What are 2 HY live attenuated vaccines which can be given to HIV patients with CD4 count > 200?

▼ Answer
MMR & VZV Vaccines

Q25

A 45-year-old man comes to the office for a health maintenance examination. He had smoked 1 pack of cigarettes daily for 30 years until he quit 3 years ago. Physical examination shows a painless white patch on the lateral border of the tongue. A photomicrograph of a biopsy specimen of the lesion is shown. Which of the following changes is most likely to occur next if this patient's lesion is left untreated?



- A. Dissemination of viral infection
- B. Dissemination to distant sites
- C. Infiltration of the perineural spaces
- D. Invasion of the submucosa
- E. Spontaneous regression

▼ Explanation

- **Answer is D (Invasion of the submucosa)**

- **IMP Clues**
 - Smoked 1 pack of cigarettes daily for 30 years (Tobacco smoking is a risk factor)
 - Painless white patch on the lateral surface of the tongue (Classical Leukoplakia description)
 - Biopsy of lesion is shown (shows dysplastic / abnormal cells)
 - Q asks what would happen if it was left untreated

- **Dx → Leukoplakia**

- **Precancerous lesion of Squamous Cell Carcinoma.**
- If seen, it **MUST be biopsied immediately** to see if it has **invaded the basement membrane → Malignant**
- So, if the lesion is **left untreated → Invasion of submucosa → Invasion of basement membrane → Metastasis**

Picture below shows Leukoplakia:



***** You differentiate between Leukoplakia & Oral Candidiasis by scraping:**

- Leukoplakia ⇒ **CAN NOT** be scrapped off
- Oral Candidiasis ⇒ **CAN** be scrapped off

Q26

A 75-year-old woman has stress urinary incontinence with sphincteric incompetence. Pelvic floor muscle exercises and the use of a vaginal pessary provide inadequate improvement, and the patient refuses surgical intervention. Administration of a drug with which of the following mechanisms of action is most appropriate?

- A. Antagonism of α -adrenoreceptors
- B. Antagonism of β -adrenoreceptors
- C. Stimulation of α -adrenoreceptors
- D. Stimulation of β -adrenoreceptors
- E. Stimulation of muscarine receptors

▼ Explanation

• Answer is C (Stimulation of α -adrenoreceptors)

◦ IMP Clues

- 75-year-old woman has stress urinary incontinence with sphincteric incompetence (So a case of stress incontinence due to weak sphincter)
- Pelvic floor exercises and vaginal pessary provided inadequate improvement + patient refused surgery (Kegel exercise strengthen the external voluntary sphincter and the pessary also help with incontinence. But all of that failed)
- Q asks for a drug that would help

- Stress incontinence due to sphincteric incompetence can be treated by **stimulation of sphincter contraction**.

◦ What receptors cause sphincteric contraction?

- **Alpha 1 Adrenergic Receptors.**
- So, **stimulation of alpha-adrenoreceptors will cause sphincteric competency**

? 67F complains of urine leaks during coughing and laughing. She is advised by her doctor to start Kegel exercises. What muscle is NOT strengthened by these exercises?

- a) Pubococcygeus
- b) Puborectalis
- c) Iliococcygeus
- d) Internal anal sphincter
- e) External anal sphincter

▼ Answer
Choice D (Internal Anal Sphincter)

- Point of this Q is to assess that you know that Kegel exercises strengthen skeletal muscles. Internal anal sphincter is smooth muscle & non-voluntary. You can't train or make it stronger.



Types of Urinary Incontinence

1. Stress Incontinence

- Leakage of urine with actions that **increase intra-abdominal pressure** (coughing - sneezing - laughing - squatting - sitting up) in **old females or multigravida**
- **Treatment → Kegel Exercises, Vaginal pessaries, Sling Surgery, or alpha agonists**

2. Urge Incontinence (Detrusor Hyperactivity)

- Leakage of urine as soon as the patient **gets an urge to pee**. Examples are when the patient **hears running water, thinks about peeing**, or when the **urine comes in contact with the detrusor muscle causing it to contract**
- **Multiple Sclerosis**. Putting this here because it is HY AF. 32F + episodes of blurry vision + ankle clonus + urine leak. This is URGE Incontinence.
- **Treatment → Oxybutynin (Muscarinic Receptor Antagonist)**

3. Overflow Incontinence (Neurogenic Bladder)

- Dripping of urine due to **inability of bladder to empty itself**. Urine accumulates and bladder pressure increases → **few drops of urine escape**
- Common in **Diabetics** & patients with **BPH**
- **Treatment → Bethenchol (Muscarinic Receptor Agonists)**
 - We use **alpha-1 blockers (-azosin) in people with BPH**

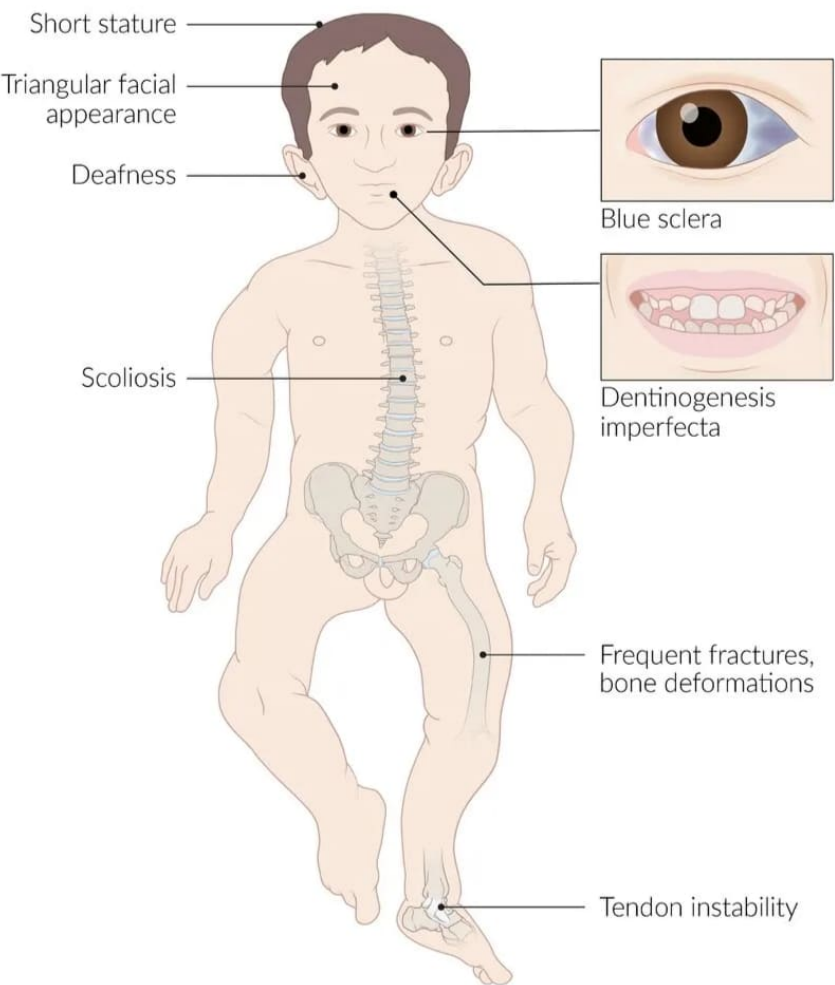
Q27

A female newborn develops respiratory distress. Her respirations are 80/min. There was poor prenatal care. Physical examination shows intercostal retractions. A chest x-ray shows multiple rib fractures. Skeletal x-rays show multiple fractures of the long bones at various stages of healing; the skull bones have a wormian appearance. There is no family history of recurrent fractures. Which of the following is the most likely diagnosis?

- A. Ehlers-Danlos syndrome, hypermobility type
- B. Ehlers-Danlos syndrome, vascular type
- C. Marfan syndrome
- D. Osteogenesis imperfecta, type I
- E. Rickets

▼ Explanation

- Answer is D (Osteogenesis Imperfecta, type I)
 - IMP Clues
 - CXR shows multiple rib fractures + Skeletal x-ray shows multiple fractures of long bones at various stages of healing (Important DD is IO, Abuse, and Osteopetrosis)
 - Skull has a wormian appearance (very HY clue that establishes IO as the dx)
 - Dx → Osteogenesis Imperfecta
 - AD; caused by a mutation in COL1A1/COL1A2 genes, resulting in abnormal Type 1 Collagen
 - Type 1 Collagen forms bones, teeth, and sclera
 - Result ⇒ Weak bones which are liable to fractures (hence IO is also known as brittle bone disease)
 - Presents as recurrent fractures in a child with blue sclera & conductive hearing loss
 - CHL is caused by defective middle ear bones (the ossicles)
 - The “wormian appearance” is due to abnormal ossification of skull bones



? What step of collagen synthesis is defective in patients with Osteogenesis Imperfecta?

- ▼ Answer
- Formation of hydrogen bonds for collagen’s secondary structure integrity - Caused by Glycine → Alanine
- If glycine is replaced by alanine → less hydrogen bonding → abnormal secondary structure of collagen → Weak collagen

Q28

A 22-year-old man is brought to the emergency department 30 minutes after a friend found him unconscious on the floor. A drug overdose is suspected. His pulse is 120/min, respirations are 4/min with apparent low tidal volumes, and blood pressure is 120/100 mm Hg. Physical examination shows mild cyanosis. He is intubated and mechanically ventilated with positive pressure ventilation (rate = 12/min, $V_T = 7$ mL/kg) using 10 cm H₂O positive end-expiratory pressure (PEEP). Which of the following sets of findings best describes the effects of the mechanical ventilation with PEEP on this patient's alveolar (P_A) and intrapleural (P_{ip}) pressures?

Choices	Peak Inspiratory P _A	End-Tidal P _A	Peak Inspiratory P _{ip}	End-Tidal P _{ip}
A	Positive	positive	positive	positive
B	Positive	zero	positive	negative
C	Zero	zero	zero	negative
D	Zero	negative	zero	zero
E	Negative	positive	positive	positive
F	Negative	zero	negative	negative

▼ Explanation

- Answer is A
 - Patient is on a ventilator so air is getting pushed inside the lungs causing positive inspiratory alveolar pressure → pushes on surrounding tissue causing positive inspiratory intrapleural pressure.

- Q also says there is a **PEEP** (which basically is additional air pressure exerted during expiration, so alveoli keep open and prevent their collapse)
 - So the **End-Tidal pressure of alveoli is positive** → in turn the **End Tidal intrapleural pressure is also positive**

Q29

A 3-month-old girl is brought to the physician by her parents because of a 2-month history of an enlarging red spot on her abdomen. She appears well developed and well nourished. She is at the 65th percentile for length and 70th percentile for weight. A photograph of the lesion is shown. Microscopic examination of the lesion is most likely to show which of the following?



- A. Arterioles in a fibrous stroma
- B. Arteriovenous malformations
- C. Cavernous vascular spaces
- D. Densely packed capillaries
- E. Dilated lymphatic vessels

▼ **Explanation**

• **Answer is D (Densely packed capillaries)**

◦ **IMP Clues**

- 3-month-old (age is important to differentiate between cherry & strawberry hemangiomas)
- Enlarging Red spot on her abdomen (Yes, it does enlarge, which get parents worried, so they come in)
- Photograph of the lesion is shown (Strawberry Hemangioma)

◦ Q asks what would be seen upon microscopic examination of the lesion?

- **Strawberry Hemangioma is a benign vascular tumor in children**
- They enlarge rapidly **BUT REGRESS OVERTIME**
- It is just **abnormal angiogenesis, which shows densely packed capillaries on microscopic examination**

? Differentiate between Strawberry Hemangiomas & Cherry Hemangiomas.

▼ **Answer**

Strawberry Hemangioma

- In *children*
- *Larger* in size
- *Regresses*

Strawberry Hemangioma shown below:



Cherry Hemangiomas

- In *adults*
- *Smaller* in size
- *DOESN'T* Regress

Cherry Hemangioma shown below:



Q30

A 44-year-old woman, gravida 2, para 2, comes to the physician for a health maintenance examination. Physical and pelvic examinations show no abnormalities. Results of a Pap smear show dysplastic columnar ciliated cells. If this patient were healthy, columnar cells seen on the patient's Pap smear would most likely originate from which of the following areas?

- A. Cervical canal
- B. Endometrium
- C. Posterior fornix of the vagina
- D. Vaginal portion of the cervix
- E. Vaginal vestibule

▼ Explanation

• Answer is A (Cervical Canal)

- Q asks where would columnar cells be seen in the female genital tract?
- There is actually a few Qs on the NBMEs that ask for the epithelium of different organs, so let's go through them:
 - Vulva → Stratified Squamous Epithelium (Keratinized)
 - Vagina & Ectocervix (vaginal part of the cervix) → Stratified Squamous Epithelium (Non-keratinized)
 - Cervical Canal (Endocervical canal/Endocervix) → Simple Columnar Cells
 - Uterus → Simple Columnar Cells
 - Proliferative phase → with long tubular glands
 - Secretory phase → with Coiled glands
 - Fallopian tubes → Simple Columnar Cells (Ciliated)
 - Ovaries → Simple Cuboidal Cells
- So, best answer is **Choice A (Cervical Canal)**



Let's Recap:

1. From Vulva to Ectocervix → **Stratified Squamous Epithelium**
2. Transformation Zone → **Squamocolumnar junction**
 - Junction between Ectocervix & Endocervix
 - Most common site of cervical cancer, so site of pap smear
3. From Endocervix to Fallopian Tubes → **Columnar Epithelium**
4. Ovaries → **Simple Cuboidal**

▼ Other Choices

You answer, we just reviewed them.

- **Choice B** → Columnar Epithelium with glands depending on phase
- **Choices C, D, and E** → Stratified Squamous Epithelium

Q31

Which of the following best explains impaired action potentials in the affected axons in patients with demyelinating diseases?

- A. Cessation of fast axonal transport
- B. Degeneration of the axon
- C. Degeneration of voltage-gated Ca^{2+} channels
- D. Depolymerization of axonal microtubules
- E. Increase in axonal capacitance

▼ Explanation

• Answer is E (Increase in axonal capacitance)

- Q asks how does demyelinating diseases affect action potential
- **First what is the function of Myelin?**
 - Allows saltatory conduction
 - **Decreases capacitance** (reduces the amount of charge that can be stored)

- **Increases membrane resistance**

◦ So, if you lose the myelin in a demyelinating disease what happens?

- **Loss of saltatory conduction**
- **Increase capacitance**
- **Decreases membrane resistance**

◦ So, correct answer is **Choice E Increase in axonal capacitance**

▼ Other Choices

- **Choices A & D** → refers to axonal transport, which is not the same as AP.
- **Choice B** → Demyelinating diseases damage the myelin NOT the axon itself
- **Choice C** → Affects the AP in the synapses not across the myelin

Q32

A 70-year-old man with severe congestive heart failure has had progressive orthopnea for the past 4 weeks. He has not been taking his medications. During this time, his urine output has progressively decreased to 300 mL/day. Which of the following sets of laboratory findings is most likely?

Choices	Serum Urea Nitrogen (BUN) (mg/dL)	Serum Creatinine (mg/dL)	Urine Na ⁺ (mEq/L)	Urine Specific Gravity
A	10	1	50	1.010
B	20	2	40	1.025
C	30	2	30	1.005
D	40	2	5	1.025
E	50	4	10	1.010

▼ Explanation

- **Answer is D**

◦ **IMP Clues**

- Severe congestive heart failure has had progressive orthopnea (CHF = Rt + Lt side HF, Blood is accumulating into the LV, causing decreased CO and backing up of blood into lungs → Orthopnea)
- He has not been taking his medications (that's why probably)
- Urine output decreased to 300mL/day (urine decreased meaning that the kidney is not getting enough blood, so thinking we are hypovolemic → reabsorbs water & Na)

- Q asks for expects labs

◦ **First, CHF means that there is LV failure causing:**

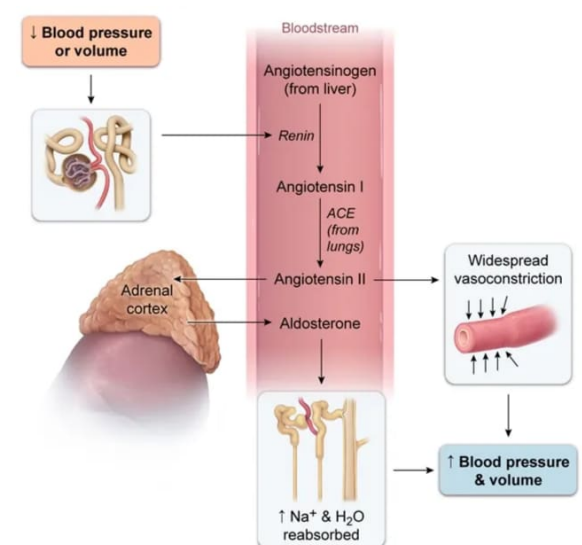
- **Decreased CO** → **decreased blood flow to kidney** → **activation of RAAS**
- **Blood backs up into atria** → **lungs** → **Increased hydrostatic pressure** → **Extravasation of intravascular fluid into lungs** → **Orthopnea + possible LL edema & ascites** → **decreased effective intravascular plasma volume**

◦ **Decreased Effective Plasma Volume** causes kidney to **reabsorb as much water (and Na) as possible** so that it "fixes" the perceived "decreased plasma volume" → **Decreased Urine Output & Hypervolemia** (which is actually bad as the body is actually overloaded already, the fluid is juts in the body cavities not the arteries)

- **This is called pre-renal azotemia**

- Decreased blood supply to kidney → **Increased Creatinine Levels**
- Expected Labs of pre-renal azotemia → **BUN/Creat >20, while FeNa < 1%**
 - Basically, Urea (BUN) is reabsorbed into the medulla to make the medulla hyperosmolar, causing water reabsorption → Increased BUN way more than the increased Creatinine.
 - Fraction of excreted Na (FeNa) is the amount of Na excreted. It is decreased as Na is reabsorbed, so that water follows it back, causing water reabsorption

◦ **So, end result would be:**



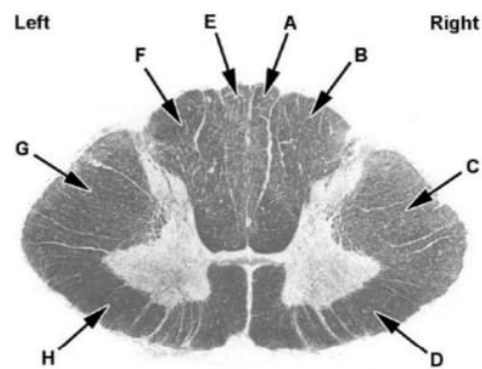
- **Increased Creatinine Levels**
- **Increased BUN/Creatinine ratio**
- **Decreased FeNa (Na in urine)**
- **Decreased water in urine (decreased urine output volume & high urine specific gravity)**


Values of Pre-renal vs Post/Intra-renal azotemia:

- **Pre-renal azotemia (hypovolemia):**
 - BUN/Creatinine >20
 - FeNa < 1%
- **Intra-renal (renal pathology) & Post-renal (stone, BPH, cervical cancer):**
 - BUN/Creatinine <20
 - FeNa > 1%

Q33

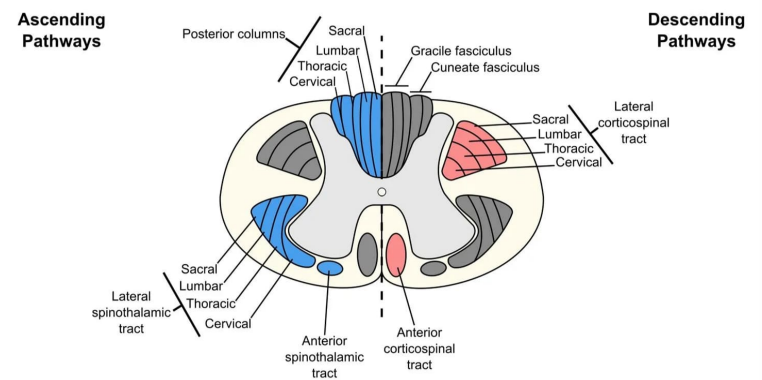
A 44-year-old man with invasive pancreatic cancer is brought to the emergency department because of a 2-week history of severe right-sided back and abdominal pain. The patient states that he has had a 6.8-kg (15-lb) weight loss during the past month. Physical examination shows no abnormalities. An operation is scheduled to relieve the pain. The most likely target of pain relief is which of the following labeled sites in the photograph of a myelin-stained cross section of the spinal cord shown?



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

▼ Explanation

- **Answer is H**
 - Basically, Q wants the site that conveys pain. We know it's the Spinothalamic tract. So. all we need to do is find the correct label.
 - **Choices A & E → Gracilis Fasciculus of Dorsal Column.** Conveys fine touch, proprioception, and vibrations from the **lower limb**
 - **Choices B & F → Cuneate Fasciculus of Dorsal Column.** Conveys fine touch, proprioception, and vibrations from the **upper limb**
 - Now Sometime I get confused between which is the spinothalamic vs which is the corticospinal. I remember which is which by **"No 2 sensation tracts are next to each other on a hemi-cord"**
 - **Dorsal Column at the back (Sensation), Below it CAN'T be sensation tract, so must be motor (Corticospinal), then below it CAN be a sensation tract (Spinothalamic)**
 - Based on what I said above, **Choices G & C → Corticospinal tracts**, which convey motor action
 - **Choices H & D → Spinothalamic tracts.** Conveys temperature & pain sensations.



- Q says that the pain is on the **RIGHT SIDE**, so we choose **contralateral side** → **LEFT SPINOTHALAMIC TRACT (CHOICE D)**

Q34

A 40-year-old man has had enlarging breast tissue for the past 3 months. He began taking a diuretic 6 months ago. Which of the following drugs most likely caused this adverse effect?

- A. Amiloride
- B. Furosemide
- C. Hydrochlorothiazide
- D. Spironolactone
- E. Triamterene

▼ Explanation

- **Answer is D (Spironolactone)**
 - **IMP Clues**
 - Man has had enlarging breast tissue (gynecomastia, causes are HY)
 - Began taking a diuretic (probably the reason)
 - Q asks which drug most likely cause this?
 - Easy Pharm Q. Adverse effects of different Diuretics are super HY.
 - **Spironolactone (Aldosterone Receptor Antagonist + Anti-androgen activity)**
 - HY Side effects → **Hyperkalemia** (K sparing diuretic) & **Gynecomastia** (Anti-androgen effect)
 - How does Spironolactone work?
 - Prevents Aldosterone binding to Cytosolic mineralocorticoid Receptors in the Collecting Ducts:
 - In Principle Cells:
 - Inhibits ENac → decreased permeability to sodium → **decreased sodium reabsorption [asked on NBME]**
 - Inhibits ROMK → decreases potassium secretion → **decreased potassium wasting**
 - Inhibits Water Reabsorption → **diuresis**
 - In α-Intercalated cells:
 - Inhibits H-ATPases → decreases H excretion → **Metabolic Acidosis**



HY Causes of Gynecomastia on the USMLE:

- Drug-Induced**
 - Spironolactone** (Highest Yield of All)
 - Cimetidine** (H2-Blocker)
- Liver-Cirrhosis**
 - Liver breaks down estrogen, if diseased → Estrogen accumulates
- Estrogen-Over-Production**
 - Granulosa Cell Tumors**
- Androgen-Over-Production** (androgen gets aromatized into estrogen)
 - Sertoli-Leydig Cell Tumors**
 - Adrenal gland hypersecretion**
 - Body-Building Androgen pills**
- Others
 - Hyperprolactinemia** (presents as gynecomastia + impotence)
 - Choriocarcinoma** (in a male, yes it is possible)

▼ Other Choices

- **Choices A & E → K sparing diuretic (ENac blocks receptors in CD)**
 - HY Side Effects: **Hyperkalemia**
- **Choice B → Loop Diuretics**
 - HY Side Effects: **Hypocalcemia, Hypokalemia, Contraction alkalosis, Sulfa-allergy, Ototoxicity**



Patient has severe edema and the doctors decided to administer Loop diuretic, but the patient has sulfa allergy. What drug should the patient be given?

▼ Answer

Ethacrynic acid - a loop diuretic given if patient has sulfa allergy

- **Choice C → Thiazide Diuretics**

- HY Side Effects: [📄] **"HyperGLUC" + others**
 - **Hyperglycemia**
 - **Hyperlipidemia**
 - **Hyperuricemia (can cause gout)**
 - **Hypercalcemia**
 - **Hypokalemia**
 - **Contraction alkalosis**
 - **Lithium toxicity (if co-ingested with lithium)**

Q35

A 35-year-old woman comes to the physician because of a 6-month history of intermittent fever, fatigue, and unexplained weight loss. She has had an 18-kg (40-lb) weight loss during this period. Her temperature is 37.2°C (99°F). Laboratory studies show a CD4+ T-lymphocyte count of 60/mm³ (N>500) and a plasma HIV viral load of 600,000 copies/mL. The most appropriate treatment for this patient includes a drug that targets which of the following steps of viral replication?

- A. Absorption to and penetration into susceptible host cells
- B. Disruption of viral receptors
- C. Release of viral particles from the cells
- D. Synthesis of viral DNA
- E. Uncoating of viral nucleic acid

▼ **Explanation**

• **Answer is D (Synthesis of viral DNA)**

◦ **IMP Clues**

- CD4 T-lymphocytes of 60/mm³ (AIDS patient as CD4 count < 200)
- Plasma HIV viral load of 600,000 copies/ml (really high viral load, meaning he's not taking his drugs or the virus is drug-resistant)
- Q asks the most appropriate ttt for this patient targets which step of viral replication?

• **HIV's main ttt is Antiretroviral therapy (NRTIs & NNRTIs)**

- They are just **Reverse Transcriptase inhibitors**
- Reverse transcriptase causes **synthesis of DNA from RNA** (normally it's RNA from DNA)
- So best answer is **Choice D (Synthesis of viral DNA)**



What are the general side effects of NRTIs vs NNRTIs?

▼ **Answer**

NRTIs → Lactic acidosis & Bone marrow suppression

- If USMLE asks for what NRTI is the most known for BMS → **Zidovudine**

NNRTIs → Hepatotoxicity & Rash

Q36

A 78-year-old man is found unresponsive in his yard by a neighbor. Paramedics arrive and begin resuscitation. Twenty-five minutes later, he regains a stable cardiac rhythm. He is brought to the emergency department, and mechanical ventilation is initiated. His temperature is 36.4°C (97.5°F), pulse is 76/min, respirations are 14/min (with spontaneous respiratory efforts), and blood pressure is 98/60 mm Hg. He remains unresponsive. After the patient is admitted to the hospital, his neighbor says, "He always said he wouldn't want to be kept on life support if there was no hope of recovery. His wife died 5 years ago, and I've been cooking for him and helping him with errands since then." The patient has no children or close relatives. The physician believes that the patient has sustained significant anoxic brain injury and his prognosis is poor. It is most appropriate for the physician to state to the neighbor which of the following at this time?

- A. "The hospital lawyer must be consulted since we do not know if your neighbor had an advance directive."
- B. "Since the patient has already been put on life support, he will have to remain on life support at this time."
- C. "Thank you for telling me this. Your friend's previous statements to you can be helpful in making decisions for him."
- D. "Thank you for your concern, but since you are not a relative of the patient you cannot make decisions for him."

E. "Unfortunately, your friend is brain-dead, so there is no need to make life support decisions at this point."

▼ Explanation

- **Answer is C ("Thank you for telling me this. Your friend's previous statements to you can be helpful in making decisions for him.")**
 - **IMP Clues**
 - He remains unresponsive (Patient is comatosed, so he can't take his own decisions. This is where surrogate decision maker comes in)
 - His wife died 5 years ago (no wife) + has no children or close relatives (no children/family/relatives)
 - I've been cooking for him & helping him with errands since then (So, this neighbor is very close to the patient, not just a stranger)
- This Q tests if you know the **Hierarchy of Surrogate Decision Makers** (given that there is **NO** advanced directive):
 - **Wife/Husband → Adult Children → Parents → Adult Siblings → Other close Relatives or Friends**
 - The Q says that the wife is dead, he has no children, and no close relatives (this includes parents/siblings) → **Just the close neighbor left.**



Unusual scenarios where the USMLE can trick you:

1. Patient has a **court-appointed guardian** → **Highest in hierarchy & takes the decisions**
2. Patient has **absolutely no one** (not even relatives) → **Physician take the decisions**

Q37

A 60-year-old man has had easy fatigability, loss of appetite, and significant weight loss over the past 3 months. Routine blood studies show a marked increase in serum calcium concentration. Radiographic examination does not show bone metastases. This patient is most likely to have cancer of which of the following organs?

- A. Colon
- B. Lung
- C. Pancreas
- D. Prostate
- E. Thyroid gland

▼ Explanation

- **Answer is B (Lung)**
 - **IMP Clues**
 - Easy fatigability, loss of appetite, and significant weight loss (buzzy for cancer)
 - Increase in serum calcium (Cancer + hypercalcemia is 1 of 3 things on the USMLE: 1) Metastasis 2) PTHrP-secreting tumor 3) Multiple Myeloma)
 - Radiographic examination does not show bone metastasis (This excludes option 1)
- **Dx → Squamous Cell Carcinoma (SCC) of the Lung**
 - **Central mass** that mostly affects **smokers** with cavitation
 - Origin = Epithelial cells
 - Biopsy shows **Keratin pearls (like any other SCC) + stains positive for Keratin**
 - Associated with **"Cavitations"** on the USMLE; they show you a **picture of a lung with cavitations with NO other info** & ask for the diagnosis.
 - Releases **PTHrP** → **Hypercalcemia**
 - USMLE may convey this as renal stones in a patient with hemoptysis & weight loss



Tumors that metastasize to bones cause local osteolysis, which releases calcium into bloodstream

- This is why **ONLY** bone metastasis of tumors that cause **osteolytic lesions** are usually associated with **hypercalcemia**.
- Tumors that cause **osteoblastic lesions**, however, **DON'T CAUSE** hypercalcemia as they are **"bone-forming"**
 - Most HY tumor that causes osteoblastic lesions on the USMLE is ⇒ **Prostate Cancer**



What other HY tumor can this patient have if "Lung" was not an answer choice?

- ▼ **Answer**
Renal Cell Carcinoma - secretes PTHrP & EPO

? What would this patient's arrows of PTH, Calcium, Phosphate be?

▼ Answer

- **LOW** PTH
- **HIGH** Calcium
- **LOW** Phosphate

PTHrP is not the same as PTH. It does its job yes, but it is not the same molecule. Calcium is increased & Phosphorus is decreased. This cause PTH to go **down**.

? What other lung cancer(s) are central in site?

▼ Answer

Small Cell Lung Cancer

"SSSS"

Sentral (Central) lung cancers are small cell carcinoma & squamous cell carcinoma and are associated with smoking.

Q38

A 39-year-old woman with obesity and recently diagnosed hypertriglyceridemia comes to the physician for a follow-up examination. She started a diet 3 months ago that was recommended by the physician. She also has peptic ulcer disease. She has smoked 1 pack of cigarettes daily for 10 years. She does not appear to be in distress. Her pulse is 80/min and regular, respirations are 12/min, and blood pressure is 145/92 mm Hg. The lungs are clear to auscultation and percussion. Cardiac examination shows no abnormalities. Abdominal examination shows normal bowel sounds; there are no masses or organomegaly. There is mild epigastric tenderness to deep palpation. Serum studies show a total cholesterol concentration of 210 mg/dL, HDL-cholesterol concentration of 20 mg/dL, and triglyceride concentration of 350 mg/dL. Which of the following is the most appropriate pharmacotherapy for this patient?

- A. Atorvastatin
- B. Cholestyramine
- C. Colestipol
- D. Ezetimibe
- E. Gemfibrozil

▼ Explanation

- Answer is E (Gemfibrozil)
 - IMP Clues
 - Recently diagnosed hypertriglyceridemia
 - Total cholesterol concentration of 210mg/dL (slightly increased, should be <200)
 - HDL-cholesterol concentration of 20 mg/dL (low, so we need to increase it)
 - Triglyceride concentration of 350 mg/dL (high, so we need to lower it)
 - Q asks for recommended pharmacotherapy for this patient
 - When answering these Qs, you have to look at the given concentrations, and choose what is **BEST** for the patient.
 - Here the patient has **high TAGs** with **low HDL**, so the ttt given must be **efficient at lowering TAGs** and **increasing HDL**.
 - **Fibrates** (can be referred to as "**fibric acid derivative**")
 - Stimulates **PPAR-α** → **upregulates LPL** → causes **FFA** (from **TAGs in chylomicrons & VLDLs**) to **enter** adipose cells → **decreases TAG serum levels [MAJOR EFFECT]**
 - **PPAR-α** is a *nuclear transcription factor* which also causes **increases Apo-A I & Apo-A II transcription** → **Increases HDL production**.
 - This is why **Fibrates are the most effective drug class in patients with high TAGs & low HDL**

? What are the HY side effects of fibrates?

▼ Answer

1. **Hepatotoxicity**
2. **Myopathy** (especially gemfibrozil when combined with statins)
3. **Gallstone formation** (due to **inhibition of 7-α-hydroxylase** → decreased bile salts formation → less solubility of fats in bile → increased liability of gallstones formation)

**Don't Get It Mixed-up:**PPAR-***α*** ⇒ **Fibrates**PPAR-***γ*** ⇒ **Thiazolidinediones** (pioglitazone, rosiglitazone)**▼ Other Choices**

- **Choice A → Statins** ***Inhibits HMG CoA reductase*** (rate limiting enzyme of cholesterol synthesis) → less cholesterol synthesized by the body
 - This causes **Up-regulation of LDL receptors** → Cholesterol scattered around the body is **picked-up by the LDL-receptors to the liver. So, it is the drug of choice in patients with high LDL-cholesterol.**
 - Side Effects: **Hepatotoxicity & Myopathy** (especially, if combined with fibrates)



Patient on statins + fibrates and developed high CK levels. What is the dx & cause of above finding?

▼ Answer

Myopathy (Rhabdomyolysis) due to CYP450 inhibition [asked on NBME]



What are the mRNA levels of HMG CoA reductase in a patient that uses statins?

▼ Answer

mRNA levels of HMG CoA reductase INCREASED.

- You inhibit the production of the enzyme. This makes the body want to produce more, hence increase mRNA levels of that enzyme.

- **Choices B & C → Bile Resins/Sequestrants** ***bind to acids & prevent their recycling*** (in the enterohepatic circulation), so the body pulls cholesterol from the blood into the liver to make more bile acids (***via upregulation of LDL receptors***) → **Lowers Cholesterol levels & increases HDL levels.**
 - Almost always used as ***adjuvant therapy*** & never a correct "lone" drug choice.
 - HY side effects: **GI disturbance & Drug malabsorption (and Fat-Soluble Vitamins "KEDA")**
- **Choice D → Ezetimibe** ***inhibits intestinal absorption of cholesterol***, so mainly **decreases LDL.**
 - Like Bile Acid Sequestrants, ***never the correct "lone" drug choice.***
 - HY Side effects: **GI disturbance**



What transporter on enterocytes is blocked by ezetimibe?

▼ Answer

***NPC1L1* Transporter (Neimann-Pick C1-like 1 Transporter)**

Q39

A 6-month-old girl is brought to the office for a well-child examination. She has no history of major medical illness and receives no medications. The patient and her mother recently emigrated from a rural region of China, where they did not receive regular health care. The patient's growth and development are appropriate for age. Physical examination shows no abnormalities. Screening for which of the following is the most appropriate next step in management?

- A. Adenovirus
- B. Cytomegalovirus
- C. Epstein-Barr virus
- D. Hepatitis B
- E. Parvovirus
- F. Respiratory syncytial virus

▼ Explanation

- **Answer is D (Hepatitis B)**
 - **IMP Clues**
 - 6-month-old girl + no hx of major medical illness and receives no medication + patient's growth & development are appropriate for age (the girl is just fine, no medical hx, no ttt, and growth is perfect)
 - Recently emigrated from a rural region of China, where they did not receive regular health care (on the USMLE, emigrated people are either sick or non-vaccinated. This is really HY association)
 - Q asks screening for which of the following is appropriate?

- As the girl is **perfectly healthy** at the moment with **no signs of chronic/congenital infections**, this makes us screen for routine diseases that are screened for in the US medical system.
- **Only Hepatitis B Virus is indicated as a pediatric vaccine for children in the USA.**
 - This is more of STEP2, but HBV vaccine is given in 3 doses:
 - Dose 1 → At Birth
 - Dose 2 → 1-2 months
 - Dose 3 → 6-18 months

Q40

A prospective study is done to assess the relative efficacy of two different antihypertensive medications, both of which were shown to be efficacious in placebo-controlled trials. In the study, patients with hypertension were randomly assigned to receive one of two antihypertensive medications. At the conclusion of the study, some participants reported inconsistent adherence to their medication regimen, while others reported discontinuing their study medication altogether before the primary outcome (blood pressure measurement after 30 days) was obtained. A few of these patients who discontinued their study medication were prescribed the other group's study medication by their primary care physician and were taking it at the time of the primary outcome measurement. In their primary analysis, which of the following methods should the investigators use to analyze data from the patients who were not adherent to the medication regimen?

- A. Exclude the outcome for only those who inadvertently switched to the other study medication
- B. Exclude the outcome for only those who reported stopping the medication altogether
- C. Include the outcome for each participant in the group to which he or she was randomized
- D. Include the outcome for those who took more than a prespecified fraction of medication doses

▼ Explanation

- **Answer is C (Include the outcome for each participant in the group to which he or she was randomized)**
 - This is **intention-to-treat analysis**. On the USMLE, when managing 2 groups of patients who were randomized to receive a certain medications placebo/another medication, we expect to have noncompliance/discontinuation of ttt or even switching to the other groups regimen. **To make results easier to analyze, 9/10 times we are going to analyze the data as *intention-to-treat*.**
 - Basically, **we sort the nonadherent participants to their original groups that they were randomized in.**
 - So, for example, 1000 participants receive the new medication (Group 1), and 1000 participants receive a placebo.
 - We intended to have 1000 participants in each group, so in an intention-to-treat analysis → **We count the participants in the original distribution we intended.**

Q41

A 65-year-old man is scheduled for physical therapy 3 days following a right shoulder operation. As part of a regimen to strengthen his right rotator cuff muscles, he begins therapy to strengthen the subscapularis muscle. Which of the following movements of the arm should this patient perform against resistance?

- A. Abduction
- B. Adduction
- C. Extension
- D. Lateral (external) rotation
- E. Medial (internal) rotation

▼ Explanation

- **Answer is E (Medial (internal) rotation)**
 - Patient here begins therapy to strengthen the **subscapularis muscle**. Q asks what movement should be done against resistance. Basically, Q asks for action of subscapularis muscle.
 - **Rotator Cuff Muscles are HY and are 4 muscles:**
 1. **Supraspinatus**
 - Action → **Abduction (0 → 15 degrees)**
 - Nerve Supply → **Suprascapular nerve**

2. Infraspinatus

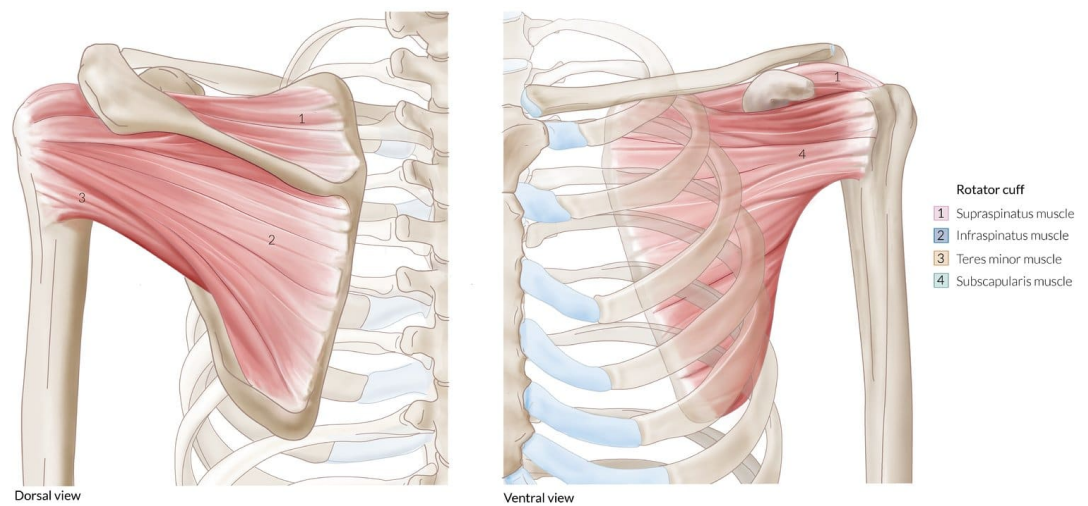
- Action → **External Rotation**
- Nerve Supply → **Suprascapular nerve**

3. Teres Minor

- Action → **External Rotation** (and weak adduction)
- Nerve Supply → **Axillary Nerve**

4. Subscapularis

- Action → **Internal Rotation** (and weak adduction)
- Nerve Supply → **Subscapular nerve** (upper & lower)

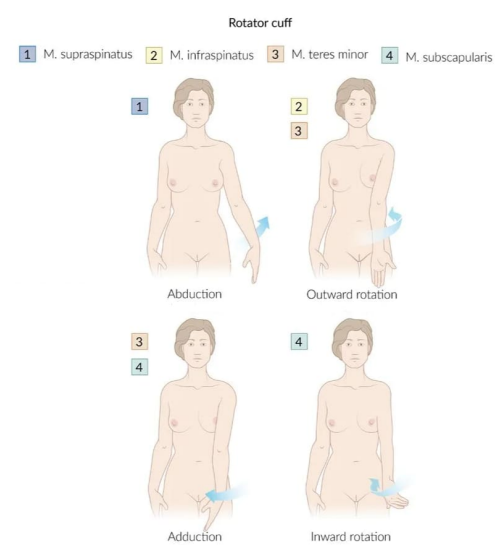
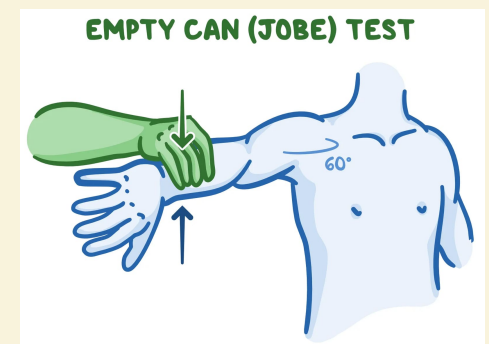


? What is the most common rotator cuff injury?

▼ Answer

Supraspinatus tear - presents as **pain and weakness/loss of shoulder abduction of FIRST 15 DEGREES**

- Tested for by **"Empty Can Test"**
 1. Patient raises arms 90 degrees in the scapular plan
 2. Patient fully rotates his arms internally, so that his thumb is pointing to the floor "as if emptying a can"
 3. Doctors pushed down on arm while patient resists → **Patient feels pain = positive test**



Q42

A 61-year-old man is prescribed fluoxetine for major depressive disorder. This drug has its initial effects on neurons arising in which of the following structures?

- Amygdala
- Insular cortex
- Locus caeruleus
- Raphe nuclei
- Substantia nigra

▼ Explanation

- **Answer is D (Raphe nuclei)**
 - Man is prescribed **fluoxetine** (which is a **SSRI**) for MDD.
 - **SSRI = Selective Serotonin Reuptake Inhibitor.**
 - **Serotonin is synthesized & released** by neurons of the **raphe nuclei** ⇒ Mood Regulation
 - SSRIs → inhibit serotonin reuptake → increase serotonin in synaptic cleft → mood regulation.



Site of origin of HY Neurotransmitters on the USMLE:

1. **Serotonin** ⇒ **Raphe Nucleus** (Midbrain)
2. **GABA** ⇒ **Nucleus Accumbens** (Basal Forebrain) [Found in high concentrations in **cerebellum**]
3. **Norepinephrine** ⇒ **Locus Coeruleus** (Pons)
4. **Acetylcholine** ⇒ **Nucleus Basalis of Maynert** (Basal Forebrain)
5. **Dopamine** ⇒ **Substantia Nigra** (Midbrain)
6. **Histamine** ⇒ **Tuberomammillary nucleus** (Posterior Hypothalamus)

? Which of the following agents are SSRIs?

- A) Citalopram
- B) Desvenlafaxine
- C) Duloxetine
- D) Escitalopram
- E) Fluoxetine
- F) Milnacipran
- G) Paroxetine
- H) Sertraline
- I) Venlafaxine

▼ Answer

A) Citalopram - D) Escitalopram - E) Fluoxetine - G) Paroxetine - H) Venlafaxine

Other Choices

Remaining choices are **SNRIs**

? What are the HY side effects of SSRIs you must be aware of on the USMLE?

▼ Answer

1. **Anorgasmia** (SSRIs are used for premature ejaculation, which sometimes can cause anorgasmia)
2. **SIADH** (vs Lithium which causes DI)
3. **Serotonin Syndrome** (when overdosed or when combined with *SNRIs/TCAs/MAO inhibitors/Tramadol/Linezolid*)
4. **Sleep/wake cycle disturbance**

Q43

A 50-year-old man who lives in eastern Minnesota comes to the physician in July because of a 3-day history of fever and malaise. His temperature is 39.4°C (102.9°F), pulse is 84/min, respirations are 14/min, and blood pressure is 100/70 mm Hg. Physical examination shows no abnormalities. Laboratory studies show a hemoglobin concentration of 13.6 g/dL, leukocyte count of 3500/mm³, and platelet count of 90,000/mm³. The result of a polymerase chain reaction test for *Anaplasma phagocytophilum* is positive. The causal organism in this patient is transmitted via the same vector as which of the following pairs of pathogens?

- A. *Babesia microti* and *Borrelia burgdorferi*
- B. *B. microti* and *Rickettsia rickettsii*
- C. *B. microti* and *Yersinia pestis*
- D. *B. burgdorferi* and *R. rickettsii*
- E. *B. burgdorferi* and *Y. pestis*
- F. *R. rickettsii* and *Y. pestis*

▼ Explanation

- Answer is A (*Babesia microti* and *Borrelia burgdorferi*)

- 2 ways you can solve this Q:

1. You have no fucking idea what *Anaplasma phagocytophilum* is, so you just exclude answer choices based on if they have the same vector or not.

- **Choice A → *Babesia* (causes babesiosis) & *Borrelia burgdorferi* (causes Lyme disease) are BOTH transmitted with *Ixodes tick*. So, work & is the correct answer.**
- **Choice B → *Babesia microti* by *Ixodes tick*, while *Rickettsia rickettsii* by *Dermacentor tick*. Nope, NO MATCH.**
- **Choice C → *Babesia microti* by *Ixodes tick*, while *Yersinia pestis* by fleas. Nope, NO MATCH.**
- **Choice D → *Borrelia burgdorferi* by *Ixodes tick*, while *Rickettsia rickettsii* by *Dermacentor tick*. Nope, NO MATCH.**
- **Choice E → *Borrelia burgdorferi* by *Ixodes tick*, while *Yersinia pestis* by fleas. Nope, NO MATCH.**
- **Choice F → *Rickettsia rickettsii* by *Dermacentor tick*, while *Yersinia pestis* by fleas. Nope, NO MATCH.**

- So, only possible answer is **Choice A (*Babesia microti* and *Borrelia burgdorferi*)**

2. **[For Nerds]** *Anaplasma phagocytophilum* is also transmitted via *Ixodes tick*.

| **The following is all you need to know about *Anaplasma phagocytophilum*:**

- Gram **negative**, **obligate intracellular** bacteria, which are characterized by "**morulae-containing leukocytes**" or "**berry cluster organisms**" (These distinctive features are also shared with *Ehrlichia chaffeensis*)
- Transmitted by ***Ixodes tick***
- ttt → **Doxycycline**

Q44

A child with septicemia has an antibiotic clearance (CL) of .09 L/hr/kg. the steady state serum concentration for the antibiotic is 12 µg/mL. Which of the following is the maintenance dose (in mg/kg/day)?

- A. 2.5
- B. 5.1
- C. 26.0
- D. 51.8
- E. 55.0

▼ Explanation

- Answer is C (26.0)
 - Q asks for the maintenance dose (in mg/kg/day)
 - Formula is $(C_{ss} \times CL \times t) / F$
 - C_{ss} = steady state serum concentration (convert 12 µg/mL → mg; so, 12 µg / 1000 → 0.012mg)
 - CL = clearance (convert 0.09L → mg; so, 0.09L x 1000 → 90mg/hr)
 - $t = 24$ (how do we know the time? the Q says he wants the does in mg/kg/day)
 - $F = 1$ (F is bioavailability, which is 100% or 1 as it is given as IV)
 - Maintenance Dose is → $(0.012 \times 90 \times 24)/1 = 25.92 = \sim 26.0$ (Choice C)

Q45

A 63-year-old woman comes to the physician because of a 2-month history of progressive shortness of breath with exertion. Her pulse is 80/min, respirations are 8/min, and blood pressure is 125/80 mm Hg. Physical examination shows no other abnormalities. A chest x-ray shows a mass pressing against the outside of the trachea just above the carina. Pulmonary function testing is most likely to show which of the following sets of results in this patient?

Choices	FVC	FEV ₁ /FVC	Peak Expiratory Flow Rate	Peak Inspiratory Flow Rate
A	Normal	normal	normal	↓
B	Normal	normal	↓	normal
C	Normal	normal	↓	↓
D	Normal	↓	normal	normal
E	↓	normal	normal	normal
F	↓	↓	normal	↓
G	↓	↓	↓	normal
H	↓	↓	↓	↓

▼ Explanation

- Answer is H
 - IMP Clues
 - CXR shows a mass pressing against the outside of the trachea just above the trachea (so a mass “obstructing” the trachea, we’d expect Obstructive Lung Disease Pattern)
 - Dx → Obstructive Lung Disease
 - In obstructive lung disease, the air is trapped inside the lungs → so LESS air enters & LESS air exits.
 - This means that the expiratory & inspiratory flow rates are *decreased*.
 - Also, we know that obstructive lung diseases cause LOW FVC & FEV₁/FVC.



Obstructive VS Restrictive Lung Diseases PFTs:

Let me fill in you guys on a hack, when getting a PFTs Q on the USMLE, do the following:

- If the pattern is **restrictive**, choose ↓↓↓ for everything except **FEV1/FVC ratio**, choose **normal/↑↑↑**
- If the pattern is **obstructive**, choose ↑↑↑ for everything expect **FEV1, FVC**, and **FEV1/FVC ratio**, choose ↓↓↓

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

Q46

A 26-year-old woman comes to the physician because of a progressive itchy red rash on her arms over the past 2 weeks. She began working in an animal clinic 2 months ago. She says that she has not been bitten, but she was scratched on both arms while caring for a litter of kittens. Physical examination shows annular erythematous plaques with central clearing and advancing scaly borders. There is no regional lymphadenopathy. Which of the following is the most likely diagnosis?

- A. Atypical mycobacterial infection
- B. Cat-scratch disease
- C. Disseminated toxoplasmosis
- D. Psoriasis
- E. Tinea corporis

▼ Explanation

• Answer is E (Tinea corporis)

◦ IMP Clues

- Progressive itchy red rash on arms over the past 2 weeks
- She began working in an animal clinic 2 months ago
- She has not been bitten, but she was scratched
- Annular Erythematous plaques with central clearing and advancing scaly borders
- No regional lymphadenopathy

• Dx → Tinea Corporis

- The description of "annular erythematous plaques with central clearing and advancing scaly borders" is **buzzy** for **tinea corporis** (aka ringworm)
 - "Corporis" means **body**, which tells us the site of the rash
- Transmission can be via **animals** (like here) or **person-to-person via direct contact or contaminated objects**
- The rash can also be described as "itchy or pruritic," "circular," and "expands centrifugally" on the USMLE.
- Dx is clinical, but USMLE likes:
 - KOH preparation of skin scrapings shows **branching septate hyphae**
 - Wood lamp UW light of **Microsporum fluoresces green**, while Trichophyton & Epidermophyton don't.
- Treatment → **TOPICAL azoles**

"I remember it by thinking the **M** in **Microsporum** is just an **inverted W** of **Wood lamp**."



What layer of the skin does tinea colonize?

▼ Answer

Stratum Corneum

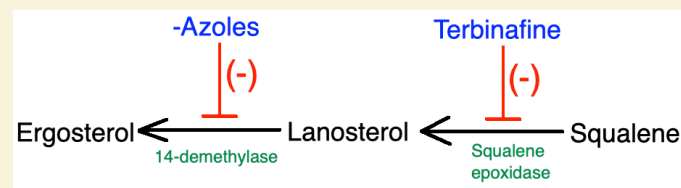


? What is the mechanism of action & HY side effects of azoles?

▼ Answer

MOA → inhibits **14-demethylase** (inhibits ergosterol synthesis/fungal plasma membrane)

HY Side Effect → **Hepatotoxicity**



Q47

A 48-year-old man comes to the physician because of a 24-hour history of severe abdominal pain and blood-tinged vomiting. He smokes 2 packs of cigarettes and drinks eight 12-ounce cans of beer daily. His temperature is 37.7°C (99.9°F), pulse is 110/min, respirations are 16/min, and blood pressure is 120/90 mm Hg. Abdominal examination shows absent bowel sounds, involuntary guarding, and epigastric tenderness with rebound tenderness. An x-ray shows free air in the abdominal cavity. Which of the following is the most likely diagnosis?

- A. Acute cholecystitis
- B. Acute pancreatitis
- C. Alcoholic gastritis
- D. Appendicitis
- E. Perforated peptic ulcer

▼ Explanation

- Answer is E (Perforated peptic ulcer)

- IMP Clues

- Severe abdominal pain and blood-tinged vomiting (vomiting blood on the USMLE is usually either PU, varices, or MW tears; however, blood-tinged is hinting more towards PU or MW tears. Varices are massive hematemesis)
- Smokes 2 packs of cigarettes & drinks eight 12-ounces cans of beer daily (heavy smoker & drinker, which are risk factors for PU)
- Abdominal examination shows absent bowel sounds, involuntary guarding, and epigastric tenderness with rebound tenderness (signs of peritonitis, so this hints to a perforated PU → peritonitis)
- X-Ray shows free air in the abdominal cavity (air under the diaphragm is buzzy for perforated PU)

- Dx → Perforated Peptic Ulcer

“HY AS FUCK SO CONCENTRATE AS WE HAVE A SHIT TON OF INFO TO COVER.”

1. First let's discuss peptic ulcers

- Could refer to either Gastric Ulcers or Duodenal Ulcers.

- How to differentiate?

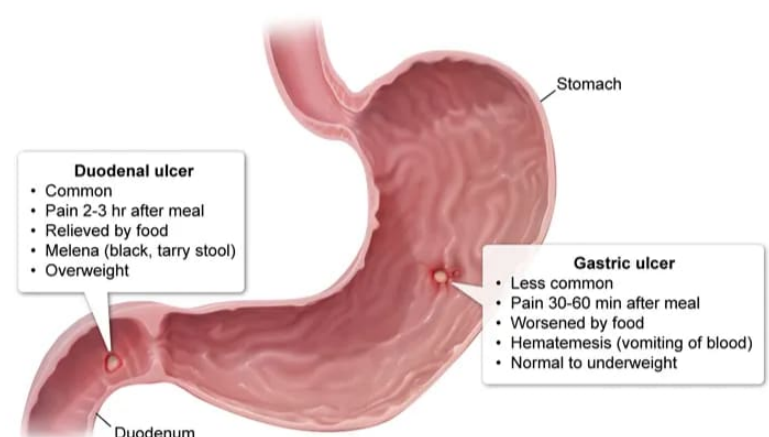
- **Gastric Ulcer**

Most common site of GU is **lesser curvature of antrum**

- **Pain with eating** that is **relieved by vomiting**, so patient typically **loses weight** as he is scared to eat.

- Eating → **induces** gastric secretion → more mucosal inflammation
- Vomiting → **less** acid in stomach → less mucosal inflammation

- **Duodenal Ulcer (more common)**



Most common site of DU is **anterior wall of 1st part of duodenum**, aka "anterior duodenal bulb"

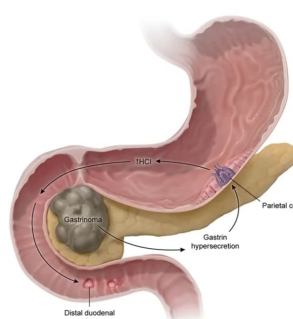
- **Pain with hunger** that is **relieved by eating**, so patient typically **gains weight** as he is scared of hunger pain.
 - Hunger → **less** bicarb secretion in duodenum → more mucosal inflammation
 - Eating → **induced** bicarb secretion in duodenum → less mucosal inflammation

• **Risk Factors**

- **H.pylori infection (most common overall)**
- **NSAIDs**
 - decreases PGs → decreases mucosal protection → ulcer formation
 - NSAIDs-induced ulcers are treated with **misoprostol (PGE2 analogue)**
 - Also, switch the patient to a **selective COX-2 inhibitor (Celecoxib)**
 - COX 1 → responsible for **integrity of gastric mucosa (PGE2/PGI2)** & TXA2 formation (causes PLTs aggregation)
 - COX 2 → responsible for inflammation, pain, and vasodilation.

• **Gastrinomas (Zollinger-Ellison Syndrome)**

- presents as **recurrent, ttt-resistant duodenal & jejunal ulcers**, diarrhea, abdominal pain + **pancreatic HEAD mass**
- **HY AF to know that Gastrin levels remain elevated/increases AFTER SECRETIN ADMINISTRATION**



• **Stress ulcer (Curling & Cushing's)**

- USMLE asks for mechanisms so know them:
 - **Curling** (**Bu**rn → fluid loss → **hypovolemia** → decreased perfusion → ischemic injury & ulcer formation)
 - **Cush**ing's (**h**ead injury → **increased ICP** → **increased vagal stimulation** → increased Ach → increased acid secretion)

• **Smoking & Alcohol**

? What type of acid-base imbalance is caused by vomiting?

▼ Answer

Hypokalemic Hypochloremic Metabolic Alkalosis

? What hormone controls bicarb secretion into the duodenum?

▼ Answer

Secretin - hormone produced by **S cells of duodenum** in response to **acidic chyme** (from the stomach)

- Causes secretion of **bicarb-rich secretions** that **neutralizes acidic chyme & decreases gastrin levels**, which decrease acid production

USMLE might show you a **graph of pancreatic secretions** with **increasing "volume"**, but **unchanged "enzymes concentration."** They then ask for **what hormone caused this?**

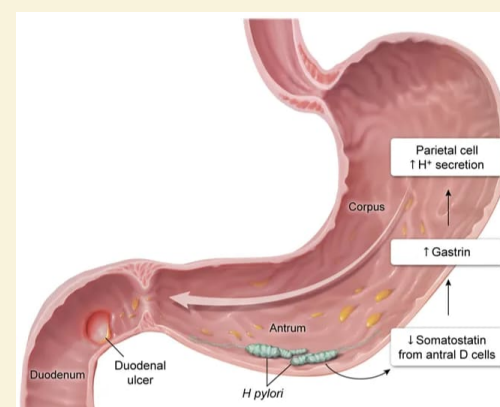
- Answer is **Secretin** as it **increases bicarb-rich secretions with NO increase in digestive enzymes.**

? How does H.pylori cause ulcers?

▼ Answer

H.pylori produces **urease**, which cleaves **urea** → **ammonia & CO2**

- **Ammonia** is **alkaline** causing the bacteria to survive in the **acidic environment**
- **Ammonia** also irritates the surrounding **mucosa** → **mucosal damage & ulcer formation**
 - Cell destruction of **somatostatin-secreting D-cells** → **increase gastrin secretion** → **increased gastric acid production** by **parietal cells** → further **mucosal damage** → **ulcer formation**



? What is a HY future complication of untreated H.pylori?

▼ Answer

Untreated H.pylori causes **MALT (Mucosa-Associated Lymphoid Tissue) Lymphoma** due to **chronic inflammation** [asked on NBME]

- Chronic inflammation → **chronic lymphocytes stimulation** → **B-cell lymphoid follicles start forming in the gastric mucosa/submucosa** → overtime chronic polyclonal proliferation can cause mutations → **monoclonal proliferation → Lymphoma**
 - Hence the name "mucosa-associated lymphoid tissue lymphoma"

2. Perforated Peptic Ulcer

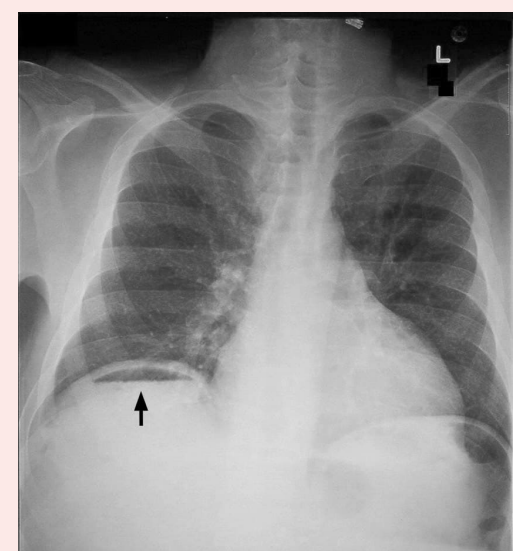
- It is the **most common cause of hematemesis** worldwide
 - On the USMLE, **hematemesis** is either **Peptic Ulcer, Esophageal/Gastric Varices, Mallory Weiss Tears**, or rarely **cancer**.
 - **Peptic Ulcer** → they give you **hx of weight loss/gain, smoking, alcohol, stress, obesity, H.pylori infection** + **signs of peritonitis** (absent bowel sounds, involuntary guarding, and epigastric tenderness with rebound tenderness)
 - **Varices** → they give you **hx of liver cirrhosis** or **left gastric vein thrombosis (esophageal varices) / splenic vein thrombosis (gastric varices)**
 - they can be tricky and just say "chronic alcoholic" or give you signs of cirrhosis (spider angiomas, ascites, gynecomastia, flapping tremors)
 - **MW tears** → hx of **retching or vomiting**; USMLE likes **"partial mucosal tears"** for what would be seen on endoscopy.
 - **Cancer** → hematemesis, weight loss, **early satiety (buzzy for gastric cancer)**, **progressive dysphagia (buzzy for esophageal cancer)**
- **Qs on Perforated PU are usually:**
 1. Give you **hx of risk factors** (smoking, alcohol, stress, obesity, or H.pylori infection) + **signs of peritonitis** (absent bowel sounds, involuntary guarding, and epigastric tenderness with rebound tenderness) and **ask for the diagnosis**. (like they did here)
 2. Ask for the **type of shock** depending on the findings given:
 - a. **Hypovolemic Shock** → **low CO, low PCWP, high HR, high SVR + cold skin**
 - b. **Septic Shock** → **high CO, low PCWP, high HR, low SVR + hot skin**
 3. **Ask for Expected radiology** or **give you the radiology and ask for the diagnosis** → **Air under the diaphragm**, which can also be referred to **"intraperitoneal air"** or **"pneumoperitoneum"**
 4. Rare (but seen) Qs give you **"air under the diaphragm"** & ask for **most likely SITE of perforation**
 - a. **GU** → **anterior wall of lesser curvature**
 - b. **DU** → **anterior wall of 1st part**

Note that POSTERIOR PERFORATIONS are possible, (again, STEP2 shit but if they show up then fair game)

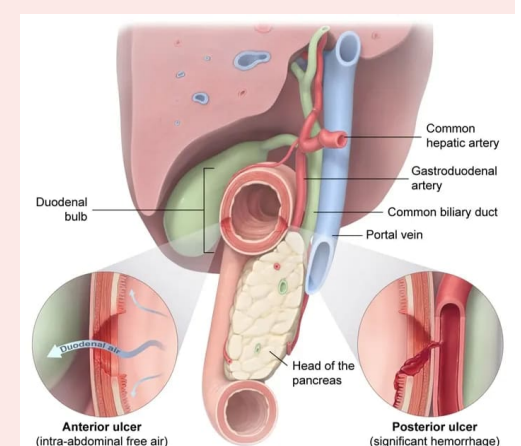
- posterior **GU** perforation causes erosion into **Left Gastric Artery** → **MASSIVE UPPER GI BLEEDING & SHOCK**
- Posterior **DU** posterior causes erosion into **gastroduodenal artery** → **MASSIVE UPPER GI BLEEDING & SHOCK**

Regarding Duodenal Ulcers:

Anterior DU perforation causes "Air Under the Diaphragm" on CXR:



Anterior vs Posterior DU Perforation:



▼ Other Choices

- **Choice A → Acute Cholecystitis** on the USMLE presents as **RUQ pain +/- nausea +/- vomiting** in a patient with **risk factors (Obese, female in her 40s, hx of gallstones, hyperlipidemia)** + US can show **gallstones** or "**pericholecystic fluid accumulation**."
- **Choice B → Acute pancreatitis** presents as **backpain/epigastric pain** with **nausea, vomiting** in a patient with **hx of trauma, TAGs > 1000mg/dL, hx of gallstones, alcohol drinking** + Labs show **high serum amylase & lipase**.
- **Choice C → Alcoholic gastritis** presents as **diffuse epigastric pain +/- nausea and vomiting**. If erosions bleed, patient can present with **hematemesis** (but rare on the USMLE). Signs of peritonitis are **not present** in alcoholic gastritis.
- **Choice D → Appendicitis** present as **peri-umbilical pain that later localizes to the RLQ**. USMLE likes to ask *for the reason of the change of pain site*; answer is **inflammation of parietal peritoneum**.
 - Basically, at first the appendix is inflamed, so inflammation **spreads to overlying visceral peritoneum**, which **sucks at conveying pain** → patient feels **vague non-localized umbilical** pain.
 - Then, inflammation **spreads over to parietal peritoneum**, which is **great at conveying pain** → patient feels **localized RLQ** (site of appendix) pain.

Q48

A 45-year-old man is brought to the emergency department after being found unconscious in the desert. Twenty-four hours ago, he had been hiking and lost consciousness after falling and striking his head on a rock. His pulse is 124/min and blood pressure is 80/40 mm Hg. He is mildly confused. Physical examination shows multiple ecchymoses on the upper and lower extremities and a large contusion on the left forehead. Which of the following best explains the hypotension?

- A. Anaphylaxis
- B. Hypothermia
- C. Hypovolemic shock
- D. Increased intracranial pressure
- E. Myocardial infarction

▼ Explanation

- **Answer is C (Hypovolemic shock)**
 - **IMP Clues**
 - Found unconscious in the desert after falling and striking his head on a rock
 - Pulse is 124/min and blood pressure is 80/40 mmHg
 - Multiple ecchymoses on the upper and lower extremities and a large contusion of the left forehead.
 - Q asks what best explains the hypotension
- **Dx → Hypovolemic Shock**
 - Patient hit his head & **bled** (ecchymoses on extremities & head contusion) + passed out in the desert (which is hot af, so probably **dehydrated** too)
 - Vitals support the hypovolemia → **Hypotension & Reflex Tachycardia**

? What would this patient's arrows be? [CO - HR - PCWP - SVR]

▼ Answer

- **DECREASED** CO & PCWP
- **INCREASED** HR & SVR

Explanation

Hypovolemia → decreased preload → **decreased LA pressure (PCWP)** → **decreased CO** → decreased carotid baroreceptor pressure → decreased impulses → decreased parasympathetic activity & increased sympathetic activity → **increased HR and increased SVR**

? What would this patient's arrows be?
[Carotid baroreceptor pressure - Carotid baroreceptor impulses
- Parasympathetic activity]

▼ Answer

- **DECREASED** Carotid baroreceptor pressure
- **DECREASED** Carotid baroreceptor impulses
- **DECREASED** Parasympathetic activity

Carotid baroreceptors detect pressure levels. When pressure gets *high*, carotid baroreceptor impulses **activate parasympathetic centers** to *decrease HR*.

- Patient is **hypotensive** so *less pressure* in baroreceptors
- This causes *less impulses* from carotid baroreceptors to parasympathetic centers
- So, **Parasympathetic activity decreases**
 - **Sympathetic activity INCREASES** ⇒ **Increases HR**

"You might be inclined to choose Choice D (increased ICP) because he hit his head."

- Head trauma causes **Cushing's triad** → Increased ICP, Hypertension, and Bradycardia

Q49

A 21-year-old man comes to the physician because of a 1-month history of fever and abdominal pain, he also has had a 6.8-kg (15-lb) weight loss during this period. He is a consultant to nongovernmental organizations that support organic farming. He returned from a 2-month trip to the Middle East 3 weeks ago. His temperature is 39°C (102.2°F). Physical examination shows generalized lymphadenopathy and hepatosplenomegaly. Laboratory studies show pancytopenia. The most likely cause of these findings is an organism belonging to which of the following genera?

- A. Acinetobacter
- B. Leishmania
- C. Plasmodium
- D. Schistosoma
- E. Trypanosoma

▼ Explanation

- **Answer is B (Leishmania)**
 - **IMP Clues**
 - Fever
 - He returned from a 2-months trip to the Middle East 3 weeks ago.
 - Generalized lymphadenopathy and hepatosplenomegaly
 - Pancytopenia
 - **Dx → Visceral Leishmaniasis (Kala Azar Fever)**
 - Transmitted by **Sand Fly**, on the USMLE it is classically found in "**hot areas**" (Middle East, Africa, South America)

- Causes Leishmaniasis, which has 2 HY presentations:

1. Visceral Leishmaniasis (Kala Azar Fever)

“Remember that visceral leishmaniasis is caused by *Leishmania donovani*.”

- Presents as a classic triad of **hepatosplenomegaly, pancytopenia, and fever** +/- weight loss & hyperpigmented skin lesions
 - Promastigotes (inactive in female sandfly) → blood → **phagocytosed by macrophages** → transforms into **amastigotes** → multiply → spread via reticuloendothelial system
 - **Liver & Spleen** ⇒ **Hepatosplenomegaly**
 - **Lymph Nodes** ⇒ **Generalized Lymphadenopathy**
 - **Bone Marrow** ⇒ **Pancytopenia**
- Diagnosis → seeing the **amastigotes in macrophages**

2. Cutaneous Leishmaniasis

- Presents as a **treatment-resistant ULCER**
 - Qs could be so vague and is usually “a **military personal** that is sent to the **Middle East**, who slept in a **hot area** + got **bitten** and the bite then **ulcerated/became ttt-resistant**.”

? How is Visceral Leishmaniasis vs Cutaneous Leishmaniasis treated on the USMLE?

▼ Answer

- Cutaneous Leishmaniasis ⇒ **Sodium Stibogluconate**
- Visceral Leishmaniasis ⇒ **Amphotericin B**



? What type of immunity is essential for disease control?

▼ Answer

Th1 (Cell Mediated Immunity) as it is intracellular.

Q50

A 21-year-old man is brought to the emergency department 30 minutes after sustaining knife wounds to the abdomen in a gang-related fight. He is in shock. He undergoes immediate operative repair of a perforation of the small intestine and a bleeding puncture wound to the liver. Recovery is uneventful and the patient is discharged. Six months later, he is admitted to the hospital for treatment of an intestinal obstruction caused by peritoneal adhesions. During the corrective abdominal operation, it is observed that one site of his previous injury has regenerated without any evidence of fibrous scarring. Which of the following sites is most likely being described?

- A. Fibroadipose subcutaneous tissue
- B. Liver
- C. Skeletal muscle
- D. Skin
- E. Small intestine

▼ Explanation

- Answer is B (Liver)
 - IMP Clues
 - Knife wounds to the abdomen
 - He undergoes operative repair of a perforation of the small intestines (Full thickness tear → perforation)
 - Bleeding puncture wound to the liver (Just punctured)
 - Q asks which organ would be regenerated without any evidence of fibrous scarring?

- Garbage Q. Basically, the guy here had a stab wound.
 - Layers affected:
 1. **Skin & Subcutaneous tissue (*penetrated*)** → skin epithelial cells regenerate perfectly (*labile cells*), *however*, if the **dermis is affected** or if the **wound size is "larger"**, → **wound repairs via fibrosis**.
 - Here the skin is completely penetrated, so the epidermis, dermis, and the underlying subcutaneous tissue are injured ⇒ **Repair by Fibrosis**
 2. **Abdominal skeletal muscles (*penetrated*)** → Skeletal muscles are **permanent cells**. They don't "regenerate". They are repaired via **satellite cells** via **fibrosis**.
 3. **Intestines (*penetrated & perforated*)** → Intestinal epithelium are *labile cells* that regenerate; however, **full thickness (transmural) injury causes repair via adhesions & fibrosis**.
 4. **Liver (*punctured*)** → The Liver is only punctured; the **stroma is essentially intact**. This allows the liver to **regenerate completely WITH NO FIBROSIS**, as liver cells are **stable cells**.

?
 Differentiate between labile, stable, and permanent cells.

▼ Answer

	Labile Cells	Stable Cells	Permanent Cells
HY Examples	- GIT Epithelium - Hair Follicles - Skin epithelium - Bone Marrow - Germ Cells	- Hepatocytes - Lymphocytes - Renal Tubular Cells - Smooth muscle	- RBCs - Neurons - Skeletal muscle - Cardiac muscle
Cell Cycle	Remains in G1 forever & never enter G0 (the quiescent phase)	Goes from G0 → G1 when stimulated .	Always in G0 & regenerates from stem cells (limited regeneration)
Regenerative Capacity	HIGHEST	MODERATE	NONE
HY Notes	Most Affected by chemo/anti-cancer drugs due to rapid turnover	Regenerates if the structural framework is preserved : - If the reticulin structure is <u>preserved</u> , Liver regenerates with NO FIBROSIS - If <u>destroyed</u> → Fibrosis	- Dead Neurons (Pos-Stroke) in CNS are replaced by gliosis . - Dead Cardiocytes (Post-MI) are replaced by scar tissue



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