



NBME EXPLANATIONS

NBME 20 Block 1

from CrackNBME

NBME 20 - Block 1

Q1

A 14-year-old girl is brought to the physician because of a 1-month history of migraine-like headaches, vomiting, and multiple left-sided focal seizures. She has had hearing loss since the age of 11 years. Her mother and maternal grandmother have high-tone deafness. Physical examination shows loss of vision in one half of the visual field of the right eye and weakness of the right upper and lower extremities. Serum and cerebrospinal fluid concentrations of lactic acid are increased. This patient most likely has a mutation of which of the following?

- A. Endoplasmic reticulum glycosyltransferase
- B. Lysosomal α -glucosidase
- C. Mitochondrial tRNA^{Leu}
- D. Nuclear proteasome activator
- E. Peroxisomal catalase

▼ **Explanation**

- **Answer is C (Mitochondrial tRNA^{Leu})**
 - **IMP Clues**
 - Migraine-like headaches
 - Multiple left-sided focal seizures
 - Hearing loss
 - Her mother and maternal grandmother have high-tone deafness
 - Loss of vision in one half of visual field
 - Weakness of the right upper & lower extremities
 - CSF & Serum concentrations of lactic acid are increased
 - Q asks where is the mutation?
- **Dx → MELAS**
 - MELAS stands for **Mitochondrial Encephalopathy, Lactic Acidosis, and Stroke-like Episodes**
 - **Mitochondrial Encephalopathy** (Migraine-like headaches, Multiple left-sided focal seizures, Hearing loss)
 - **Lactic Acidosis** (CSF & Serum concentrations of lactic acid are increased)
 - **Stroke-like Episodes** (Weakness of the right upper & lower extremities, Loss of vision in one half of visual field)
 - It is one of the **mitochondrial diseases**, which follow a **maternal pattern of transmission (female → all of her children)**
 - This is hinted in the vignette by the "Her mother and maternal grandmother have high-tone deafness"
 - Affects organs with the most mitochondria (organs with most energy requirements) → Brain & Muscles
 - **Pathophysiology**
 - **Mutation in mitochondrial tRNA genes** (most HY & worth knowing is → **MT-TL1, "mitochondrial-tRNA Leu"**)
 - Fucked up mitochondria → **impaired oxidative phosphorylation** → **impaired ATP production** → **increased anaerobic respiration** → **Increased Lactic acid & Pyruvate accumulation**
 - They can say "**decreased concentration of NADH dehydrogenase**", which is an **ETC (complex 1) enzyme**. If the mitochondria are all fucked up, then chance are most of their enzymes will be too. Don't freak out.
 - **Biopsy shows** → **Ragged-red Fibers** (seen with **Gomori stain**, which stains mitochondria red) & USMLE can refer to it as "**abnormal accumulation of mitochondria under sarcolemma**"
 - USMLE can ask for cause of ragged-red fibers; answer is → **compensatory mitochondrial proliferation**



The grandmother and mother had high-tone deafness, while the daughter had a much more severe presentation (Stroke-like episodes, encephalopathy, and hearing loss). What is the reason for the difference in presentations?

▼ **Answer**

Heteroplasmy - Not all mitochondria are affected, there is a mixture of normal and abnormal mitochondria in each cell, which creates variability in presentations/severity. This is called **Heteroplasmy**



DON'T FORGET ABOUT MERRF!

Myoclonic Epilepsy with Ragged Red Fibers is also a mitochondrial myopathy that causes, well, myoclonus/epilepsy with ragged red fibers accumulation.

- Caused by **MT-TK gene** mutation



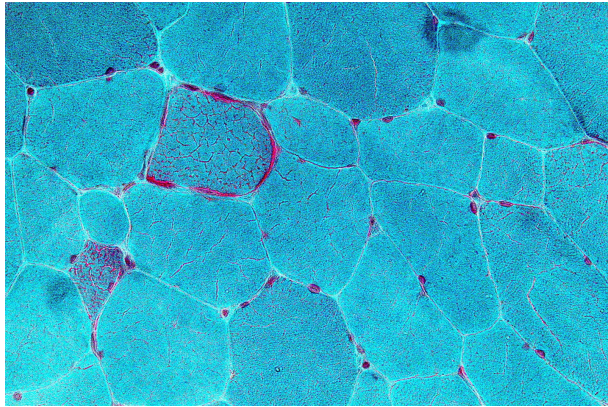
USMLE can describe the above vignette and show you a picture of a cell under EM, then proceed to ask you about site of pathology.



- All you have to do is look for the **mitochondria** (bottom left)
- How do I know that this is the mitochondria?
 - The **cristae** (the wavy lines inside) + **double membrane** around it

Leber hereditary optic neuropathy:

- Caused by → Mutations in **Complex I** of Electron Transport Chain (ETC)



- *Pathophysiology* → Impaired **oxidative phosphorylation** → neuronal death in **RETINA & OPTIC NERVE**
- *Presentation* → Subacute **bilateral vision loss** in teens or young adults (Usually permanent) +/- **neurologic dysfunction** (tremors, multiple sclerosis-like illness)

- *EM shows* → **Mitochondrial Crystalline Inclusions**
- *Labs* → **NORMAL CK & INCREASED lactate and alanine**

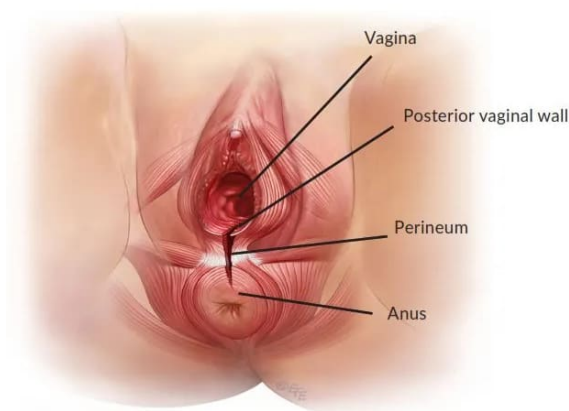
Q2

A 32-year-old woman has had fecal incontinence since giving birth to her first child 1 year ago. Which of the following is the most likely cause of the fecal incontinence in this patient?

- A. Achalasia of the internal anal sphincter
- B. Damage to the anal sphincter
- C. Increased pressure of the anal sphincter
- D. Spastic contraction of the puborectalis muscle
- E. Spastic external anal sphincter

▼ **Explanation**

- **Answer is B (Damage to the anal sphincter)**
 - **IMP Clues**
 - Fecal incontinence since giving birth to her child 1 year ago
 - Q asks for likely cause of incontinence
 - **Dx → Fecal incontinence secondary to sphincteric damage**
 - A common (and HY) complication of normal vaginal birth is **perineal tears, which sometimes can extend into the anal sphincter** → **Fecal Incontinence**
 - This is also why **posterior midline episiotomy** is **NOT** usually preferred (**due to risk of causing anal sphincter damage**)



[For Nerds/STEP2] Degrees of Perineal Tears:

- **First Degree** → Limited to vaginal mucosal
- **Second Degree** → Extends to perineal body muscles
- **Third Degree** → Involves external anal sphincter
- **Fourth Degree** → Involves rectal mucosa

▼ **Other Choices**

- **Choices A, C, D, and E** → All will cause **sphincter contraction**, which would cause **constipation** **NOT** incontinence

Q3

A 17-year-old girl comes to the emergency department because of a swollen tender ankle. An x-ray of the ankle is strongly suggestive of osteosarcoma. She and her parents are told only that "further evaluation is needed." Which of the following next steps is most appropriate?

- A. Request that an oncologist discuss the findings with them immediately
- B. Request the presence of the hospital chaplain, then discuss the findings
- C. Speak with the parents alone about the findings
- D. Speak with the patient alone about the findings
- E. Speak with the patient and her parents about the findings

▼ **Explanation**

- **Answer is E (Speak with the patient and her parents about the findings)**

- Ethics Q, asks for next step.
- Patient has osteosarcoma. She and her parents only got “further evaluation as needed”. Chances are they’re very distressed and anxious, so you need to speak to them about the findings.
- **Remember that ⇒ “Physicians should always encourage healthy minor-guardian communication.”**

▼ **Other Choices**

- **Choice A** → You, the primary care physician, should first talk to the patient & her family. Give them the news, have empathy, validate their feelings, and answer their Qs. THEN we could refer them to the oncologist.
- **Choice B** → Garbage and never the correct answer on the USMLE
- **Choices C & D** → You’re not following the “Physicians should always encourage healthy minor-guardian communication.” Unless there is a reason to withhold the information from someone.
 - Patient asks you not to tell anyone → **ASSESS THE CAPACITY**
 - **if capacity is intact** → **DON’T TELL THE PARENTS**
 - Parents approach you & tell you that they’d like if you hid the diagnosis from the patient → FIRST: **assess why & risks (depression/suicide)**
 - If patient is well → **Tell the patient**
 - If a risk is found → **Don’t tell the patient**

Q4

An otherwise healthy 16-year-old girl comes to the physician because of a 2-month history of episodes of wheezing and shortness of breath while participating in track meets with her high school team. Her respirations are 12/min. Physical examination shows no abnormalities. A diagnosis of exercise-induced asthma is made. Exposure to which of the following is most likely to precipitate a similar episode in this patient in the future?

- A. Cold, dry air
- B. Cold, moist air
- C. Warm, dry air
- D. Warm, moist air

▼ **Explanation**

- **Answer is A (Cold, dry air)**

- **IMP Clues**
 - Episodes of wheezing & SOB while participating in track meets + diagnosis of exercise-induced asthma is made
 - Q asks exposure to which of the following would precipitate a similar episode?
- Asthma attacks are caused by **irritation in presence of airway hypersensitivity** → **contraction of airway** → **symptoms of asthma**
 - What can cause airway irritation ⇒ **cold dry air**.
 - This is why we have a ton of airway air-warming mechanisms:
 - **Nasal Hairs** → Removes dust
 - **Turbinates** → **Removes dust & Rich in blood vessels to facilitate warming/humidifying the air**

- When exercising, **RR increases** → air spends **less time** going through the respiratory tract → **insufficient removal of dust & warming/humidifying of air** (Same as getting exposed to cold/dry air) → **Airway irritation** → **mast cell degranulation** → **release of histamine, LTs, PGs** → **bronchoconstriction**
 - Additionally, during exercise mouth breathing increases, which lacks protective mechanisms.

?

All of the following Leukotrienes are involved in bronchoconstriction except?

A) LT-B4
B) LT-C4
C) LT-D4
D) LT-E4

▼ Answer

A) **LT-B4** as it is primarily a **chemotactic molecule**.

Other Choices

- LTs-C4/D4/E4 are all key mediators of bronchoconstriction

?

15-year-old boy with no known allergies presents with dry cough that appears during football practice. Brother has history of eczema. Cough becomes severe and makes him want to quit. Examination shows MVP. Dx?

▼ Answer

Exercise-Induced Asthma

- MVP doesn't cause dry cough ONLY during exercise.
- "No KNOWN allergies" = No allergies diagnosed YET.
 - Brother with eczema is an important hint!

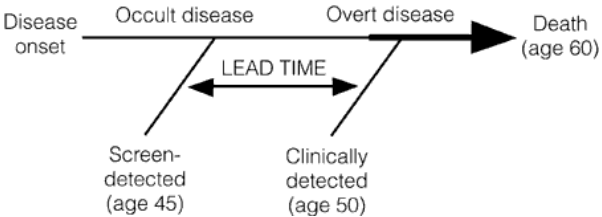
Q5

A study is conducted to assess the effect of a new screening test on the mortality rate of prostate cancer. Prior to implementation of screening, the overall 5-year survival rate was 70%. After initiating the screening in the randomly selected study population, the 5-year survival rate increases to 85%. During this time, there were no changes in the treatment of prostate cancer. The apparent decrease in mortality could be due to which of the following types of bias?

- Compliance
- Lead-time
- Recall
- Selection

▼ Explanation

- Answer is B (Lead-time)
 - Q says that the survival rates of prostate cancer were 70%, but after implementation of screening, the survival rate increased. They also mention that no changes in ttt happened.
 - This means that essentially what we have here is caused by early discovery of the cancer via the screening that was implemented. This is called **Lead-time bias**.
 - With **no screening**, patients presented when they were symptomatic; this is often when the cancer progressed to further stages, which **increased mortality rates and decreased survival rates**.
 - With **screening**, however, occult cancer can be detected before symptoms arise & before the cancer progresses. **Early-stage cancer has less mortality rates and more survival rates. So, this causes an "apparent" improvement of survival time, despite the patient's lifespan is essentially unchanged.**



Q6

A new antiplatelet agent is developed for the prevention of recurrence of stroke. In a large randomized clinical trial with equal numbers of men and women, the rates of stroke are lower in patients receiving the new agent than in patients receiving the standard treatment. Results are shown:

Recurrent Stroke Rates per 1000 Person-Years		
	Standard Treatment	New Antiplatelet Drug
Women	.12	.04
Men	.24	.08
Overall	.18	.06

Based on the results, which of the following is the absolute risk reduction in women?

- 8%
- 12%
- 16%
- 33%
- 50%

F. 62%

G. 67%

H. 75%

▼ Explanation

- **Answer is A (8%)**
 - Simple Biostat Q.
 - Asks for ARR in women
 - **ARR = Risk % of A - Risk % of B**
 - A = Standard ttt = .12
 - B = Antiplatelet drug ttt = .04
 - ARR = 0.12 - 0.04 = 0.08 = **8%**



Using the above data, what is the Relative Risk Reduction in women?

▼ Answer

Choice G (67%)

- **RRR = (Risk % of A - Risk % of B) / Risk % of A**
- $(0.12 - 0.04) / 0.12 = 0.08 / 0.12 = 0.6666 = \sim 67\%$ (Choice G)

Q7

A previously healthy 32-year-old woman is brought to the emergency department because of a 2-hour history of severe epigastric pain, nausea, and vomiting blood. Her temperature is 37°C (98.6°F), pulse is 125/min, respirations are 18/min, and blood pressure is 85/45 mm Hg. Physical examination shows cool skin and a tender abdomen. A decrease in which of the following hemodynamic parameters is the most likely cause of this patient's hypotension?

- A. Heart rate
- B. Left ventricular compliance
- C. Left ventricular contractility
- D. Preload
- E. Systemic arterial resistance

▼ Explanation

- **Answer is D (Preload)**
 - **IMP Clues**
 - Severe epigastric pain, nausea, and vomiting of blood (sounds like a perforated PU)
 - Blood Pressure is 85/45mm Hg (she's hypotensive & hemodynamically unstable, probably due to the hematemesis)
 - Cool skin (Hypovolemic shock)
 - Q asks for a decrease in which of the following the cause of the hypotension

- Dx → Perforated Peptic Ulcer
 - Perforated PU causes **hematemesis** followed by Melena
 - This loss of blood (volume) causes **hypotension**.
 - What describes blood volume? ⇒ Preload (Choice D)
 - **Decreased Blood Volume = decreased venous return = decreased preload = decreased stroke volume = decreased cardiac output = decreased BP (hypotension)**

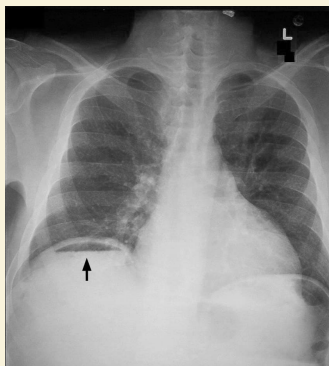


What radiological finding would be expected to be seen in this patient?

▼ Answer

Air Under the Diaphragm - often seen on CXR in patients with perforated PU or "perforated viscus"

USMLE LOVES
"perforated viscus" as an answer choice in these Qs.



How does USMLE assess Perforated Peptic Ulcer:

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

▼ Other Choices

- **Choice A** → **CO = SV x HR**; when SV goes down, the HR goes up in a trial to maintain CO (and in so maintain BP). So, **HR increases NOT decreases**.
- **Choice B** → Irrelevant really. **LV compliance decreases when there is LVH**. Often hinted to us on the USMLE by "S4 sound".
- **Choice C** → **Contractility may go up** in a trial to maintain SV, and hence maintain CO & BP.
- **Choice E** → **BP = CO x TPR**; when CO goes down due to decreased preload, the TPR increases (via arteriolar constriction) in a trial to maintain BP. So, **Total Peripheral Resistance increases NOT decreases**.

Q8

A 31-year-old man has a large, yellow, soft mass deeply infiltrating the gluteus maximus muscle. Microscopic examination of the excised mass shows irregular vacuolated cells and clear cells with frequent mitoses. Which of the following is the most likely diagnosis?

- A. Fibroma
- B. Fibrosarcoma
- C. Lipoma
- D. Liposarcoma
- E. Rhabdomyoma
- F. Rhabdomyosarcoma

▼ Explanation

- **Answer is D (Liposarcoma)**
 - **IMP Clues**
 - Large, yellow soft mass (Yellow = Fat, so either Liposarcoma or lipoma)
 - Infiltrating the gluteus maximus (infiltration is a feature of malignancy, so hinting more to Liposarcoma)
 - Irregular vacuolated cells & clear cells with frequent mitosis (sounds malignant)
 - Q asks for Dx
- **Dx → Liposarcoma**
 - **A malignant tumor of fat cells.**

Stages of Neoplasia:

- Features of malignancy:
 - **Infiltration** → “Deeply infiltrating the gluteus maximus”
 - **Pleomorphic cells with frequent mitosis/rapid turnover** → “Irregular vacuolated cells and clear cells with frequent mitoses”

 Differences between Benign & Malignant tumors:	
Benign tumors:	Malignant tumors (cancers):
• WELL-differentiated and well-demarcated • LOW mitotic activity • NO metastases • NO necrosis	• POORLY differentiation with erratic growth • HIGH mitotic activity • LOCAL invasion & METASTASIS • DECREASED apoptosis

Grade → Degree of cell **differentiation & mitotic activity** (HIGH grade = HIGH aggressiveness)

Stage → Degree of **invasion & spread** from initial site (Depth of invasion correlates to risk of metastasis)

- **STAGE HAS A MORE PROGNOSTIC VALUE THAN GRADE** (Stage determines Survival)
 - Low grade tumor with high stage **IS WORSE** than high grade tumor with low stage

▼ **Other Choices**

- **Choices A & B** → Made up of fibrous connective tissue, which appears white + microscopy would show spindle-shaped cells.
- **Choice C** → Yes, would be large yellow soft mass, but **NOT** infiltrating as it is benign. Microscopy would show **regular** vacuolated and clear cells.
- **Choice E & F** → Made up of muscle tissue. Microscopy would show striated cells.

Q9

A 25-year-old woman has a flu-like illness (fever, myalgias, fatigue) that is followed by decreased exercise tolerance and shortness of breath, particularly when lying down. Findings on examination of tissue obtained on myocardial biopsy are suggestive of a viral infection. Which of the following is the most likely cause of her illness?

- A. Adenovirus
- B. Herpesvirus
- C. Myxovirus
- D. Orthomyxovirus
- E. Picornavirus

▼ **Explanation**

- **Answer is E (Picornavirus)**
 - **IMP Clues**
 - Flu-like illness (fever, myalgia, fatigue) (probably a viral infection)
 - Followed by decreased exercise tolerance and SOB, particularly when lying down (dypnea + orthopnea, so looks like heart failure symptoms. Probably Myocarditis)
 - Myocardial biopsy are suggestive of viral infection (confirms what we said)
 - Q asks for cause of illness
- **Dx → Coxsackievirus B**
 - Coxsackievirus B is HY and causes 3 HY diseases:
 1. **Viral Myocarditis** (what we have here) → hx of flu-like illness followed by **heart failure symptoms** (Dilated Cardiomyopathy)
 2. **Pleurodynia** (Bornholm's Syndrome / Devil's Grip) → **unilateral pleuritic/stabbing** chest pain due to inflammation of intercostal muscles
 3. **Pericarditis** → chest pain that **improves on leaning forward** + **friction rub** on auscultation + diffuse ST-segment elevation and/or PR depression on ECG

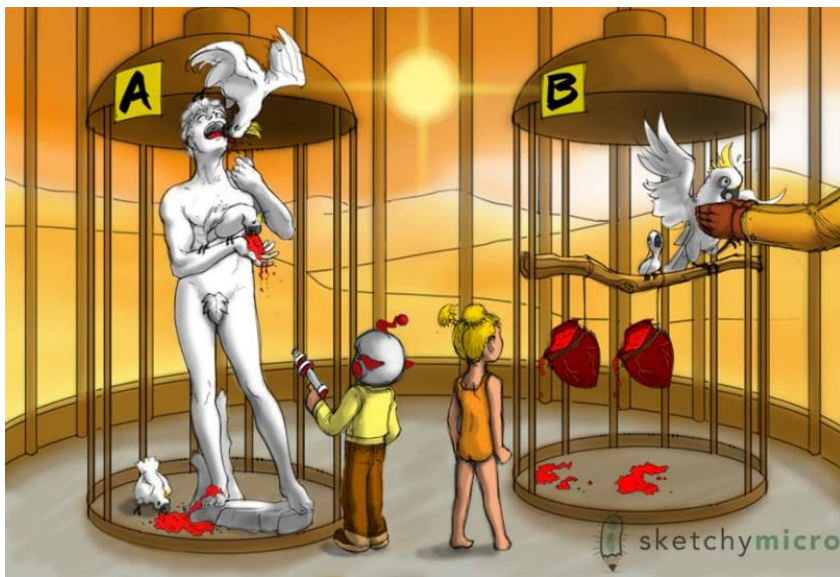
 Coxsackievirus B viral myocarditis is often referred to as **“lymphocytic infiltrate with myocyte necrosis”** on biopsy. So, keep your eyes open for this phrase in answer choices.

? How to differentiate Pleurodynia from pleurisy as their pain is very similar clinically?

▼ **Answer**

Pleurodynia has *increased* CK

- **Pleurodynia** is inflammation of muscle → ***increased*** CK
- Pleurisy is inflammation of pleura → **normal** CK



? What diseases does Coxsackievirus A cause?

▼ Answer

1. Hand-Foot-Mouth Disease
 - Mouth ulcers + Vesicular rash on palms & soles.
2. Herpangina (mouth blisters & fever)
3. Aseptic (viral) Meningitis
 - **NORMAL/HIGH** Opening Pressure
 - **HIGH LYMPHOCYTES** Cell Type
 - **NORMAL/HIGH** Protein
 - **NORMAL** Glucose

Ways USMLE assess Coxsackievirus A:

- Vignettes will describe a **child** who went to **summer camp**, and developed a **rash on their hands and feet** + **vesicles in their mouth (herpangina)** and ask for causative organism ⇒ **Coxsackievirus A**
- They can also give you **child** in **summer camp** + **meningitis**, then ask about structure of causative virus ⇒ **Naked positive-sense ssRNA virus**

Q10

A 10-year-old boy with mild mental retardation is brought to the physician by his parents because of a 2-week history of frequent staring spells. Examination of the skin shows pale oval-shaped areas on the trunk. A CT scan of the head without contrast shows multiple calcified subependymal and cortical lesions. Which of the following is the most likely diagnosis?

- A. Cysticercosis
- B. Hyperparathyroidism
- C. Metachromatic leukodystrophy
- D. Oligodendroglioma
- E. Tuberous sclerosis

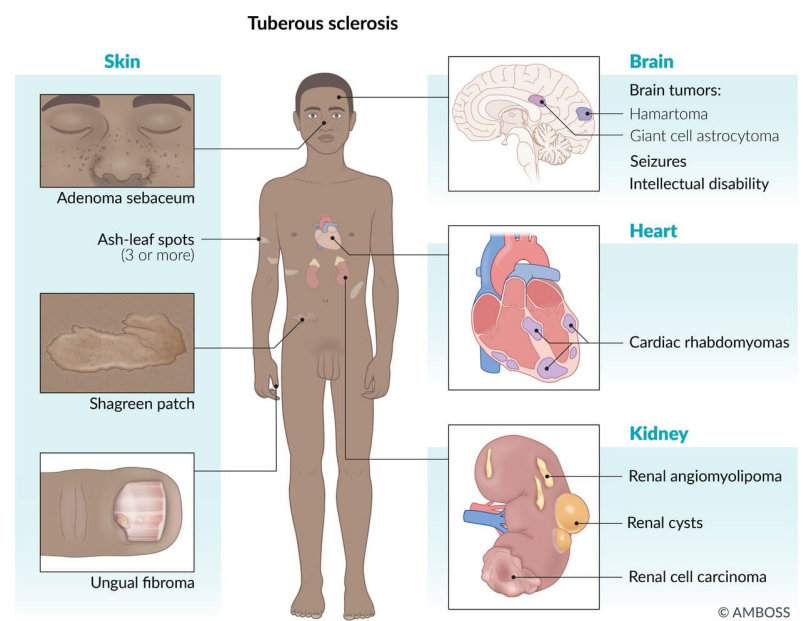
▼ Explanation

- Answer is E (Tuberous Sclerosis)
 - IMP Clues
 - Mental Retardation (seen in tuberous sclerosis, as the brain lesions affect development)
 - Staring spells (a type of seizure, again from the brain lesions)
 - Pale oval-shaped area on the trunk (Ash-leaf spots)
 - Multiple calcified subependymal and cortical lesions (MRI findings confirm)
 - Q asks for Dx

- **Dx → Tuberous Sclerosis**
 - **AD** Neurocutaneous disorder
 - **TSC1/TSC2** (Hamartin/Tuberin) gene mutation on **chromosomes 9 & 16**, respectively.

[[]] TSC2 (Two) = Tuberin = six Teen

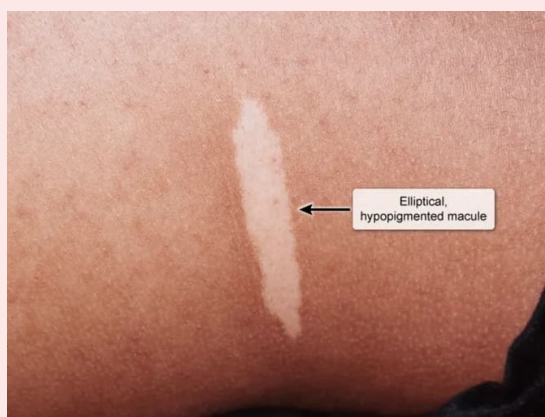
- HY Features include:
 - **Tubers "Periventricular Nodules"** (causes seizures & mental retardation/Autism)
 - **Ash-Leaf spots** (*Hypopigmented lesions*)
 - **Shagreen patches** (*Hyperpigmented lesions*)
 - **Cardiac rhabdomyoma** (can present on the USMLE as a ball-in-valve murmur that disappears when patient is repositioned or child with obstructive symptoms)
 - **Renal angiomyolipoma**
 - Others: **Angiofibromas & Subungual fibromas**



? What are TSC1/TSC2?
 ▼ Answer
Tumor Suppressor Genes

Pictures of Tuberous Sclerosis Complex Features:

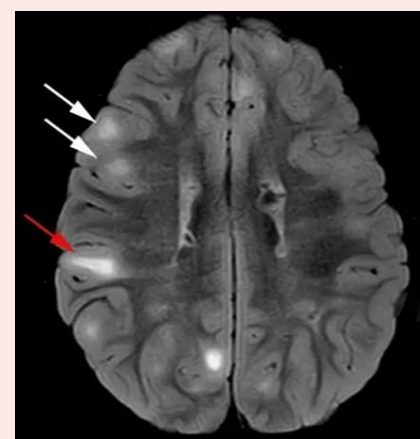
Ash-leaf Spots:



Shagreen Patches:



Periventricular Nodules:



▼ Other Choices

- **Choice A → Neurocysticercosis** would present as seizures in a patient who **ingested tinea solium eggs**. Patient will not have mental retardation or skin skin patches. **CT would show multiple brain calcifications with scolexes (the parasite's head).**
- **Choice B →** Would cause decrease hypercalcemia, renal stones, and osteolytic bone lesions + bone pain.
- **Choice C → Metachromatic leukodystrophy:** a Lysosomal storage disease.
 - Deficiency → **Arylsulfatase A**
 - Accumulation → **Cerebroside sulfatase**
 - Features → **Dementia, Ataxia, Demyelination** (central & peripheral)
- **Choice D → Oligodendroglioma** - A brain tumor
 - Origin → **Oligodendrocytes**
 - Histology → **Fried-Egg appearance + chicken-wire capillary pattern**

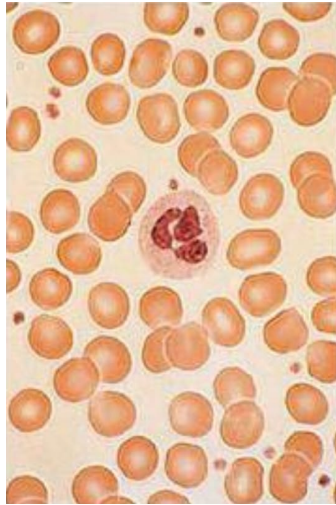


Oligodendrocytes HY Factoids

- Cells that **myelinate neuron** in CNS
- Targeted by **Multiple Sclerosis** → T-cell mediated destruction of **oligodendrocytes** → **demyelination**
- **Schwann cells** are the equivalent of Oligodendrocytes in PNS

Q11

A 57-year old man has a hemoglobin concentration of 18.5 g/dl. A peripheral blood smear is shown. These findings are most consistent with which of the following disorders?



- A. Agnogenic myeloid metaplasia
- B. Chronic obstructive pulmonary disease
- C. Hereditary hemochromatosis
- D. Hypersplenism
- E. Myelodysplastic syndrome

▼ Explanation

• Answer is B (Chronic obstructive pulmonary disease)

◦ IMP Clues

- Hemoglobin concentration of 18.5g/dl (Polycythemia)
- Smear is shown (RBCs are normal, they're just increase. PLTs look normal. Neutrophils normal too)

• Dx → COPD

- COPD patients have **chronic hypoxia** → **increases EPO** production from **kidney** → **increased RBCs** production from bone marrow → **Polycythemia**
- This is called **Reactive Polycythemia**.
 - Smear just shows **isolated increased RBCs**, with no abnormal forms of RBCs, WBCs, PLTs, or their progenitor cells.

? How is Reactive Polycythemia different from Polycythemia Vera

▼ Answer

Polycythemia Vera is characterized by an **increase in RBCs + an increase in at least another cell line (PLTs or WBCs)**
Due to the increase of RBCs → negative Feedback on EPO, so **EPO decreased**.

Mechanism is **JAK2 mutation** → **Hypercellular Bone Marrow** (increased hematopoietic progenitor cells) [asked on NBME]

? What are 3 HY causes of chronic hypoxia on the USMLE?

▼ Answer

COPD - Living at **high altitudes** - **Smoking** (chronic CO exposure)

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

- HY Side Effect of B2 Agonists ⇒ **Tremors**

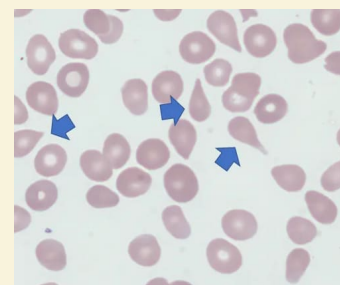
▼ Other Choices

📌 **COPD Rapid Review:**

- **Most Important risk factor for COPD is smoking.**
- Features of COPD:
 - **Chest Hyperinflation** (air is trapped inside) & **Diminished air entry**
 - **Chronic productive cough** (dysfunctional cilia + mucus gland hyperplasia/hypersecretion)
 - **Wheezing & Exertional Dyspnea**
 - **Chronic Hypoxia**
 - **Increased PCO₂**, so kidney stimulates HCO₃ reabsorption to balance the acidosis → **Increased blood HCO₃**
- HY Complications:
 - Increased EPO → **Secondary Polycythemia**
 - **Pulmonary HTN & Cor pulmonale**
- PFT Pattern: **↑↑↑ for everything expect** FEV₁, FVC, and FEV₁/FVC ratio, choose **↓↓↓**
- Management: **B2 agonist** (Albuterol) + **Muscarinic Antagonist** (Ipratropium)
 - **B2 Agonists** → **stimulates B2 receptors** in the lungs → **bronchodilation**
 - **Muscarinic Antagonists** → **Block M receptors** in the lungs → **inhibit** bronchoconstriction

- **Choice A → Primary Myelofibrosis** (a type of chronic myeloproliferative disorders)
 - **JAK2 mutation** → proliferation of **Fibroblasts & Megakaryocytes** → deposition of **collagen in bone marrow** → **Bone Marrow Fibrosis** (USMLE describes this as **"Dry Tap on BM aspiration"**)
 - Peripheral smear shows **Teardrop RBCs (Dacrocytes)**
 - **Patients are anemic** as there is BM fibrosis & decreased RBC production.
 - Patients usually have **Splenomegaly** (due to extramedullary hematopoiesis)

 **Teardrop RBCs (Dacrocytes):**



- **Choice C → Hereditary Hemochromatosis**
 - **Increased Intestinal Iron Absorption** *[asked on NBME]* → **iron overload & deposition in organs** causing their **dysfunction** (heart, liver, testes, pituitary, hypothalamus, pancreas, joints, skin)
 - Hb levels are relatively not affected, unless maybe anemia of chronic diseases (rare on USMLE, and not really assessed)
- **Choice D → Hypersplenism would cause anemia not polycythemia**
 - **Hypersplenism on USMLE = Splenic Sequestration**
 - Spleen destroys RBCs, PLTs, and WBCs → **Anemia, Thrombocytopenia, and Leukopenia.**
 - **Finding these labs + enlarged spleen ⇒ Hypersplenism**
- **Choice E → Myelodysplastic Syndrome** was assessed once or twice on all NBMEs as far as I can remember.
 - Presents as a **patient with hx of chemo & radiation**
 - Labs show **pancytopenia**
 - Physical examination shows **NO HSM** or **lymphadenopathy**
 - Peripheral Smear shows **Oval macrocytic red cells & hyposegmented neutrophils & abnormal platelets**
 - **Dx → Myelodysplastic Syndrome; How to confirm ⇒ BM biopsy shows "Increased cellularity with Dysplastic Progenitor Cells"**

Q12

At a postnatal checkup, a 6-week-old female newborn weighs 20 ounces less than at delivery. Her mother says she vomits and regurgitates bile-tinged fluid after every feeding. Which of the following is the most likely cause of this abnormality?

- A. Annular pancreas
- B. Hiatal hernia
- C. Meckel diverticulum
- D. Pyloric stenosis
- E. Tracheoesophageal fistula

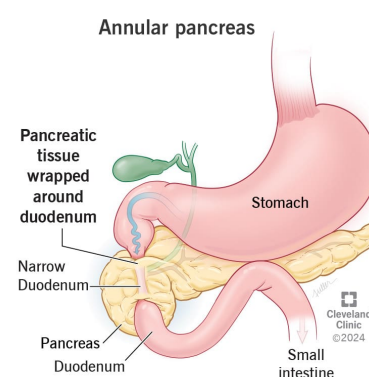
▼ **Explanation**

- **Answer is A (Annular pancreas)**
 - **IMP Clues**
 - 6-week-old female newborn weighs 20 ounces less than at delivery (weight of newborns should increase. a decrease usually means that something is wrong)
 - Vomits and regurgitates bile-tinged fluid after every feed (bile-tinged tells us that the level of the obstruction is at or below the duodenum, as bile is secreted into the intestines at the duodenum)
 - Q asks for most likely cause?
- **Dx → Annular Pancreas**
 - **On the USMLE, this exact presentation can be cause by annular pancreas or duodenal atresia.**
 - Both present with **bile-tinged vomiting/regurgitation + double bubble sign on AXR.**
 - Embryological cause → **Failure of ventral pancreatic bud rotation** *[asked on NBME]* → **compresses duodenum → causes duodenal obstruction**

"Your STEP 1 exam might trick you by showing different imaging modalities like they do on STEP2 (if they do, they are honestly assholes)"

 - CT/MRI → pancreas encircles the duodenum
 - Upper GI contrast → concentric duodenal narrowing

 - Associated with **Down Syndrome**



? Neonate + greenish vomiting + AXR shows below imaging. Differentiate between the possible causes.



▼ Answer

	Annular Pancreas	Duodenal Atresia
Presentation	bile-tinged vomiting/regurgitation	bile-tinged vomiting/regurgitation
AXR	Double Bubble Sign	Double Bubble Sign
Embryological causes	Failure of ventral pancreatic bud rotation	Failure of duodenal recanalization
HY Syndromic Association	Down Syndrome	Down Syndrome

The X-Ray provided shows the "double-bubble sign"

- The bubble on the right (small one) → **Duodenum**
- The bubble on the left (big one) → **Stomach**

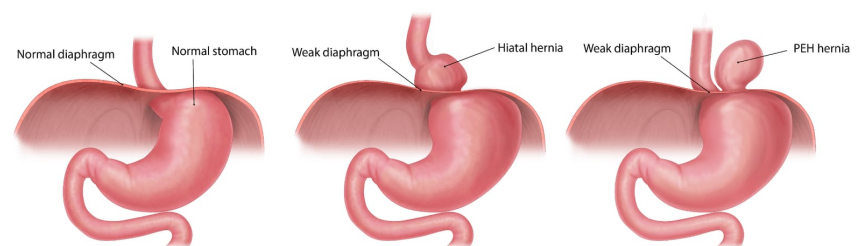
▼ Other Choices

• Choice B → Hiatal Hernia

- Usually presents in **adults with increase intraabdominal pressure (obesity, pregnancy)**

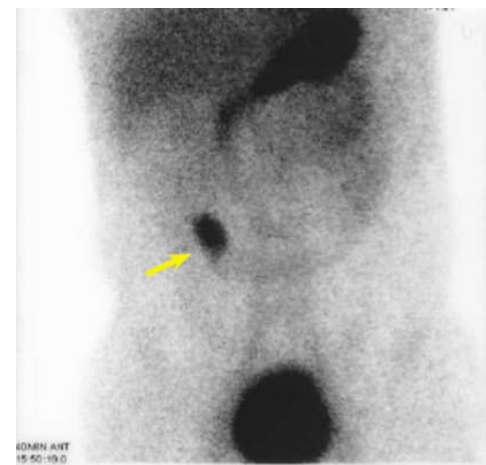
• Has 2 Types:

1. **Sliding Hiatal Hernia** → Cardia of the stomach "slides" into the LES, and **now cardia is above GEJ** → **GERD**
 - a. More common (~95% of hiatal hernia)
 - b. Risk factor for **Barrett's Esophagus & Adenocarcinoma of the stomach**
2. **Paraesophageal Hernia** → **Defect in phrenoesophageal membrane** → usually the fundus of the stomach herniates. **Cardia of the stomach is in its normal site (below GEJ)**
 - a. Less common (~5%)
 - b. Liable for **strangulation** → Emergency



• Choice C → Meckel Diverticulum

- Presents as a healthy **child with bloody stools**
- One of the omphalomesenteric duct (aka vitelline duct) disorders spectrum.
- Cause of bleeding is → presence of **ectopic (heterotopic) gastric/pancreatic tissue** → inflammation of mucosa → bleeding
- Site → **Terminal Ileum** ("**2 feet from the ileocecal valve**" is the classic textbook site)
- Radiology → **Tc99 uptake scan (also called Meckel scan) shows ectopic gastric mucosa in terminal ileum**
 - Shown below is a Tc-99m scan → Upper black is stomach mucosa, yellow arrow is ectopic gastric mucosa in Meckel's diverticulum, below is bladder.



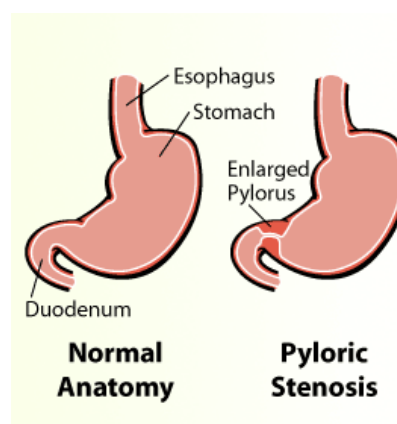
? What type of diverticulum is Meckel's diverticulum?

▼ Answer

Meckel's → **True Diverticulum** (contains mucosa, submucosa, and musculosa)
Zenker's → **False Diverticulum** (contains only mucosa & submucosa)

• Choice D → Pyloric Stenosis

- Presents as a child with **projectile NON-bilious vomiting** after feeding.
- Child is "eager to eat" (hungry) and dehydrated
- Physical examination can show an **olive-shaped mass in the abdomen** (the hypertrophied pyloric muscles) +/- **abdominal peristalsis**.



? 2M + non-bilious vomiting + olive-shaped mass + peristalsis. What is expected arrows for K, Cl, Na, HCO₃, PCO₂, and pH?

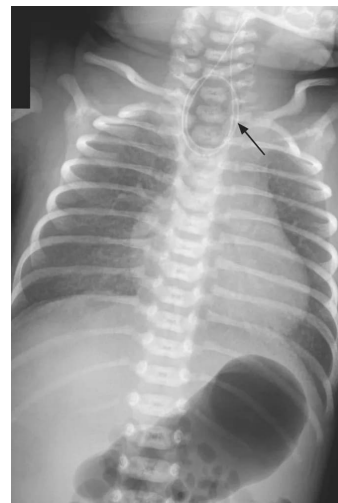
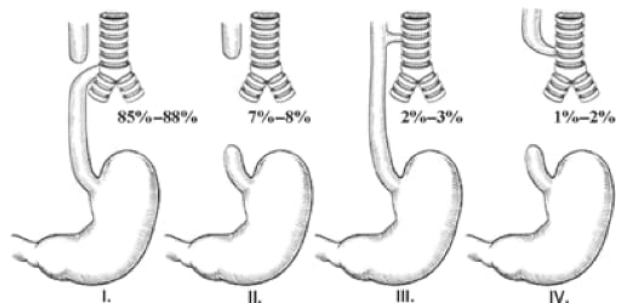
▼ Answer

Vomiting causes **hypokalemic hypochloremic metabolic alkalosis**. so expected arrows are:

- **Decreased K**
- **Decreased Cl**
- **Normal/decreased Na**
- **Increased HCO₃**
- **Increased PCO₂**
- **Increased pH**

• Choice E → Tracheoesophageal fistula

- Has many presentations; **most common Atresia of esophagus + Fistula between lower part of esophagus & trachea.**
- presents as **non-bilious vomiting/choking/coughing immediately after feeding.**
- They can also show you a scan, where a **feeding tube can't go all the way in & coils mid-esophagus**
 - also note the **gastric bubble/air in intestines**, this tells us that there is a **distal fistula**
 - If **absent** → **pure esophageal atresia WITH NO** fistula.



Q13

A 55-year-old man comes to the physician because of constipation since starting an over-the-counter medication 2 weeks ago for a chronic, persistent cough and sinus congestion. Which of the following ingredients in this medication is the most likely cause of this patient's new symptom?

- A. Acetaminophen
- B. Dextromethorphan
- C. Guaifenesin
- D. Loratadine
- E. Phenylephrine

▼ Explanation

• Answer is B (Dextromethorphan)

◦ IMP Clues

- Constipation since starting an OTC medication 2 weeks ago (must be a drug-induced side effect)
- For chronic, persistent cough, and sinus congestion (ok so the drug tested is for cough/sinusitis)
- Q asks which drug is responsible for symptoms

◦ Dextromethorphan

- MOA → **NMDA-receptor antagonist used for cough suppression**
 - Acts **centrally** on the **cough center** **[For Nerds → In Medulla]**
 - It has **low addictive potential** (in comparison to opioids) & weak peripheral effect
- HY side effect → **constipation**

▼ Other Choices

- Choice A → **Acetaminophen** is a **central COX inhibitor** used for fever and pain.

- **Choice C** → **Guaifenesin** is an **expectorant** which thins bronchial secretions → facilitates coughing up of mucus
- **Choice D** → **Loratadine** is an 2nd-generation **antihistamine** drug that is used for allergy (here we have sinusitis and persistent chronic cough, not episodes).
 - **Side effects of antihistamines (1st gen) are HY** → **anti-cholinergic (urine retention/constipation), anti-alpha adrenergic (hypotension), and anti-H1 (sedation)**
- **Choice E** → **Phenylephrine** is an **alpha-1 agonist** used for nasal congestion, not cough. **HY side effect is *Rhinitis medicamentosa* (rebound nasal congestion)**
 - **IF USMLE ASKS FOR *MECHANISM OF RHINITIS MEDICAMENTOSA*, CHOOSE *TACHYPHYLAXIS*.**

Q14

A 19-year-old man who is a college student is brought to the emergency department because of the sudden onset of right-sided chest pain and difficulty breathing after an accident in which he was thrown from his bicycle. He has difficulty walking and cannot climb stairs because of pain and shortness of breath. He is slightly cyanotic, afebrile, and tachypneic. Which of the following is most suggestive that fractured ribs caused the respiratory problem?

- A. Bronchophony
- B. Expiratory stridor
- C. Inspiratory stridor
- D. Subcutaneous crepitus
- E. Succession splash

▼ Explanation

- **Answer is D (Subcutaneous crepitus)**
 - **IMP Clues**
 - Sudden onset right-sided chest pain and difficulty breathing after an accident (this is either pneumothorax or rib fracture, causing pleuritis)
 - Pain and Shortness of breath (pain being highlighted here suggests more of a rib fracture)
 - Cyanotic & Tachypneic (Suggests that this is not just a rib fracture, but a complicated rib fracture that caused something else)
- Q asks what is most suggestive of rib fracture?
 - Okay, so what happened here is **the patient had a *rib fracture***
 - The rib fracture caused a **penetrating injury** which caused a ***pneumothorax***.
 - The air escaping the lungs, escaped through the injured tissue and ***accumulated under the skin***, causing **Subcutaneous Emphysema**
 - Subcutaneous Emphysema can be detected be palpating the chest wall, which would cause ***crackling sensation*** (the air underneath the skin), this is what is referred to as **Subcutaneous Crepitus (Choice D)**

?
What nerve conveys pain caused by rib fractures?

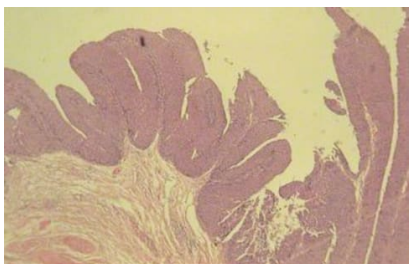
▼ Answer
Intercostal nerve

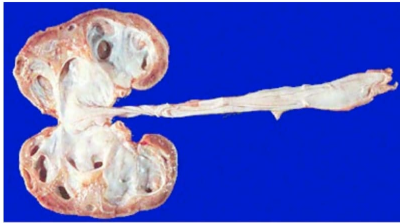
▼ Other Choices

- **Choice A** → Can be seen in pneumonia
- **Choices B & C** → Can be seen when there is upper air way narrowing
- **Choice E** → Can be seen when there is IO or paralytic ileus. The distended stomach with fluids causes this “splash” sound when the patient is moved from side to side. This more of STEP2 but knowing that gastric outlet obstruction causes it is HY.

Q15

A 66-year-old man is brought to the emergency department 30 minutes after sustaining injuries in a motor vehicle collision. He is pronounced dead on arrival. A photograph of the left kidney and a photomicrograph of a section of the distal left ureter taken at autopsy are shown. Examination of the right kidney and ureter shows no abnormalities. Which of the following was the most likely predisposing factor in the development of the ureteral lesion in this patient?





- A. Alcoholism
- B. Arylamine exposure
- C. Cigarette smoking
- D. Radiation exposure
- E. Schistosomiasis
- F. Vinyl chloride exposure

▼ Explanation

• Answer is C (Cigarette smoking)

◦ IMP Clues

- Distal Ureter taken at autopsy is shown (okay so we know this is ureter tissue, which is made up of transitional epithelium)
- Blue picture is garbage and is found in many Qs all over the USMLE. That same picture is used for children with chronic pyelo & for tumors. Don't count on that picture.
- Q asks for most likely predisposing factor for that lesion

◦ Dx → Transitional Cell Carcinoma

- How the hell did I know that it is cancer? I don't. But why would they show you a picture of transitional epithelium? Especially that of the ureter. Not assessed on the USMLE except for cancer, so that's how I know.
- **What is most likely risk factor → Smoking > Arylamine exposure**
 - Smoking is like the go-to answer in risk factor Qs. If you get a Q on your test & the choices mention "Smoking", 8/10 times it will be the correct answer.

▼ Other Choices

- **Choice A** → Highest Yield is **Gout**. USMLE tells you **patient with swollen big toe + asks for most likely risk factor** → **Alcohol (especially home-distilled)**

◦ Other HY things are

- **Elevated liver enzymes in someone who drinks. Most likely to prevent these findings** → **Alcohol cessation**
- HY cause of **SCC of esophagus** (with smoking)
- Hard one → **patient who drinks regularly + low calcium. Calcium supplements are given & levels don't go up.** What is cause → **Alcohol. Alcohol causes hypomagnesemia (causes hypocalcemia/hypokalemia refractory to ttt)**
- Patient with **confusion + ataxia + ophthalmoplegia**, what is greatest risk factor for this presentation → **Alcohol. This is Wernicke's**
- **Baby with long, smooth philtrum**, what is most likely cause → **Alcohol ingestion by mother. This is fetal alcohol syndrome.**

- **Choice B** → HY cause of **Transitional Cell Carcinoma**. But if you had to choose between smoking & -amines, choose smoking.

- **Choice D** → **Papillary Thyroid Carcinoma & Lymphoma**

- **Choice E** → **Only cause of SCC of bladder on the USMLE**

- **Choice F** → **Hepatic angiosarcoma**

Q16

A 12-year-old girl is brought to the physician by her mother after the dentist found many unerupted and supernumerary teeth. Physical examination shows frontal bossing, hypertelorism, and retained deciduous teeth. When prompted, the patient is able to place her shoulders together anteriorly. Serum studies show a decreased alkaline phosphatase activity. A chest x-ray shows hypoplasia of the clavicles. Skull x-rays show open sutures and multiple Wormian bones. Genetic testing shows a mutation in the CBFA1 gene. Which of the following cell types is directly affected by the mutation in this patient?

- A. Chondroblasts
- B. Chondroclasts
- C. Chondrocytes
- D. Osteoblasts
- E. Osteoclasts
- F. Osteocytes

▼ Explanation

- **Answer is D (Osteoblasts)**

- This is a bluff Q. Condition is LY and never mentioned in FA or any other USMLE prep source, and to be honest you don't need to know that condition.
- You can make an educated guess based on **"Serum studies show a decreased alkaline phosphatase activity." We know ALP reflects osteoblast function. So, if we have decreased ALP, when most likely we'd have defective Osteoblasts (Choice D).**
- This makes sense too, when looking back at the C/P of this disease. **Defective bone formation causing unerupted retained teeth, hypoplasia of the clavicles, and open sutures + wormian bones of skull.**

[For Nerds, like me]

This is **cleidocranial dysplasia**

- Caused by a **mutation**, which causes **impaired osteoblast function**
 - Osteoblastic activity is reflected by ALP
 - **decreased** osteoblastic activity ⇒ **low** ALP
- Impaired osteoblast function → characteristic features:
 - **Absent/Hypoplastic clavicles**
 - **Delayed closure of skull sutures**
 - **Retained deciduous teeth & other dental abnormalities**

Q17

A 70-year-old woman is transferred to a rehabilitative service 2 days after operative repair of a fracture of the right femur. She weighs 65 kg (143 lb). Findings on physical and mental status examinations are unremarkable. Which of the following is the most important predictor of success in the rehabilitation of this patient?

- A. Activity level before the fracture
- B. Age
- C. Postoperative hemoglobin concentration
- D. Serum calcium concentration
- E. Serum vitamin D concentration

▼ **Explanation**

- **Answer is A (Activity level before the fracture)**

- This is another risk factors Q disguised as a normal Q. Basically, we have an old woman that had a femur fracture.
- **Femur Fractures are the most common fractures in osteoporotic patients.** She is an old woman (Almost definitely osteoporotic to some degree)
- Now the Q asks what will be the most important predictor of success in the rehab of this patient.
 - In other words, what is the most important factor that would predict that her bones will regenerate & will become healthy again?
- **Do you know what is the number one most protective action that decreases incidence of osteoporosis + strengthens the bones?**
 - **Weight-bearing exercises.**
 - **If a patient has osteoporosis, number one prescribed ttt is → Weight-bearing exercises THEN Calcium & Vitamin D supplementation THEN drugs.**
- So, the **activity level of the patient before the fracture (Choice A)**, determines the degree of osteoporosis she had → predicts bone strength → predicts success of rehabilitation.

Q18

A physician prescribes a newly marketed drug to 45 patients. Over the next several weeks, she notes that the drug has good therapeutic efficacy, but it increased serum liver enzyme activities three times the normal value in 5 of the 45 patients. The physician is unable to find any official data linking the new drug with liver dysfunction. Which of the following is the most appropriate action by the physician?

- A. Continue the drug in all patients but inform the drug company about the association
- B. Discontinue the drug in all patients but study the results again to identify any other possible causes of the abnormal findings
- C. Discontinue the new drug in affected patients and file MedWatch reports on the FDA's Web site
- D. Discontinue the new drug in all patients and take no further action
- E. Do nothing, since the drug company most likely previously conducted all necessary research

▼ **Explanation**

- **Answer is C (Discontinue the new drug in affected patients and file MedWatch reports on the FDA's Web site)**
 - This is a **phase 4** of drug testing (a newly marketed drug; if it is on the market, then this is phase 4)
 - **In phase 4, we follow up the side effects of drugs for a long time & we report back to the FDA if there is any side effects, which the researchers were not aware of.**

▼ **Other Choices**

- **Choice A** → Of course not. Increase in liver enzymes 3x UNL is something to worry about, so we can't just continue the drug in these patients.
- **Choice B** → We stop the drugs in the affected patients.
- **Choice D** → You can't just "take no further action", you have to find out why this happened.
- **Choice E** → No body would do that.



Bottom Line:

In phase 4 of clinical trials/drug testing, if a drug shows a side effect that we are unaware of → stop the drug in affected patients & report to FDA

Q19

A sedentary 50-year-old man with hypertension comes to the physician because of a 6-week history of depression, anxiety, difficulty sleeping, fatigue, decreased appetite, and poor memory and concentration. He had an anterior wall myocardial infarction 3 months ago. He has one glass of wine each evening. He is 165 cm (5 ft 5 in) tall and weighs 67 kg (148 lb); BMI is 25 kg/m². His pulse is 104/min, respirations are 16/min, and blood pressure is 177/89 mm Hg. His ECG is unchanged from his last appointment. Laboratory studies show a hemoglobin concentration of 13.8 g/dL and serum LDL-cholesterol concentration of 127 mg/dL; serum LDL-cholesterol concentration was 117 mg/dL at his last visit. Which of the following is most likely to decrease this patient's risk for mortality over the next 2 years?

- A. Abstinence from alcohol
- B. Diet high in omega-3 fatty acids
- C. Low-calorie diet
- D. Antidepressant therapy
- E. Anxiolytic treatment

▼ **Explanation**

- **Answer is D (Antidepressant therapy)**
 - **IMP Clues**
 - 6-week hx of depression, anxiety, difficulty sleeping. decreased appetite, poor memory and concentration (Classic depression criteria)
 - Hypertension
 - Hx of anterior wall MI
 - Drinks one glass of wine each evening
 - LDL-cholesterol concentration of 127mg/dL
 - Q asks what will most likely decrease risk of mortality over next 2 years?
 - **Depression on the USMLE = Immediate assessment of suicidal thoughts.**
 - USMLE has this all over the NBMEs/Free120s. **If a patient is found to be depressed, YOU MUST ASSESS IDEAS OF SELF HARM or HARM TO OTHERS.**
 - This is because **risk of mortality from suicide exceeds risk of other morbidities (like HTN, Dyslipidemia, Alcoholism), especially on the short run.**

Q20

A 23-year-old woman has had fever, hypotension, and disseminated intravascular coagulation for 24 hours. She has a history of splenectomy following trauma. Which of the following bacteria is the most likely cause of this overwhelming sepsis?

- A. Escherichia coli
- B. Listeria monocytogenes
- C. Pseudomonas aeruginosa
- D. Staphylococcus aureus
- E. Streptococcus pneumoniae

▼ Explanation

- **Answer is E (Streptococcus pneumoniae)**
 - **IMP Clues**
 - Fever + hypotension (sounds like sepsis)
 - DIC (sepsis progressed to DIC)
 - Hx of splenectomy + asks for what bacteria most likely caused this overwhelming sepsis
 - **Dx → OPSI (Overwhelming Post-Splenectomy Infection)**
 - People who undergo **splenectomy (either elective - emergency - or even auto splenectomy in sickle cell anemia patients)** are at risk of something called **OPSI "Overwhelming Post-Splenectomy Infection"**.
- This patient here had **hx of splenectomy**, so she should have been vaccinated & she must be prescribed prophylactic antibiotics
- Otherwise, she is at **massive risk of developing sepsis → DIC (already happened) → Death**
- The Infection is caused by **encapsulated organisms**.
 - Most Commonly **Streptococcus pneumoniae**
 - Other common ones include **H.influenza, N.meningitides, and E.coli**.
 - E.coli is listed here as **choice A**, yes it is encapsulated and is a common cause of OPSI. However, if you had to choose between Streptococcus pneumoniae and E.coli, Choose → **Streptococcus pneumoniae**

? What smear finding would be expected in a patient with sickle cell disease that warrants prophylactic antibiotics and vaccinations?

- ▼ Answer
- Howell-Jolly bodies - DNA fragments** that are normally removed from the RBCs by the spleen
- Presence of Howell-Jolly Bodies = **functional asplenia** due to repeated infarcts
 - The other HY cause is **post-splenectomy**.

Q21

A 44-year-old woman comes to the physician for a follow-up examination after two separate Pap smears showed atypical squamous cells of undetermined significance. Results of a molecular diagnostic test show the presence of the viral E6 protein of human papillomavirus. This protein is known to promote cell growth and malignancy by causing cellular p53 protein degradation. This degradation most likely begins when the p53 protein is targeted to which of the following types of cellular enzymes?

- A. Lysine acetyltransferase
- B. Lysosomal protease
- C. Serine protease
- D. Tyrosine kinase
- E. Ubiquitin ligase

▼ Explanation

- **Answer is E (Ubiquitin ligase)**
 - Let's understand HPV oncoproteins
 1. **HPV E6 Protein**
 - Binds to & inhibits **p53** (p53 is a **tumor suppressor gene**)
 - **Causes ubiquitination of p53 → decreased p53 → decreased apoptosis → Cancer**
 2. **HPV E7 Protein**
 - Binds to & inhibits **Rb** (Rb is also a **tumor suppressor gene**)
 - **Rb is bound to E2F (forms Rb-E2F complex) → inhibition of Rb → release of E2F → promotes proliferation → Cancer**

? What parts of the cell cycle does p53 and Rb regulate?

- ▼ Answer
- G1 → S**

Q22

A 43-year-old woman, gravida 2, para 1, at 10 weeks' gestation comes to the physician for an initial prenatal visit. Physical examination shows a uterus consistent in size with a 10-week gestation. This patient is at increased risk for a child with Down syndrome if she has which of the following sets of ultrasound and serum findings?

Choices	Fetal Ultrasound Nuchal Translucency	Maternal Serum Pregnancy-associated Plasma Protein	Maternal Serum Human Chorionic Gonadotropin
A	↑	↑	↑
B	↑	↓	↑
C	↑	↓	↓
D	↓	↑	↓

Choices	Fetal Ultrasound Nuchal Translucency	Maternal Serum Pregnancy-associated Plasma Protein	Maternal Serum Human Chorionic Gonadotropin
E	↓	↓	↑
F	↓	↓	↓

▼ Explanation

- **Answer is B**
 - Easy Q, which asks for Down Syndrome US/Serum findings. Let’s master them:
 - **US** → They always assess **Nuchal Translucency** ⇒ **ALWAYS** ↑↑↑
 - **SERUM**
- 📋

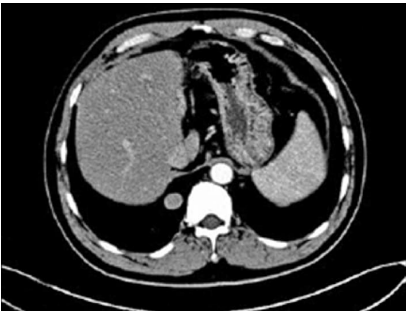
“Always choose ↑↑↑ for “H” in Down Syndrome”

 - Triple Test → ↓ AFP - ↑↑↑ hCG - ↓ E3
 - Quad Test → ↓ AFP, ↑↑↑ hCG, ↓ E3, ↑↑↑ Inhibin
 - Combined Test → ↓ PAPPA - ↑↑↑ hCG

“You don’t need to know the names of tests, just know whatever test has the letter “H” in it, choose ↑↑↑”

Q23

A 36-year-old woman comes to the office because of a 1-month history of joint pain, frequent headaches, and fatigue. Her temperature is 37.6°C (99.6°F). Physical examination shows edema of the upper and lower extremities. An abdominal CT scan is shown. Which of the following additional findings was most likely seen in this patient?



- A. Enlarged liver
- B. Gallstones
- C. Gastric perforation
- D. Pancreatic mass
- E. Splenomegaly

▼ Explanation

- **Answer is E (Splenomegaly)**
 - **IMP Clues**
 - Joint pain
 - Fatigue
 - Temperature is 37.6
 - Edema of upper and lower extremities
 - CT scan is shown
 - Q asks what else would be seen in this patient
- **Dx → Felty Syndrome**
 - It’s one of the **extraarticular manifestations of Rheumatoid Arthritis**
 - Mnemonic is “**SANTA**” → **S**plenomegaly, **A**nemia, **N**eutropenia, **T**hrombocytopenia, **A**rthritis
 - Patient has Joint pain → **Arthritis**
 - Patient has fatigue → **Anemia**
 - Patient temperature 37.6 → Low-grade fever hinting to **neutropenia**
 - Patient has Edema of upper & lower extremities → Chronic inflammation of RA causes **decrease in albumin & pre-albumin (negative acute phase proteins)** → decreased oncotic pressure → **Edema**
 - Q asks what else is likely to be seen ⇒ **Splenomegaly (Choice E)**

? What is the MOA of Rheumatoid Arthritis?

- ▼ Answer
- Autoimmune disease characterized by **CD4 T-cell activation** in response to **antigen-antibody complex deposition**, causing release of cytokines that induce **pannus formation** (synovial hyperplasia by proliferative granulation tissue)
- This results in **erosion of articular cartilage and bone**
 - The autoantibodies are **Rheumatoid Factor** and **anti-cyclic citrullinated peptide (anti-CCP, specific)**
- As the main immunological mechanism is antigen-antibody complexes deposition, causing T-cell activation; **This is Type 3 Hypersensitivity Reaction.**

Q24

A 25-year-old woman comes to the physician because of a 2-day history of fever, malaise, and a rash. She had a single painless lesion on her labia 3 weeks ago, but it resolved spontaneously. She is sexually active, but she and her partner do not use condoms consistently. Her temperature is 38°C (100.4°F). Physical examination shows a diffuse erythematous rash that includes the palms and soles. A sensitive but nonspecific rapid serologic screening test that uses which of the following reagents is most likely to support a diagnosis?

- A. Antitreponemal antibody on beads
- B. Dead commensal treponemes on beads
- C. Live *Treponema pallidum* on glass slides
- D. A phospholipid (cardiolipin) on charcoal particles
- E. Soluble fluorescent treponemal antibodies
- F. Treponemal antigens on ELISA plates

▼ Explanation

• Answer is D (A phospholipid (cardiolipin) on charcoal particles)

◦ IMP Clues

- Single painless lesion on her labia 3 weeks ago that resolved spontaneously (Painless lesion on genitals = Chancre until proven otherwise)
- She and her partner do not use condoms inconsistently (this phrase on the USMLE means think STDs, if they mention that they use condoms consistently, think something else)
- Examination shows a diffuse erythematous rash the includes palms and soles (DD of rashes that include palms & soles are super HY)
- Q asks for the sensitive serological test NOT the most sensitive test.

◦ Dx → Syphilis

“I’m going to mention everything you need to know about syphilis because it is HY”

▪ Primary Syphilis

- Chancre = **painless ulcer**
- Syphilis causes **endarteritis obliterans**. In other words, it obliterates end arteries. Obliteration of end arteries causes decreased blood supply to tissue (causing ulcers) and peripheral nerves (hence, painless ulcers) **[asked on NBME]**
- If **Primary Syphilis** is left untreated, the **chancre** heals after 3-6 weeks

• Secondary Syphilis then develops

◦ Secondary = Systemic disease

- **Maculopapular rash** that covers all body **including** palms & soles
- Condyloma Lata can also be seen (DD Condyloma acuminata of HPV)

? What is the DD of Rashes that involves palms & soles?

▼ Answer

- **Secondary Syphilis** - *Treponema pallidum*
- **Hand-Foot-Mouth Disease** - *Coxsackievirus A*
- **Rocky Mountain Spotted Fever** - *Rickettsia Rickettsii*
- **Kawasaki Disease** - *autoimmune disease*
- **Meningococcemia** - *Neisseria meningitides*

◦ If Secondary syphilis is left untreated, the rash resolves then **tertiary syphilis** develops after years

• Tertiary Syphilis → Gummas, Tree Bark Aortitis, Tabes dorsalis, Argyll's Robertson pupil

- **Gumma** → **painless** firm necrotic ulcer (granulomatous lesion)
- **Tree Bark Aortitis** → Ascending aorta aneurysm with tree bark look (due to destruction of vasa vasorum, the blood supply of the aorta)
- **Tabes Dorsalis** → Destruction of the dorsal column of spinal cord: presents as loss of proprioception & vibration + positive Romberg sign
- **Argyll's Robertson pupil (aka prostitute's pupil)** → Accommodates but doesn't react
 - mnemonic: Argyll's Robertson = AR = Accommodate but doesn't Reat
 - Caused by lesion in pretectal area
 - Accommodation is intact but light reflex is absent



HY to know:

- **Primary & secondary syphilis** → biopsy of lesions **demonstrates the organism**
- **Tertiary syphilis** → biopsy of lesions **DO NOT** demonstrate the organism

A tricky Q may tell you that this patient has syphilis + describe a painless lesion & asks what will be seen on biopsy.

- MAKE SURE TO DIFFERENTIATE, is this a Chancre? or a Gumma?
 - **Chancre** → **spirochetes seen**
 - **Gumma** → **NO** spirochetes seen.
 - What is seen is a **granuloma + inflammatory cells**

◦ Lastly, Syphilis is one of the **TORCH infections**.

- **Congenital syphilis causes: Saddle nose, Saber chins, SNHL, and Hutchinson teeth (notched incisors) or mulberry molars**

• Investigations

- What shape is Syphilis under the microscope → **Spirochetes**
- How can you directly visualize treponema → **Dark Field Microscopy** [*CAN'T BE SEEN IN TERITERY INFECTION*]

- Most common *screening tests* for syphilis → **VDRL & RPR** [*THEY DON'T DETECT THE BACTERIA ITSELF, BUT THE BODY'S REACTION TO CELL DEATH CAUSED BY THE BACTERIA*]
 - **RPR (Rapid Plasma Reagin)** which detects non-specific antibodies called reagin by introducing a **cardiolipin**-lecithin-cholesterol antigen to the patient's serum.
 - **VDRL (Venereal Disease Research Laboratory)** also detects antibodies produced by cell death in response to syphilis-causing bacteria

? 34F + hx of joint pain + hx of recurrent 2nd trimester abortion + positive VDRL/RPR. What is diagnosis?

▼ **Answer**

Anti-Phospholipid Syndrome (APS) - This female has **SLE + antiphospholipid syndrome**

- SLE → Arthritis (Joint pain)
- APS → most common cause of recurrent 2nd trimester abortion
 - **APS is associated with false positive VDRL/RPR.** No syphilis here.

- What's the *confirmatory test* for syphilis → **FTA-ABA** [*DETECT ANTIBODIES AGAINST TREPONEMA PALLIDUM ANTIGENS THEMSELVES*]

• **Treatment → Penicillin**

- What if the patient is allergic to penicillin → **Desensitize the patient THEN give penicillin.** It is **THAT** effective.
- What are some complications expected during ttt of penicillin → **Jarisch-Herxheimer reaction**
 - **Rapid release of cell wall components/organism products ⇒ LPS-like reaction ⇒ Fever, chills, hypotension**
 - HY to know that this reaction **can also happen in other spirochetes infection**, like **Lyme Disease**, and **not** just unique to syphilis [*asked on NBME*]

Q25

An 80-year-old man with type 2 diabetes mellitus is brought to the physician because a 2-month history of severe constipation. Use of over-the-counter laxatives has not relieved his symptoms. Abdominal examination shows distention. Colonoscopy shows no abnormalities. This patient most likely has dysfunction of which of the following nerves?

- A. Hypogastric
- B. Inferior rectal
- C. Pelvic splanchnic
- D. Perineal
- E. Sacral sympathetic

▼ **Explanation**

• **Answer is C (Pelvic Splanchnic)**

- **IMP Clues**
 - Type 2 Diabetes mellitus + Constipation (DM-related GI conditions are HY)
 - Abdominal examination shows distension (GI not moving as it should be + constipation causing obstruction-like state)
 - Colonoscopy shows no abnormalities (this excludes organic causes of GI obstruction)

• **Dx → Diabetic Gastroparesis**

- **As I said, DM-related GI conditions are HY**
 1. Neuropathy of **Pelvic Splanchnic nerve** (Parasympathetic supply) → **Constipation** (what we have here)
 2. Increase of **bacterial growth** in small intestines → **Diarrhea**
 - This is called **Small Intestinal Bacterial Overgrowth (SIBO)**
 3. Neuropathy of **Vagus nerve** → **Diabetic Gastroparesis (GERD-like symptoms)**



Clinical Scenarios

54M + heartburn + regurgitation of food.

- Dx → **GERD**
- ttt → **trial of PPIs/H2 Blockers for 2 weeks**
 - **If failed** → **Endoscopy**

54M + DM + heartburn + regurgitation of food.

- Dx → **Diabetic Gastroparesis**
- ttt → **Metoclopramide then Erythromycin**

Yes. The difference is just the **presence of DM** in the vignette. Nothing else will be different.

Q26

Following a wedding reception that was attended by 75 people, 25 adults develop low-grade fever, abdominal cramping, vomiting, and diarrhea. The symptoms begin 24 to 36 hours after the event and resolve without treatment in 3 to 4 days. Studies of stool specimens from several of the patients show no occult blood; no leukocytes are seen on microscopic examination, and stool cultures grow no pathogens. Several family members exhibit similar symptoms 3 days after the initial outbreak. Which of the following is the most likely causal organism?

- A. *Giardia lamblia*
- B. Norovirus
- C. Rotavirus
- D. *Shigella dysenteriae*
- E. *Staphylococcus aureus*

▼ Explanation

• Answer is B (Norovirus)

◦ IMP Clues

- 25 adult (yes, this is a keyword to differentiate between Rotavirus & Norovirus)
- Low-grade fever, abdominal cramping, vomiting, and diarrhea that began 24-36 hours after the event & resolved 3-4 days after (so short incubation period + self-limiting; This excludes parasites, and invasive bacteria)
- Stool studies show no occult blood, no leukocytes, and culture grows no pathogens (again, this excludes invasive bacteria)
- Q asks which of the following is the most likely causal organisms

• Dx → Norovirus Infection

- Norovirus (*Calicivirus* family) is a **positive-sense ssRNA Naked virus**
- **Most common cause of diarrhea in children > 5 years of age OR Rotavirus-immunized children**
- Known for its “**Explosive Diarrheal Illness**”, but not mentioned here



HY TO KNOW THE DIFFERENCE

- **Rotavirus** → Most common cause of diarrhea in **children < 5 years OR non-immunized children**
- **Norovirus** → Most common cause of diarrhea in **children > 5 years & adults OR Rota-immunized children**

Remember how USMLE hints to “non-immunized children”

- A child that came from [insert some other non-US/non-Western country] with no past medical records.
 - Okay, Mr.USA amazing health system.

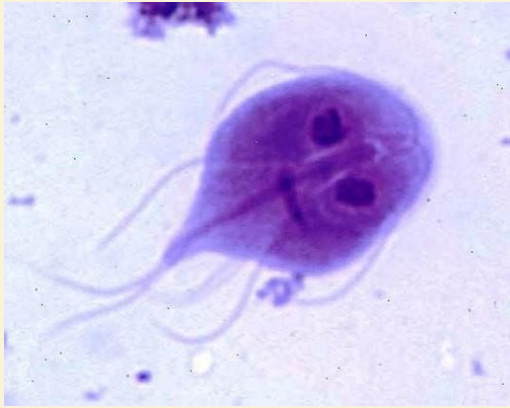


▼ Other Choices

- **Choice A** → USMLE presents *Giardia* infections as **people who went camping & drank unclean water + now have steatorrhea “foul smelling bulky greasy loose stools that float” [These keywords are buzzy & mentioned in almost all cases of giardia]**
 - They can also be tricky & mention travel to a country (like Indonesia/Honduras) where they drank tap water + developed loose stools that floats.
 - *Giardia* doesn't cause fever or vomiting + Stool microscopy would show the trophozoites



A couple traveled to Bali & ran out of clean water. They now present with 2w hx of foul smelling shiny stools. The doctor ordered a stool analysis and the following organism was found. What is the mechanism of action of appropriate treatment?



▼ Answer

Production of metabolites that damage microbial DNA.

- Treatment is **Metronidazole**.
- **Metronidazole** produces a metabolite that produces ROS that causes damage to microbial DNA → Cell Death



- **Choice C** → **Rotavirus** causes diarrhea in children **under 5 years of age**. Here they said adults were affected. This is why this a very important keyword.
- **Choice D** → **Shigella** is an invasive GI bacterium that would cause **fever, abdominal pain, bloody + mucoid stools**. There would be leukocytes too, in addition to positive growth on stool culture.
 - Highly associated with HUS (caused by Shiga Toxin or Shiga-like Toxin of EHEC)



What are the features of Hemolytic Uremic Syndrome?

▼ Answer

1. **Hemolytic Anemia + Schistocytes** on peripheral smear
2. **Renal Failure**
3. **Thrombocytopenia**

- **Choice E** → **Staphylococcus aureus** exotoxin (the one that causes food poisoning) causes similar symptoms; however, it starts within a few hours after ingestion & resolves in 24 hours. Timing her doesn't matchup really.

Q27

An investigator compares the DNA sequences of a group of newborns with achondroplasia with the sequences of a group of healthy newborns. DNA sequence analysis shows a G → C mutation in the fibroblast growth factor 3 receptor (FGR3) gene on chromosome 4. The sequences for the two groups are shown:

	Sequence
Achondroplasia	5'-TAC <u>C</u> GGGT-3'
Healthy	5'-TACGGGGT-3'

As a result of this mutation, an MspI restriction enzyme site is created that allows for a convenient diagnostic test. Which of the following sequences most likely represents the substrate specificity of MspI?

- A. 5' AATT
- B. 5' ACCG
- C. 5' AGGG
- D. 5' CCGG
- E. 5' GGCC
- F. 5' TACC

▼ Explanation

- **Answer is D (5' CCGG)**
 - To answer this Q, all you had to know that restriction enzymes bind to **5'-CCGG-3'** or **3'-GGCC-5'**.
 - Out of these 2, 5' CCGG is present. **Choice D**.
 - Bullshit? Yes. Deal with it.

“FYI, I DIDN’T STUDY BIOCHEM FOR MY STEP EXAM. Yes, you heard me right. Just the HY conditions, none of that molecular bullshit.”

Q28

A female newborn delivered at 36 weeks' gestation is in respiratory distress. Apgar scores are 3 and 5 at 1 and 5 minutes, respectively. Physical examination shows cyanosis. Endotracheal and nasogastric tubes are placed. The x-ray shown depicts the nasogastric tube in the left hemithorax, displacement of the mediastinum to the right, and absence of bowel gas in the abdomen. This condition most likely results from which of the following embryologic events?



- A. Failure of epimere to migrate
- B. Failure of hypomere to migrate
- C. Hypoplasia of the lungs
- D. Incomplete formation of pleuroperitoneal membrane
- E. Malrotation of bowel

▼ Explanation

- **Answer is D (Incomplete formation of pleuroperitoneal membrane)**

- **IMP Clues**

- Newborn delivered at 36 weeks' gestation is in respiratory distress (respiratory distress in premature ~24 weeks newborns is usually NRDS; but here we have a near term baby so NRDS unlikely)
- Cyanosis (DD is cardiac or respiratory)
- CXR shows NGT in left hemithorax, displacement of the mediastinum to the right, and absence of bowel gas (okay, so when we put a NGT in through the nose → stomach; we see that the NGT in the thorax area. This means that the stomach is in the thorax. Also, the displacement of the mediastinum to the right, means that the stomach on the left is pushing the mediastinum to the right)

- **Dx → Congenital Diaphragmatic Hernia**

- Caused by **"Incomplete formation of the pleuroperitoneal membrane"**

- The **absence** of the pleuroperitoneal membrane (the membrane between the pleura & the peritoneum) **causes herniation of the abdominal content into the chest.**

- Most common site is **Left Side** → **Mediastinal shift to the opposite site.**

- **Why the left?**

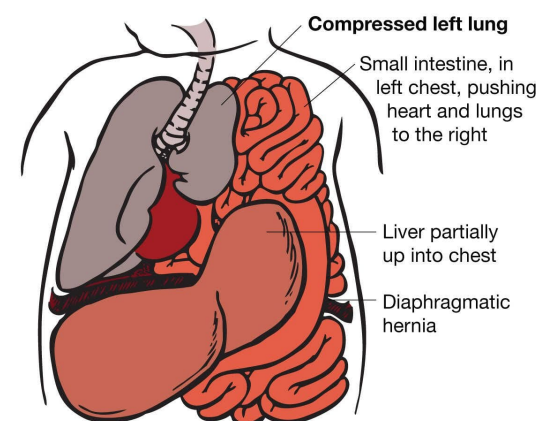
- **Left pleuroperitoneal canal closes later & the Liver protects the right side.**

- This causes compression of the adjacent lung tissue → **Lung hypoplasia** (the cause of respiratory distress & death)

- **NGT is found in the chest** (site of stomach)

- HY Findings that may hint to the condition are:

- 34w NB + resp distress + **persistent cyanosis despite O2 therapy**
- 34w NB + resp distress + **decreased breath sounds on left side**
- 34w NB + resp distress + **intestinal sounds on chest auscultation**
- 34w NB + resp distress + **intestinal loops/NGT in chest on CXR**



▼ Other Choices

- **Choices A & B → Epimere & Hypomere** are parts of the myotome that go on to form different muscles

▮ **"You don't need to know this bullshit, I'm just explaining"**

- Epimere → Intrinsic back muscles
- Hypomere → Limbs & Abdominal muscles

- **Choice C** → Tricky as, yes, the cause of the respiratory distress is hypoplasia of the lung, but the Q asks "this condition most likely results from which of the following embryologic events?" The whole condition (the distress + the NGT tube in the chest) is due to the "Incomplete formation of pleuroperitoneal membrane."

- **Choice E → Malrotation of bowel** or referred to as **"Midgut Malrotation"**

- **Abnormal rotation of abdominal organs, which causes:**

- Compression of **duodenum** → **Bilious Vomiting**
- Compression of **SMA** → **SMA Syndrome**

- Other HY findings are **presence of Ladd bands and Jejunum on the right**

Q29

An 82-year-old woman is brought to the physician because of a 1-week history of episodes of light-headedness and fainting. She has hypertension currently treated with propranolol. Her pulse is 45/min, and blood pressure is 90/50 mm Hg. Physical examination shows no other abnormalities. An ECG shows normal, regular P waves followed by normal QRS complexes. The physician decreases the dose of propranolol. Five days later, the patient's pulse is 80/min, and her symptoms have resolved. Which of the following is the most likely explanation for this patient's low pulse while taking the higher dose of propranolol?

- A. Decreased activation of fast sodium channels
- B. Decreased rate of repolarization phase
- C. Decreased slope of diastolic depolarization
- D. Increased calcium influx during late phase of slow depolarization
- E. Increased potassium influx during rapid depolarization phase
- F. Increased sodium efflux during early repolarization phase

▼ Explanation

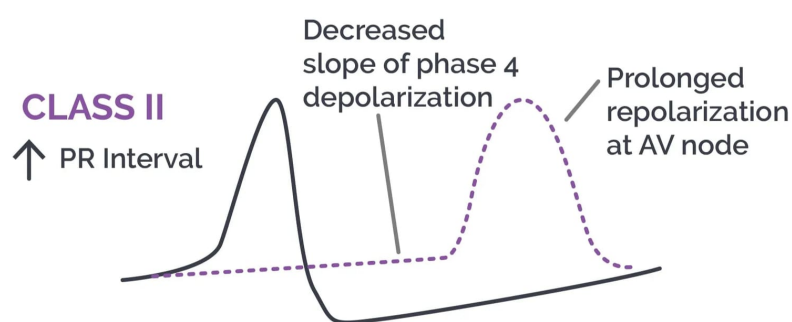
- Answer is C (Decreased slope of diastolic depolarization)

- IMP Clues

- Woman is brought to the physician because of 1-week history of episodes of light-headedness and fainting (these are signs of Low CO in cardio)
- She has HTN treated with propranolol + her pulse is 45/min and BP is 90/50 mmHg (she's taking a BB which caused her to be bradycardic and hypotensive)
- ECG is normal
- Physician decreases the dose of propranolol and 5 days later her pulse is 80/min & her symptoms resolved (okay, so the BB was the cause of the bradycardia & hypotension)

- Q asks what is most likely explanation for this patient's low pulse while taking the higher dose of propranolol?

- The SA Node is what controls the Heart Rate & Rhythm
 - HR increases when there is **increased adrenergic stimulation (via B1 agonism)** → B1 → **increases cAMP** → **increases Ca influx** → **increases slope of diastolic depolarization** → heart fills faster & pumps faster.
 - **If a Beta Blocker (Class II antiarrhythmics) is taken** → **decreased cAMP** → **decreases Ca influx** → **decreased slope of diastolic depolarization** → heart fills slower & pumps slower.



? What is the antidote for Beta Blocker overdose?

▼ Answer

Glucagon (increases cAMP) - If you want to be more clinically accurate, proper steps are fluids → atropine → glucagon.

▼ Other Choices

- **Choice A** → Fast Na channels are NOT for Nodal AP. They are present in atrial & ventricular myocyte AP
- **Choice B** → Decreased rate of depolarization is what causes the bradycardia (decreased Nodal firing) not repolarization
- **Choice D** → Increasing Ca influx would increase the HR, not decrease it
- **Choice E** → K influx DOESN'T happen during depolarization. Ca influx does
- **Choice F** → Na is the driving ion for atrial & ventricular myocyte AP. Nodal AP is mainly driven by Ca channels & Funny Channels

Q30

A 30-year-old man comes to the physician because of a 3-month history of pain in his jaw and left arm. He also has had intense thirst and increased urination during this period. He was found to have peptic ulcer disease 2 months ago. Physical examination shows no abnormalities. Serum studies show a calcium concentration of 13.5 mg/dL and an intact parathyroid hormone concentration of 110 pg/mL (N=10-65). An x-ray of the left humerus shows no abnormalities. Which of the following biologic mechanisms best explains the impaired calcium homeostasis in this patient?

- A. Decreased calcium reabsorption by renal tubules

- B. Decreased expression of parathyroid hormone receptors on osteoblasts
- C. Decreased hydroxylation of vitamin D by renal tubule epithelial cells
- D. Increased calcitonin secretion by thyroid gland
- E. Increased motility of monocytes in bone marrow
- F. Increased osteoclast maturation and activity

▼ Explanation

- **Answer is F (Increased osteoclast maturation and activity)**
 - **IMP Clues**
 - He was found to have peptic ulcer disease 2 months ago (as you read on, you'd notice that this is probably caused by a gastrinoma "pancreatic tumor" portion of MEN1)
 - Serum studies show a calcium concentration of 13.4 mg/dL and PTH concentration of 110pg/mL (so both PTH & Ca are increased, meaning this is 1ry hyperparathyroidism. The most common cause is parathyroid adenoma; also part of MEN1)
 - **Q asks what causes the impaired calcium homeostasis?**
 - This is **MEN 1 Syndrome**, which presents as a triad of *pituitary adenoma* (not present here), *pancreatic tumor* (gastrinoma, causing PUD), and *parathyroid adenoma* (causing primary hyperparathyroidism)
 - **Parathyroid Adenoma** → high PTH concentration stimulates osteoblasts → *increases* osteoblasts expression of RANK-Ligand → binds to nearby osteoclast precursors that express RANK-Receptor → *activation & differentiation of osteoclasts ("Increased osteoclast maturation and activity")* → bone resorption
 - The activation of osteoclasts is sometimes referred to as *"paracrine stimulation of osteoclasts by osteoblasts"*

? Patient with recurrent duodenal & jejunal ulcers + diarrhea + abdominal pain with family hx of neck mass in mother. What is defective in this patient?

▼ Answer

Tumor Suppressor Gene (Menin) on chromosome 11 - USMLE can sometimes be this vague. Neck mass is the parathyroid adenoma. The ulcers are the gastrinoma. They might not put the full triad in the vignettes, and thy might ask you for the diagnosis (**MEN1**) or for the genetic cause (**mutation of Menin - a tumor suppressor gene**)

? Patient has parathyroid adenoma. What are expected arrows of osteoblast activity, ALP, osteoclasts activity, and RANK-L expression?

▼ Answer

- **Increased** osteoblast activity
- **Increased** ALP
- **Increased** osteoclast activity
- **Increased** RANK-L expression

Q31

An 18-year-old woman comes to the physician because she has never had a menstrual period. Physical examination shows a 1-cm invagination where the vagina would normally be present. No uterus is palpable on rectal examination. Laboratory studies of serum show:

Follicle-stimulating hormone	8.3 mIU/mL
Luteinizing hormone	6.7 mIU/mL
Estradiol	200 pg/mL (N=30-400)
Testosterone	3 nmol/L (N=<3.5)

Which of the following structures is most likely normal in this patient?

- A. Cervix
- B. Ductus deferens
- C. Ovaries
- D. Round ligament
- E. Testes
- F. Uterus

▼ Explanation

- **Answer is C (Ovaries)**
 - **IMP Clues**
 - Never had a menstrual period (case of primary amenorrhea)
 - 1-cm invagination instead of vagina (no Vagina) + no uterus palpated (No uterus too)
 - Serum studies are all normal (So, we have a female with no uterus & vagina + normal hormones)

- **Dx → Mullerian Agenesis**
 - Also known as *Mayer-Rokitansky-Kuster-Hauser Syndrome*
 - **Mullerian (Paramesonephric) duct is what becomes the Fallopian tubes, Uterus, Cervix, and upper 3/4 of the Vagina.**
 - In **Mullerian Agenesis**, the Mullerian ducts *fails* to develop → **Female with no tubes, uterus, cervix, and upper vagina.**
 - **No Uterus → Primary Amenorrhea**
 - **Blind-End Vaginal pouch → lower 1/4 of vagina is derived from urogenital sinus (unlike upper 3/4 from Mullerian duct)**
 - **Ovaries are *normal* as they are derived from the genital ridge**

?

How to differentiate MRKH Syndrome from AIS (Androgen Insensitivity Syndrome)?

▼ **Answer**

Both do present with a “female” with primary amenorrhea (never menstruated before). They both have no uterus and they have a blind-end vaginal pouch. They most likely also present with well-developed breasts & secondary sexual characters.

<u>AIS</u>	<u>MRKH Syndrome</u>
• XY Genotype	• XX Genotype
• Testes present	• Ovaries present
• Defect in androgen receptors	• Defect in Mullerian Duct development
• Spare/No axillary & pubic hair	• Normal axillary & pubic hair
• High LH and High Testosterone	• Normal Labs

Q32

A 27-year-old woman comes to the physician because of a 3-month history of intermittent headaches and palpitations. Her initial blood pressure is 125/80 mm Hg while she sits in a chair. When asked to sit on the examination table, she has facial flushing, and her blood pressure increases to 185/115 mm Hg. Physical examination shows no other abnormalities. Which of the following is the most likely diagnosis?

- A. Coarctation of the aorta
- B. Hyperthyroidism
- C. Pheochromocytoma
- D. Primary aldosteronism
- E. Renovascular hypertension

▼ Explanation

- **Answer is C (Pheochromocytoma)**
 - **IMP Clues**
 - Intermittent headaches and palpitations (the word intermittent is key, as periodic episodes of palpitations & headaches due to catecholamines release is the cause)
 - Facial Flushing and her blood pressure increases to 185/115 mmHg (again, suddenly her BP increases from 125 to 180 mmHg; This is so buzzy for pheochromocytoma)
 - **Dx → Pheochromocytoma**
 - Most common tumor of **adrenal medulla** (Q can describe the above symptoms and *ask for origin*; answer is **medulla**)
 - Derived from **Chromaffin cells (*Neural Crest Origin*, ectoderm) [*positive for Chromogranin and Synaptophysin*]**
 - **Secretes Dopamine, Epinephrin, and Norepinephrine in *episodic manner* → Episodes of:**
 - **Hypertension**
 - **Headaches**
 - **Flushing**
 - **Palpitations**

- Diagnosis:
 - **Increased catecholamines & metanephrines (HVA & VMA) in urine & plasma**
 - Microscopy can show **Electron-dense membrane bound secretory granules**
 - Associated with some mutations:
 - RET → MEN2A & MEN2B
 - VHL → Von Hippel-Lindau
 - NF-1 → Neurofibromatosis 1
- Treatment
 - **1st** → **Phenoxybenzamine** (irreversible alpha antagonist)
 - **then** → BB
 - why this order?
 - If you give BB first & the patient gets an “episode” → **unopposed alpha agonism** → **hypertensive crisis**
 - So, we block **alpha** first **THEN beta** (A before B)

? 3M + increased HVA & VMA in urine + episodes of abnormal eye & limb movements. What is Dx?

▼ Answer

Neuroblastoma

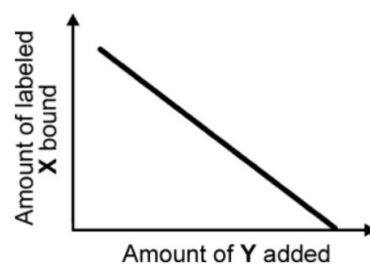
- **Pediatrics tumor** that rises from **adrenal medulla** (or sympathetic chain) that also originates from **neural crest cells**.
- Presents as a **firm irregular abdominal mass** (causing distention) that **can cross the midline** + **opsoclonus-myoclonus syndrome**
- Urine shows **high levels of HVA & VMA**
- Biopsy shows **Homer-Wright Rosettes** (*found also in Medulloblastomas*)
- Associated with **N-myc oncogen amplification** (*vs c-myc of Burkitt's lymphoma*)
 - **Neuroblastoma** = **N**-myc
 - **Burkitt's lymphoma** = **C**-myc

▼ Other Choices

- All other Choices would cause hypertension yes. However, they would cause **persistent HTN**. **Episodic HTN & palpitations are characteristic to pheochromocytoma**

Q33

Purified serum antibodies elicited by immunization with protein X are adsorbed to microtiter wells. The graph shows the amount of radiolabeled protein X that is bound by the solid-phase anti-X antibodies in the presence of varying concentrations of protein Y. With respect to the anti-X serum, which of the following interpretations regarding 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 A (Proteins X and Y express the same epitopes)**
 - Very easy Q here. As you add Y, amount of “bound” X decreases.
 - **This means that X & Y share competing for the same antibody binding sites, so they share the same epitopes (Choice A)**

Q34

A patient with a 1-week history of diarrhea has reduced tissue turgor. Arterial pH is 7.3; serum bicarbonate concentration is 15 mEq/L. This patient is also likely to have which of the following?

- A. Decreased arterial Pco2
- B. Decreased circulating level of ADH (vasopressin)
- C. Decreased circulating level of aldosterone
- D. Increased circulating level of atrial natriuretic peptide
- E. Increased serum anion gap

▼ Explanation

- **Answer is A (Decreased arterial Pco2)**
 - **IMP Clues**
 - 1 week history of diarrhea (Diarrhea is a cause of non-anion gap metabolic acidosis)
 - Arterial pH is 7.3 (acidosis) & serum bicarbonate concentration is 15 mEq/L (low bicarb, tell us that this is metabolic acidosis)
 - Q asks what else is likely to be found?
 - If the patient has **metabolic acidosis (low pH & low HCO3)**, then the body is most likely to decrease acidosis. How can this be done?
 - **Decrease CO2 levels via *increasing* Respiratory Rate**
 - *higher RR → more CO2 washout → less H in blood → **increases serum pH (as a compensatory mechanism)***
 - So, answer is **“Decreased arterial Pco2” (Choice A)**

▼ Other Choices

- **Choice B** → Patient is dehydrated (hx of diarrhea & reduced skin turgor), so this causes ***increased*** ADH levels → increase free water reabsorption
- **Choice C** → Patient is dehydrated (hx of diarrhea & reduced skin turgor), so this causes ***increased*** Aldosterone levels → increase Na reabsorption (water follows). Additionally, H is also secreted out to decrease acidosis.
- **Choice D** → Patient is hypovolemic, so ventricles & atria are not stretched → ***decreased*** ANP
- **Choice E** → Diarrhea causes ***normal*** anion gap metabolic acidosis



What are the causes of high anion gap VS normal anion gap metabolic acidosis?

▼ Answer

Causes of high anion gap: “MUDPILES**”**

- M = Methanol
- U = Uremia (Renal Failure acute or chronic)
- D = DKA
- P = Phenformin (NON-EXISTANT ON THE USMLE)
- I = Iron (HY) or Isoniazid (HY)
- L = Lactic acidosis
- E = Ethylene glycol
- S = Salicylates (Aspirin)

HY causes of normal anion gap metabolic acidosis on the USMLE:

- RTA
- Diarrhea

Q35

A 28-year-old man has excessive thirst and polyuria. The following laboratory data are obtained:

	Serum Glucose (mg/dL)	Serum Osmolality (mOsmol/kg)	Urine Osmolality (mOsmol/kg)
Baseline	75	310	175
With 12 h water deprivation	70	320	185
With ADH (vasopressin) after water deprivation	70	310	315

Which of the following is the primary site of the pathophysiologic process in this patient?

- A. Adrenal cortex
- B. Aortic baroreceptors
- C. Cerebral cortex
- D. Hypothalamus
- E. Renal tubules

▼ Explanation

- **Answer is D (Hypothalamus)**
 - **IMP Clues**

- Excessive thirst & polyuria (On the USMLE, excessive thirst & polyuria are DI, PP, or DM)
- Baseline & after 12 hours of water deprivation, there was no change in serum & urine osmolality (this means something is definitely wrong as when you deprive yourself from water, ADH will be secreted. So this is DI)
- with ADH administration, urine osmolality increases (this means the kidneys CAN respond to ADH, so the problem was ADH not being secreted)

• Dx → Central ADH

- Presents with **HIGH** serum Na, **HIGH** urine output, **HIGH** serum osmolality, **LOW** urine osmolality, **which improves with exogenous ADH (vasopressin) administration**
- Where is ADH synthesized?
 - **Hypothalamus** (Supra-optic nucleus & paraventricular nucleus) *[asked on NBMEs]*
 - They (ADH & oxytocin) are **stored** in the **posterior pituitary** **NOT SYNTHESIZED THERE**.
- Central DI is caused by **meningitis, trauma, or idiopathically**



Patient with excessive thirst & polyuria with hx of bipolar disorder. What is the cause of these symptoms?

▼ Answer

Nephrogenic DI - this caused by **lithium intake (the main line of ttt in bipolar disorder)**

- Other causes of Nephrogenic DI are **Lithium, Demeclocycline, Hypercalcemia, and NSAIDs**

Q36

A 38-year-old African American man with recently diagnosed hypertension comes to the physician for a follow-up examination. At his last visit 1 month ago, the patient agreed to initiate a regimen including increased physical activity, a low-sodium diet, and pharmacotherapy. He has had no weight loss since then. He is 175 cm (5 ft 9 in) tall and weighs 82 kg (180 lb); BMI is 27 kg/m2. His blood pressure is 150/95 mm Hg. Physical examination shows no other abnormalities. Which of the following best describes the role of ethnicity when the appropriate medication is selected for this patient?

- A. It should not play a role because cost, patient adherence, and adverse effects are of primary importance
- B. It should not play a role because use of ethnicity could lead to stereotyping
- C. It should not play a role because the variability of response to medications within a single ethnic group is greater than the different responses among ethnicities
- D. It should play a role because the adverse effect profiles differ by ethnicity
- E. It should play a role because the efficacy of certain classes of medications varies among different ethnicities

▼ Explanation

- **Answer is E (It should play a role because the efficacy of certain classes of medications varies among different ethnicities)**
 - The aim of his concept tests the reasoning behind why the ACC/AHA Hypertension guidelines mention that **there is better BP lowering with thiazides/CCBs in African American patients.**
 - Are you supposed to know that? For STEP 1? No. STEP 2? Yes.
 - Just keep these facts in the back of your head.

Q37

A 35-year-old man comes to the physician to discuss donating a kidney to his 39-year-old sister who has type 1 diabetes mellitus and chronic renal failure. He has no history of major medical illness, and physical examination shows no abnormalities. Which of the following best describes the likelihood that this donor's human leukocyte antigen type will match that of his sister?

- A. 1:1
- B. 1:2
- C. 1:4
- D. 1:6
- E. 1:8

▼ Explanation

- **Answer is C (1:4)**
 - Q asks what is the likelihood that a brother will have the same HLA type as his sister.
 - All you need to know is the following to answer these types of Qs:
 - **25% Identical HLA MATCH**
 - **25% NO MATCH**
 - **50% Shares one HLA (Heterozygous)**

- So, the answer here is **25% or 1:4 (Choice C)**

Q38

A male newborn is found to have a decreased blood thyroxine (T₄) concentration on newborn screening. Physical examination shows no abnormalities. Serum studies show decreased concentrations of triiodothyronine (T₃) and T₄. His serum free T₄ and thyroid-stimulating hormone (TSH) concentrations are within the reference ranges. Which of the following best explains these findings?

- A. Maternal antithyroid antibodies
- B. Organification defect in T₃ and T₄ synthesis
- C. Thyroid dysgenesis
- D. Thyroid hormone-binding globulin deficiency
- E. TSH deficiency

▼ **Explanation**

- **Answer is D (Thyroid hormone-binding globulin deficiency)**

- **IMP Clues**

- Decreased blood T₄ concentration (when T₄ is written without the “free” part, this usually means that this is the total T₄, the free + the bound T₄)
- Decreased concentration of T₃ and T₄ (again, total T₃ + T₄ are decreased)
- Serum free T₄ and TSH concentrations are within the reference ranges (This means we are clinically euthyroid, not hyper nor hypothyroidism is present)

- **Dx → Thyroid hormone-binding globulin deficiency**

- First, you need to understand that **total T₄ = Free T₄ + T₄ bound on THBG**
- Second, you need to understand that **the “effective” hormone is the FREE part.**
 - What I mean by this is that if you have **low free T₄, this causes hypothyroidism → high TSH**
 - If you have **normal free T₄ with low total T₄, this will NOT cause hypothyroidism → NORMAL TSH**
- So, on the USMLE if you find **normal TSH + normal Free T₃/T₄, with decreased total T₃/T₄ ⇒ THINK THBG deficiency**



A pregnant woman presents to the clinic for a follow up. Lab investigations reveal a high Total T₄, normal free T₄, and a normal TSH. What is the cause of these labs?

▼ **Answer**

Increased THBG - Increased Estrogen in pregnant women causes increase liver production of THBG.

- The increased/newly synthesized unbound THBG binds to the free T₄ → T₄ level decreases → TSH increases → Thyroid produces more free T₄ → normal free T₄ level → normal TSH level

Q might give you a pregnant lady with elevated Total T₄, and asks how do we confirm if this lady has hyperthyroidism?

- Just measure the free T₄ as it is the “effective” chunk, if it is increased → hyperthyroidism.

“This is very HY and asked on the USMLE, so knowing the relation between THBG, total, and free thyroid hormone is very important to understand.”

▼ **Other Choices**

- **Choices A, B, C, and E** → Would cause hypothyroidism (decreased Free T₃/T₄ + increased TSH)

Q39

A 29-year-old man comes to the physician because of a 1-week history of fever, muscle aches, sore throat, and nonproductive cough. His temperature is 38.9°C (102°F). Rhonchi are heard on auscultation of the chest. A chest x-ray shows bronchopneumonia of the right lower lobe. Symptoms persist after 7 days of amoxicillin therapy. A test result for cold agglutinins is positive. Which of the following features of the causal organism best explains the ineffectiveness of the pharmacotherapy in this patient?

- A. Absence of peptidoglycan
- B. Alteration of penicillin-binding proteins
- C. Impermeable outer membrane
- D. Production of a β-lactamase that inactivates amoxicillin
- E. Requirement of sterols for growth

▼ **Explanation**

- **Answer is A (Absence of peptidoglycan)**

- **IMP Clues**

- 1 week hx of fever, muscle aches, sore throat, and nonproductive cough (unspecific symptoms, but this is an infection of the lungs)
- Ronchi are heard on auscultation of the chest + CXR shows bronchopneumonia of the right lower lobe (confirmed pneumonia)
- A test result for cold agglutinins is positive (IMP KEYWORD HERE, cold agglutinins + pneumonia is Mycoplasma)
- Symptoms persist after 7 days of amoxicillin therapy + Q asks why is amoxicillin therapy ineffective

- **Dx → Mycoplasma pneumonia**

- As we know from sketchy, **Mycoplasma has NO cell wall.**
- Amoxicillin MOA is **inhibition of peptidoglycan cross-linking → inhibition of cell wall synthesis**
- There is no cell wall for it to be inhibited.

? After the discovery of the new diagnosis, what is the MOA of the drug that should be given to the patient?

▼ **Answer**

Inhibition of Protein Synthesis - Macrolides are **50s ribosomal subunit inhibitors**

- Aminoglycosides & Tetracyclines are **30s** ribosomal subunit inhibitors
- mnemonic I use to remember this is **"I will meet you AT 30 Street"**
 - **A = Aminoglycosides**
 - **T = Tetracyclines**
 - **30 Street = 30S**



? What are the HY conditions were cold agglutinins are seen?

▼ **Answer**

Mycoplasma pneumonia, Infectious Mononucleosis, CLL, HCV

Q40

A 70-year-old man has a 3-month history of weakness and a 10-kg (22-lb) weight loss. He has smoked 2 packs of cigarettes daily for 50 years. An x-ray of the chest shows a 4-cm lesion in the right upper lobe. Serum calcium concentration is 13.5 mg/dL. There are no bone metastases. A malignant lesion arising in a segmental bronchus is seen during lobectomy. Which of the following is the most likely diagnosis?

- A. Adenocarcinoma
- B. Carcinoid
- C. Leiomyosarcoma
- D. Small cell carcinoma
- E. Squamous cell carcinoma

▼ **Explanation**

- **Answer is E (Squamous cell carcinoma)**

- **IMP Clues**

- 3-month history of weakness + serum calcium concentration is 13.5 mg/dL (hypercalcemia causes weakness)
- Weight loss + CXR shows a 4-cm lesion in the right upper lobe (sounds like cancer)
- Smoked 2 packs of cigarettes daily for 50 years (okay, so we are thinking lung cancer that is associated with smoking & causes hypercalcemia, easy right?)
- A malignant lesion arising in a segmental bronchus is seen during lobectomy (confirmed that this is cancer)

- **Dx → SCC of the Lungs**

- **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 lung with a cavity** & ask for the diagnosis.
- Releases **PTHrP → Hypercalcemia**
 - USMLE may convey this as renal stones in a patient with hemoptysis & weight loss

? Patient with Lung SCC. Arrows of PTH, Calcium, Phosphate?

▼ **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.

▼ Other Choices

- **Choice A** → Usually presents as a **nonsmoker with a peripheral / apical lung lesion**
 - Associated paraneoplastic syndromes are **hypercoagulability, dermatomyositis, and hypertrophic osteoarthropathy**
- **Choice B** → Patients present with **flushing, diarrhea, diaphoresis, and TR. Biopsy shows rosettes.**
- **Choice C** → Very rare in the lungs
- **Choice D** → Similar to SCC, it presents as a **smoker with a central lesion**
 - However, associated paraneoplastic syndromes are **SIADH, ACTH secretion, Lambert-Eaton syndrome, or Neurological Syndromes**

Q41

A 78-year-old man is brought to the emergency department by his neighbor because of a 3-week history of severe weakness and fatigue; he also has had a 7.3-kg (16-lb) weight loss during this period. He lives alone, and he says that his daughter usually visits him once or twice weekly to bring him groceries. However, he has eaten nothing but small quantities of saltine crackers and black coffee since his daughter left for vacation 1 month ago. He is 173 cm (5 ft 8 in) tall and now weighs 56 kg (124 lb); BMI is 19 kg/m². His pulse is 92/min, and blood pressure is 108/76 mm Hg. Physical examination shows generalized muscle weakness. Serum studies in this patient are most likely to show an increased concentration of which of the following hormones?

- A. Cortisol
- B. Insulin
- C. Insulin-like growth factor-I
- D. Testosterone
- E. Triiodothyronine (T₃)

▼ Explanation

- **Answer is A (Cortisol)**
 - **IMP Clues**
 - Severe weakness and fatigue + generalized muscle weakness (a lot on the DD list, but after reading the options, increased cortisol can cause weakness & fatigue)
 - Weight loss + he has eaten nothing but small quantities of saltine crackers and black coffee since his daughter left for vacation 1 month ago (patient is in a catabolic state, so we are expecting the stress hormones to increase)
 - Q asks which hormone is most likely to show an increased concentration
 - Patient is in a **state of stress (fasting)**, so we expect the stress hormones to **increase**:
 - **Cortisol (our answer)** → **Increases lipolysis, gluconeogenesis, protein catabolism, and maintains blood pressure & blood glucose, but suppresses immunity**
 - **Glucagon** → **Inhibits glycolysis and increases glycogenolysis and gluconeogenesis**
 - **Epinephrine & Norepinephrine** → **Increases heart rate and blood pressure**

▼ Other Choices

- **Choice B** → Patient is fasting/catabolic, so **insulin will be decreased** not increased. As you know, insulin level increases when you EAT, not starve yourself. Insulin is anabolic.
- **Choice C** → **IGF-1 is produced by the liver** in response to GH. Its function is to regulate metabolic processes in the body; however, **in starvation the decreased protein synthesis decreases the production of IGF-1.**
- **Choice D** → Malnutrition affects GnRH-pituitary-gonadal axis. If you want me to be more specific/HY, **I'd say you need to know that Leptin (produced by Fat cells) is low in underweight people (low fat cells = low leptin), and leptin inhibits GnRH axis, causing decreased FSH & LH production, which can decrease estrogen/testosterone.**
- **Choice E** → Stress causes **euthyroid sick syndrome**.
 - **Stress hormones (Cortisol - Catecholamines - Glucagon) & cytokines (IL-1, IL-6, TNF-alpha)** increase, causing:
 - **Suppression of 5-deiodinase enzyme** which converts T4 into T3 peripherally.
 - T4 is then shunted into **reverse T3 (rT3) production**, essentially an inactive form of T3.
 - The levels of T4 essentially stays the same, so no change in TSH levels.
 - So, expected labs would be:



24F + 7-month hx of amenorrhea. BMI is 13. What is cause of above symptom?

▼ Answer

Decreased Leptin inhibiting the hypothalamus-pituitary-gonadal axis

- **Low T3**
 - **High rT3**
 - **Normal T4**
 - **Normal TSH**
-

Q42

An 18-year-old boy has just been diagnosed with schizophrenia. His identical twin brother is unaffected, but he and his parents are concerned about his likelihood of developing the disorder. Which of the following best represents the brother's risk for developing schizophrenia?

- A. 10%
- B. 25%
- C. 50%
- D. 75%
- E. 100%

▼ **Explanation**

- **Answer is C (50%)**
 - Q asks what is the risk of an identical twin to develop schizophrenia like his brother? Like how the fuck would you know?
 - Apparently, research says that:
 - Lifetime risk is 1%
 - Risk in 1st degree relatives is 6.5%
 - Non-identical twins risk is 10-20%
 - Identical twins risk is 50%
 - Bullshit info? Yes.
-

Q43

A 25-year-old man comes to the physician 8 hours after the onset of severe pain of his low back that radiates down his left leg. He started a weight-lifting regimen earlier in the day during which he tried to lift a bar loaded with 91 kg (200 lb) from the ground to over his head. The pain began almost immediately after this attempt. Which of the following is the most likely cause of this patient's pain?

- A. A fracture of a lumbar vertebra
- B. Rupture of the deltoid tendon
- C. Rupture of an intervertebral disc
- D. A tear in the sciatic nerve
- E. A torn muscle in the low back

▼ **Explanation**

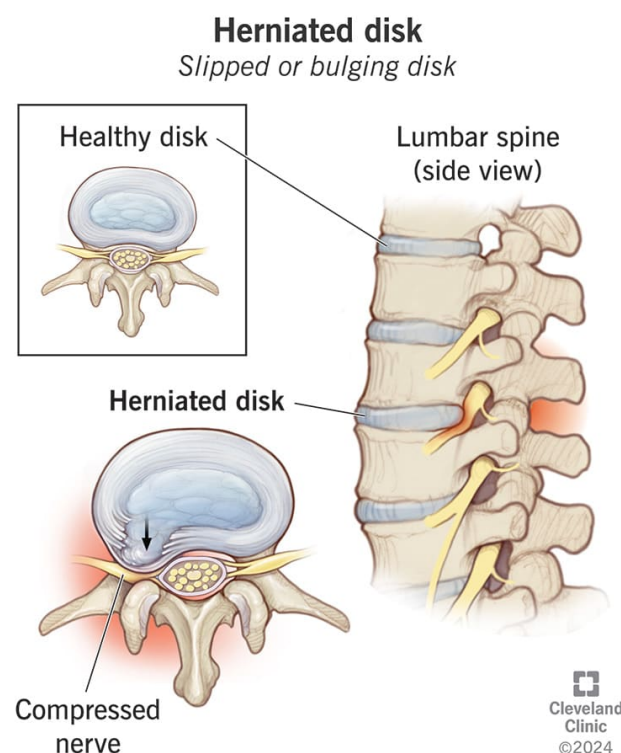
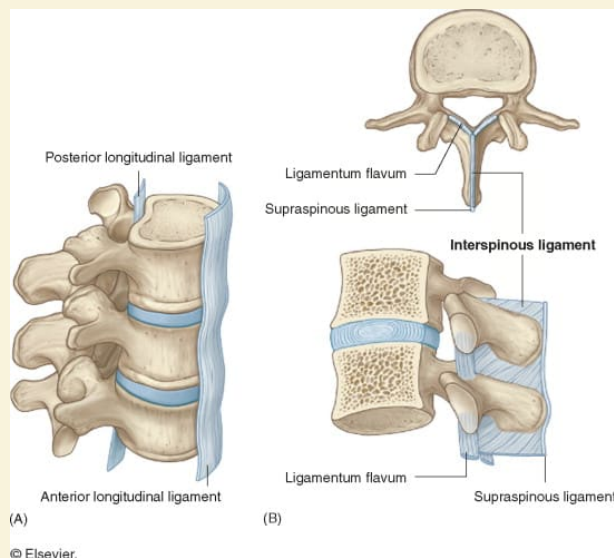
- **Answer is C (Rupture of an intervertebral disc)**
 - **IMP Clues**
 - Severe pain of his low back that radiates down to his left leg (radiating pain is radiculopathy, which usually means that a spinal cord root is being compressed by something)
 - Pain began almost immediately after his attempt of lifting a bar loaded with 91 kg (bro tried to power clean 91kg, then felt severe back pain that radiates down to his leg. This is a herniated disc. Easy)

- Dx → Rupture of an intervertebral disc
 - On the USMLE, severe radiating pain after lifting something is usually a **herniated disc**.
 - The Vertebral disc is made up of an *outer harder layer* called the **annulus fibrosus**, and an *inner jelly like layer* called the **nucleus pulposus**.
 - When **lifting a heavy object + excessive back extension** → this causes **increase pressure on the intravertebral disc**, which causes **rupture of the outer fibrous layer and expulsion/herniation of the nucleus pulposus**.

? What is the **ligament** that is pushed by the herniated matter onto the nerve root?

▼ Answer

Posterior longitudinal ligament.



▼ Other Choices

- **Choice A** → Fracture of a vertebra would present as **acute back pain with pain increasing upon palpation** of the affected vertebra. **NO radiculopathy**.
- **Choice B** → Rupture of deltoid tendon would cause **severe shoulder pain +/- bleeding below the skin + loss of deltoid function**. Why would there be LEG radiculopathy? No reason, so **NO radiculopathy**.
- **Choice D** → Extremely rare from weightlifting. Would cause loss of sciatic nerve function **NOT radiculopathy**.
- **Choice E** → Would **NOT cause radiculopathy** but would probably cause **severe pain at the site of that muscle + overlying tenderness and swelling**.

Q44

A 25-year-old woman comes to the physician 2 days after noticing a mass in her right axilla. She also has a 1-week history of malaise, headaches, and night sweats. The patient says that she recently adopted a kitten and has sustained several bite and scratch marks. Her temperature is 37.8°C (100°F). Physical examination shows edema and tenderness of the right axillary lymph node. The skin over the node is erythematous, tough, and warm. There are scratches and bite marks of various ages over the upper extremities and hands. The result of an indirect fluorescent antibody test for *Bartonella henselae* is positive. A biopsy specimen of this lymph node is most likely to show which of the following histologic patterns?

- Diffuse neutrophil infiltration
- Granulomas containing stellate microabscesses
- Large activated lymphocytes with occasional plasma cells
- Serous inflammation with abundant intravascular fibrin and few inflammatory cells
- Vascular proliferation with fibrosis

▼ Explanation

- **Answer is B (Granulomas containing stellate microabscesses)**
 - **IMP Clues**
 - A mass in her right axilla (On the USMLE, this may be a metastasis, Yersinia, or Cat-Scratch Disease)
 - Recently adopted a kitten + has sustained several bites and scratch marks (I think that it is clear that this is cat-scratch disease)
 - Edema and tenderness of the right axillary lymph nodes + skin overlying is erythematous, tough, and warm + scratches are seen over hands & upper extremities (more clues to cat-scratch disease)
 - Indirect fluorescent antibody test for Bartonella henselae is positive (confirmed)
 - Q asks what histological pattern is most likely to be seen upon biopsy of the lymph node?
 - Very straight forward Q here, **Bartonella Henselea cat scratch disease causes enlarged axillary lymph node that shows granulomas containing stellate microabscesses.**
 - HY to know that Bartonella Henselae causes 2 HY disease:
 - **Immunocompetent** → **Cat-Scratch Disease** (biopsy shows → *Granulomas containing stellate microabscesses*) [Choice B]
 - **Immunosuppressed** → **Bacillary Angiomatosis** (biopsy shows → *Vascular Proliferation with fibrosis + neutrophils infiltration*) [Choices A+E]



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

? What are the antibiotics used in ttt of Cat-Scratch Disease VS Bacillary Angiomatosis?

- ▼ **Answer**
 - Cat-Scratch Disease** → **Macrolides**
 - Bacillary Angiomatosis** → **Macrolides + Doxycycline**

Q45

A 65-year-old man is brought to the emergency department because of substernal chest pain, nausea, and sweating for 1 hour. He has a 10-year history of type 2 diabetes mellitus and hypertension. His pulse is 120/min, respirations are 24/min, and blood pressure is 98/60 mm Hg. Physical examination shows a jugular venous distention of 12 cm. Crackles are heard halfway up the lung fields posteriorly. Which of the following ECG findings is most likely in this patient?

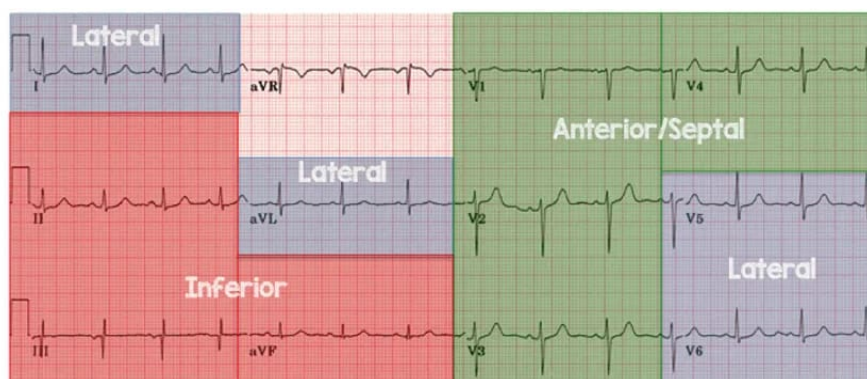
A. PR-segment depression
B. PR-segment elevation
C. QRS widening
D. QT-interval prolongation
E. QT-interval shortening
F. ST-segment elevation

- ▼ **Explanation**
 - **Answer is F (ST-segment elevation)**
 - **IMP Clues**
 - Substernal Chest pain (MUST BE WORRIED)
 - He has 10-year hx of T2DM and HTN (Major Risk Factors for MI)
 - Pulse is 120/min (tachycardic) + respirations are 24/min (tachypneic), and Blood pressure is 98/60mmHg (hypotensive due to LV failure)
 - JVD of 12 cm (Right Side HF) + Crackles are heard halfway up the lung field posteriorly (Pulmonary edema due to Left Side HF)

- **Dx → Myocardial Infarction**
 - Q asks what does MI ECG show?
 - Can be one of 2 things **mainly**:
 - **STEMI** (ST-segment elevation MI) where ECG shows ST-segment elevation (duh)
 - **NSTEMI** (Non-ST-segment elevation) where ECG shows ST-segment depression instead.
 - Do I need to know how does the ECG look like? **Yes**.



- Do I need to know what leads refer to what parts of the heart? **Yes. You also need to know what arteries supply these leads.**
 - Leads **II, III, aVF** → **Inferior heart (PDA)**
 - Leads **I, aVL, V, VI** → **Lateral heart (Left circumflex artery)**
 - Leads **V1-V4** → **Anterior heart + Septum (LAD)**



[For Nerds/STEP2]

What are all the expected ECG changes in MI?

- **Early Changes** (we're talking like minutes to hours post-MI)
 1. Peaked, hyperacute T waves
 2. ST-segment elevation (if transmural MI)
 3. ST-segment depression (if subendocardial MI)
- **Hours/Days After**
 1. T-wave inversion
 2. Pathological Q waves appear
- **Late Changes** (we're talking like weeks)
 1. Q waves persist (tell us that this patient had an MI before + cardiac tissue scarring)

Very HY & Important Clinically to know:

- If the Q **doesn't specify the coronary dominance** of the patient, the patient is **Right-Dominant** → **PDA is branch of the Right Coronary Artery**
- If the Q explicitly says that the patient is **Left Coronary-Dominant** → **PDA is branch of the Left Coronary Artery**

? What is most common cause of death post-MI?

▼ Answer

Arrhythmia - Most common cause of death in first 24-48hrs post-MI is arrhythmia

▼ Other Choices

- **Choice A** → PR depression is LY, For **Acute Pericarditis**, you must know **DIFFUSE ST-ELEVATION**. PR-depression is also found, however, for USMLE purposes it is LY.
- **Choice B** → Not even tested.
- **Choice C** → Wide QRS complexes tell you that **ventricles are contracting autonomously**. HY conditions that cause this is **VT and 3rd degree Heart Block**.
- **Choice D** → QT prolongation is HY and can be caused by **hypocalcemia, Type Ia & Type III antiarrhythmics, Metoclopramide, Macrolides, TCA, and Antipsychotics**.
 - **Risk of progression to Torsade de Pointes, which can cause Fatal VF.**
- **Choice E** → HY cause of QT shortening I can think of this **hypercalcemia**

Q46

Three elderly residents of an assisted living facility in rural Pennsylvania are admitted to the hospital within 3 days of one another because of pneumonia. All three patients have a history of chronic obstructive pulmonary disease and returned home from a weekend retreat at a residence hall 4 to 7 days ago. Forty-three other individuals attended the retreat. Two other attendees developed pneumonia shortly after returning home, but they did not require hospital admission; they were a 37-year-old woman with systemic lupus erythematosus treated with corticosteroids and a 46-year-old man with severe asthma. No other retreat attendees, including nine children under the age of 5 years, developed a respiratory illness. None of the other residents of the assisted living facility have any symptoms of respiratory illness. Which of the following infectious agents is the most likely cause of these findings?

- A. Adenovirus
- B. Influenza virus
- C. Legionella pneumophila
- D. Respiratory syncytial virus

E. Streptococcus pneumoniae

▼ Explanation

- **Answer is C (Legionella pneumophila)**
 - **IMP Clues**
 - Three elderly residents in an assisted living facility are admitted to the hospital because of pneumonia + all three had hx of COPD (Okay so COPD patients only developed the pneumonia)
 - 43 people attended the retreat + 2 other attendees developed pneumonia, but didn't require hospitalization + They had SLE treated with steroids and a man with severe asthma (I think we started seeing a pattern that immunocompromised patients are affected)
 - No other people developed the pneumonia including 9 children (helps exclude RSV)
- **Dx → Atypical pneumonia caused by Legionella pneumophila**
 - Legionella is transmitted through **aerosolized water** (ACs, closed confined spaces, conference rooms, cruise ships)
 - People at risk are **smokers, COPD patients, the elderly, and immunocompromised patients**
 - Classical Legionella Pneumonia (not mentioned here, but mentioning because it is unique so HY) is **atypical unilateral pneumonia in a smoker/elderly/immunocompromised/COPD patient + diarrhea + hyponatremia + confusion (CNS symptoms)**



 Rapid Legionella Review:

- Gram → **negative**
- Visualized under → **Silver Staining**
- Agar → **Charcoal yeast + Cysteine and Iron**
- Presentations:
 1. **Pontiac Fever** → Self-limiting fever & malaise
 2. **Legionnaire's Disease** → **Atypical pneumonia + Diarrhea + Hyponatremia (SIADH) + Confusion (CNS dysfunction)**
- Diagnosis → **Urine antigen testing**
- Treatment → **Macrolides & Fluoroquinolones**

? **What are the MOAs of Legionella treatment?**

- ▼ **Answer**
- Macrolides** → **Inhibit 50S ribosomal subunit**, causing prevention of **protein synthesis** (USMLE likes to call it "**translation**").
- Fluoroquinolones** → **Inhibits DNA gyrase** (Topoisomerase 2 & 4), causing prevention of **DNA replication/RNA synthesis** (USMLE like to call it "**transcription**").

▼ Other Choices

- **Choice A → Adenovirus** would cause conjunctivitis & tonsillitis in kids. Also, a HY DD for hemorrhagic cystitis
- **Choice B → Influenza Virus** will make much more people sick not just the elderly/immunocompromised.
- **Choice D → RSV** would make the kids sick.
- **Choice E → Streptococcus pneumoniae** would cause serious pneumonia in many of the people. Hard hitting pneumonia too.

Q47

A 56-year-old woman has frequently burned herself while cooking over the past several months. Examination shows loss of pain and temperature sensation in both upper extremities and in a portion of her trunk from the clavicles to just below the nipples. Touch, vibratory sensation, and proprioception are normal. There is some wasting of the small muscles of her hands. Which of the following findings is most likely on MRI of the head and spine?

- A. Dilated third ventricle causing damage to both sides of the thalamus
- B. Edema in the postcentral gyri on both sides secondary to multiple strokes
- C. Sclerotic plaques bilaterally in the anterolateral white matter of the spinal cord
- D. Syrxinx of the central region of the spinal cord from C-4 to T-5
- E. Tumors compressing the lateral funiculi of the spinal cord at C-4

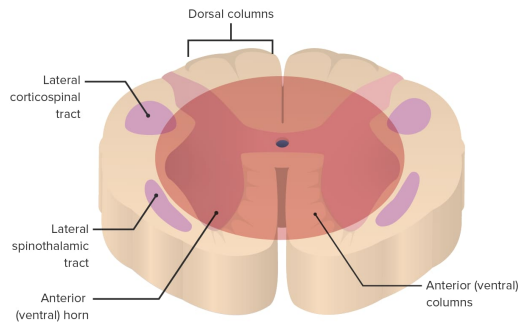
▼ Explanation

- **Answer is D (Syrinx of the central region of the spinal cord from C-4 to T-5)**
 - **IMP Clues**
 - Frequently burned herself (usually hints that she can't feel shit)
 - Examination shows loss of pain and temperature sensation in both upper extremities and in a portion of her trunk from the clavicles to just below the nipples (loss of spinothalamic sensation in a cape-like distribution, rings a bell?)

- Touch, vibration, and proprioception are normal (Intact Dorsal column)
- There is some wasting of the small muscles of hands (affection of corticospinal tract, especially the medial part of that tract that carries sensation to the upper part)

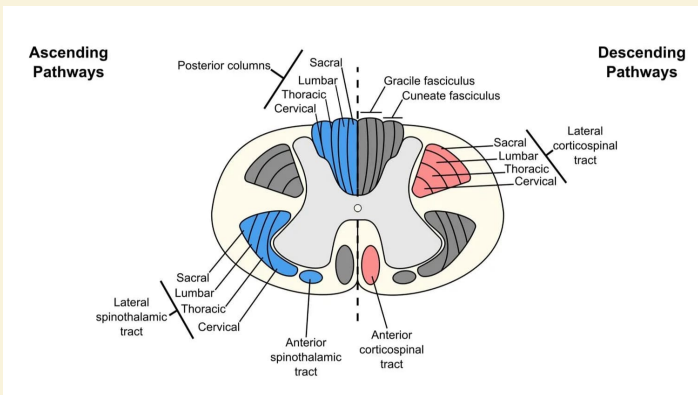
◦ **Dx → Syringomyelia / Central Cord Syndrome**

- Presents as:
 - ***Bilateral*** loss of **temperature & pain sensation (Spinothalamic tract)** in ***cape distribution*** (upper chest, shoulders, arms, and hands). Lower limb may be affected but will be less severe.
 - **+/- motor power (Corticospinal tract)**



? Why does this patient have wasting of the hands **ONLY** & not the whole upper limb?

▼ **Answer**
 The most medial part of the corticospinal tract is the tracts that carry the cervical roots, which include the C8-T1 which supply the hand muscles



- Syringomyelia is associated with **Chiari I malformation, trauma, and infection** [asked on NBME]

Q48

Which of the following changes in the cardiovascular system occurs with normal aging?

- A. Development of coronary atherosclerosis
- B. Development of mitral stenosis
- C. Increased basal heart rate
- D. Increased basal systolic blood pressure
- E. Increased cardiac muscle mass
- F. Increased compliance of arteries

▼ **Explanation**

- **Answer is D (Increased basal systolic blood pressure)**
 - Q asks which of these happens with “normal” aging?
 - **Choice A** → Development of coronary atherosclerosis isn’t “normal”, this is pathological and will kill you.
 - **Choice B** → Mitral Stenosis also isn’t normal. **HY to know that MS is the greatest risk factor for developing of AF.**
 - **Choice C** → The older you get, the more degeneration happens. An example of that is degeneration of the SAN, which decreases basal HR.
 - **Choice D (THE ANSWER)** → Arteries **lose** their elasticity and may get **calcified** as a person ages, this **increases the afterload** on the heart and causes **increase basal systolic BP**.
 - **Choice E** → Cardiac muscle mass (and overall muscle mass) decreases as you get older.
 - **Choice F** → The older you get, you lose the elasticity of the arteries & they get calcified, hence that sometimes when you palpate the arteries in older people during BP measurement, you may feel it as a cord under your fingers [asked on NBMEs]

Q49

A 28-year-old woman of Eastern European Jewish decent comes to the office 2 days after she noticed a lump in her left breast. Her maternal grandmother was diagnosed with ovarian cancer at the age of 54 years and died at the age of 60 years; her maternal aunt and mother were diagnosed with breast cancer at the ages of 36 and 40 years, respectively. The aunt died as a result of the disease at the age of 50 years. The patient is concerned that she may have inherited a genetic mutation that would predispose her to breast and/or ovarian cancer. Genetic testing of this patient and her mother are most likely to show a germline mutation in a component of which of the following pathways?

- A. DNA mismatch repair
- B. DNA polymerase proofreading
- C. DNA base excision repair
- D. DNA nucleotide excision repair
- E. Recombinational double-stranded DNA break repair

▼ Explanation

- **Answer is E (Recombinational double-stranded DNA break repair)**
 - **IMP Clues**
 - Maternal grandmother was diagnosed with ovarian cancer (so hx of breast cancer)
 - Her maternal aunt and mother were also diagnosed with breast cancer (again, hx of breast cancer)
 - Q asks which germline mutation is most likely present?
 - **BRCA gene mutation.** Easy.
 - We all know that it is BRCA gene, but what USMLE will ask you is what caused that **BRCA gene mutation**, answer is → **Recombinational double-stranded DNA break repair**



What are the HY USMLE conditions that are caused by Recombinational double-stranded DNA break repair?

▼ Answer

- **BRCA gene mutation**
- **Fanconi Anemia**

▼ Other Choices

- **Choice A** → DNA mismatch repair refers to **Lynch Syndrome**
- **Choice B** → Not really specific for anything special on the USMLE
- **Choice C** → The answer if the Q mentions **glycosylases**
- **Choice D** → The answer if the Q mentions **pyrimidine-pyrimidine dimers, UV light exposure, SCC, or Xeroderma pigmentosum**

Q50

A 50-year-old woman with a restrictive pulmonary disorder with no obstructive component is most likely to have which of the following sets of pulmonary volumes?

Choices	Functional Residual Capacity (L)	Residual Volume (L)	Vital Capacity (L)
A	↓	↓	↓
B	↓	↓	normal
C	↓	normal	↓
D	Normal	↓	↓
E	↑	↑	↓

▼ Explanation

- **Answer is A**

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 ↓↓↓**

**Obstructive VS Restrictive Lung Diseases PFTs:**

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



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