



NBME EXPLANATIONS

NBME 20 Block 4

from CrackNBME

NBME 20 - Block 4

Q1

A 65-year-old woman who has a 25-year history of chronic alcoholism is brought to the emergency department because she is vomiting blood. She eats little more than an occasional sandwich. Examination of the legs shows perifollicular hyperkeratosis and hemorrhage. Abnormally decreased function of which of the following metabolic pathways is most likely in this patient?

- A. Carboxylation of pyruvic acid
- B. Decarboxylation of pyruvic acid
- C. Decarboxylation of 2-ketoisocaproic acid
- D. Hydroxylation of proline
- E. Synthesis of porphyrin

▼ Explanation

- **Answer is D (Hydroxylation of proline)**
 - **IMP Clues**
 - Patient has 25-year history of chronic alcoholism (Alcohol has calories 7cal/g, which satiates the consumer. This predisposes patients to malnutrition as they are no getting in enough macros & micronutrients)
 - She eats a little more than an occasional sandwich (Another hint that she's not eating enough)
 - Examination shows perifollicular hemorrhage and perifollicular hyperkeratosis (buzzy and pathognomonic for Vitamin C deficiency on USMLE)
 - **Dx → Vitamin C Deficiency**
 - Vitamin C is a vital component in collagen synthesis
 - **Post-transcriptional modification in the ER → hydroxylation of Proline residue via Hydroxylase enzyme, which requires Vitamin C.**
 - If vitamin C is deficient → **Scurvy**
 - **Poor Wound healing** (due to impaired collagen synthesis)
 - **Corkscrew Hairs & Hyperkeratosis**
 - **Bleeding gums & Capillary Fragility** (Petechiae, Ecchymoses, **Perifollicular hemorrhage**, and subperiosteal hemorrhage)
 - **Inability to maintain bone matrix [asked on NBME]**

USMLE gives you a **malnourished patient who was lost on a hiking trip + got a broken leg**. After rescuing him, they found that the bone was made up of **improperly formed callus**, and they ask for diagnosis; answer is **Vitamin C deficiency**.



What mineral's absorption is enhanced by Vitamin C intake?

▼ Answer

Iron

- **Vitamin C reduces $\text{Fe}^{3+} \rightarrow \text{Fe}^{2+}$**



Patient with Methemoglobinemia + G6PD deficiency. What is appropriate ttt?

▼ Answer

Vitamin C (Ascorbic Acid)

- **Methemoglobinemia** causes formation of Fe^3
- Vitamin C is used to **reduce back $\text{Fe}^{3+} \rightarrow \text{Fe}^{2+}$**
- 1st line ttt is **Methylene blue**, however, **its use is contraindicated in patients with G6PD as Methylene blue can cause hemolysis.**

Q2

A 33-year-old woman with HIV infection is brought to the emergency department 30 minutes after she had a generalized tonic-clonic seizure. She also has a 2-month history of daily headaches. Physical examination shows no signs of meningismus. Muscle strength is 3/5 in the left upper extremity and 5/5 in the right upper extremity. Her CD4+ T-lymphocyte count is 22/mm³ (N≥500), and plasma HIV viral load is 50,000 copies/mL. A CT scan of the head shows a 3-cm lesion in the right cerebral cortex. Serologic studies show a positive IgG antibody titer to Toxoplasma gondii. Treatment with pyrimethamine and sulfadiazine is initiated. During the next 2 weeks, she has three additional seizures. Two weeks after starting antibiotic therapy, a CT scan of the head shows that the lesion has increased to 3.5 cm. Which of the following is the most likely cause of this mass?

- A. Bacterial abscess
- B. Cerebral toxoplasmosis
- C. Glioblastoma
- D. Metastatic disease

▼ Explanation

• Answer is E (Non-Hodgkin lymphoma)

◦ IMP Clues

- Woman with HIV infection + headaches + generalized tonic-clonic seizure + strength is 3/5 in left upper extremity and 5/5 in right upper extremity (Okay, this sounds like a right sided brain lesion, causing headaches, weakness and seizures)
- No signs of meningismus (NOT meningitis)
- CD4 count is 22 & HIV viral load is 50,000 (She is clearly not taking her meds, which predisposes her to all HIV-associated infections & immunosuppression)
- CT scan shows a 3-cm lesion in the right cerebral cortex (confirms what we said above)
- Positive IgG titer to Toxoplasma + ttt is initiated + she has additional seizures + CT scan shows lesion size has increased to 3.5cm (Physician though this was toxo + started ttt, however, patient didn't get any better & lesion increase in size. This means this is NOT Toxoplasmosis)

◦ Dx → Primary CNS Lymphoma

- This patient is **immunosuppressed due to the low CD 4** count as a result of noncompliance with her HIV medications, **causing major predisposition to tumors & HIV-associated infection**
- **A singular brain lesion in an HIV patient is either *Toxoplasmosis* or *Primary CNS Lymphoma* until proven otherwise (especially if they were described as enhancing lesions)**
- This patient was thought to have toxoplasmosis and ttt was started. On USMLE, there is **NO** thing as **non-responsive toxoplasmosis, so if the ttt doesn't work → IT IS NOT TOXOPLASMOSIS**
 - Which makes us reach the conclusion that this is **CNS Lymphoma**



Primary CNS lymphoma (PCNSL) is a **diffuse, large-cell non-Hodgkin lymphoma of B-cell origin** that is associated with **Epstein-Barr virus (EBV)**.



Another presentation for CNS lymphoma is a **brain enhancing lesion in a patient with hx of autoimmune diseases**



Brain Enhancing Lesions on the USMLE:

1. HIV patient + brain enhancing lesion
 - ⇒ Think **Toxoplasmosis**
2. HIV patient + brain enhancing lesion + started toxoplasmosis ttt, but patient got worse/lesion got bigger
 - ⇒ Think **CNS Lymphoma**
3. HIV patient + brain enhancing lesion + on TMP-SMX
 - ⇒ Think **CNS Lymphoma**
4. HIV patient + brain enhancing lesion + on PJP prophylaxis
 - ⇒ Think **CNS Lymphoma**
 - Prophylaxis of PJP is TMP-SMX, which is also the prophylaxis of Toxoplasmosis
5. Patient with hx of autoimmune disease + brain enhancing lesion
 - ⇒ Think **CNS Lymphoma**

▼ Other Choices

- **Choice A** → Bacterial Brain abscess on the USMLE is quite a rare sighting. The only Q I can think of was a **child with Chronic Suppurative Otitis Media, which spread to his temporal lobe causing the child to have seizures and vomiting.**
- **Choice B** → **Toxoplasmosis** would have responded to given ttt. Patient got worse after giving him the appropriate ttt, so **IT IS NOT Toxoplasmosis.**
- **Choice C** → **GBM** is usually described as a **butterfly-shaped heterogenous mass** seen at the **midline** of the brain (usually invades the corpus callosum). They can also provide you with the histology, **"Pseudo-palisading cells."**
- **Choice D** → **Metastatic disease** would present as **MULTIPLE** lesions at the **grey-white junction.**

A 16-year-old girl with cystic fibrosis is brought to the physician because of a 3-week history of generalized weakness, numbness and tingling of her arms and legs, and difficulty walking. She has not adhered to her medication regimen during the past 6 months. She appears alert and oriented. Her vital signs are within normal limits. Physical examination shows bilateral weakness and decreased deep tendon reflexes in the upper and lower extremities. She walks with an ataxic gait. The most likely cause of these findings is a deficiency of which of the following?

- A. Folic acid
- B. Vitamin A
- C. Vitamin B6 (pyridoxine)
- D. Vitamin D
- E. Vitamin E

▼ Explanation

- Answer is E (Vitamin E)
 - IMP Clues
 - Cystic Fibrosis (CF = pancreatic insufficiency = decreased absorption of fat-soluble vitamins)
 - Bilateral weakness + decreased tendon reflexes (LMN affection)
 - Numbness and tingling of her arms and legs (Sensation is affected)
 - Difficulty walking + walks with an ataxic gait (Cerebellar lesion)
- Dx → Vitamin E Deficiency
 - Patient has Cystic Fibrosis, which causes thick impacted secretions in the pancreas → Pancreatic insufficiency → Decreased absorption of Fat-Soluble Vitamins (K, E, D, A)
 - Vitamin E Deficiency is super HY on USMLE:
 - Ataxia (affection of spinocerebellar tract)
 - Peripheral Neuropathy (affection of dorsal column)
 - Myopathy
 - Hemolysis

? What is defective in patients with Cystic Fibrosis?

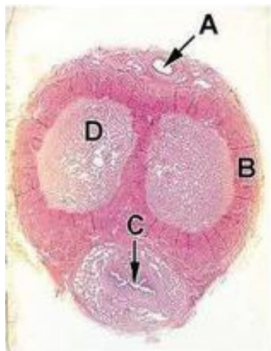
- ▼ Answer
- Protein Structure of CFTR channels
- Deletion ($\Delta F508$; deletion of phenylalanine) in the CFTR gene on Chromosome 7 → Misfolded CFTR channels (these are proteins, which are misfolded so defected protein structure) retained in the Golgi.

▼ Other Choices

- Choice A → Not usually seen in CF patients, as it is a water-soluble vitamin NOT fat-soluble vitamin.
- Choice B → Can happen in patients with CF, but present as Retinitis Pigmentosa, Corneal Ulcers, Night Blindness, Bitot Spots, and maybe a rash.
- Choice C → Not usually seen in CF patients, as it is a water-soluble vitamin NOT fat-soluble vitamin.
- Choice D → Can happen in patients with CF, but presents as Rickets or Osteomalacia

Q4

A 61-year-old man has erectile dysfunction due to spinal cord injury at L-2. Sildenafil is likely to markedly correct the dysfunction by acting at which of the following labeled structures in the transverse section of the penis?



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

▼ Explanation

- Answer is D

- Sildenafil (more commonly known as Viagra)
 - PDE-5 inhibitor that causes **vasodilation of the Deep Penile Artery** that supplies the **corpus cavernosum (Choice D)**
 - Uses: **Erectile Dysfunction & Pulmonary HTN.**
 - HY Side Effect is **hypotension** (especially if taken with other drugs that cause hypotension, like nitrates) & **bluish tint in color vision.**



How does PDE-5 Inhibitors work?

▼ Answer

PDE-5 breaks down cGMP, so **inhibiting it causes increase in cGMP levels** → **activation of protein kinase G** → **vasodilation**

▼ Other Choices

- Choice A → Deep Dorsal Vein
- Choice B → Tunica Albuginea
- Choice C → Urethra inside the corpus spongiosum

Q5

A 35-year-old man is given cyclosporine following a liver transplantation. Which of the following mechanisms best describes the utility of this drug in this situation?

- A. Decreased synthesis of interleukins
- B. Induction of calcineurin phosphatase
- C. Inhibition of B-lymphocyte proliferation
- D. Promotion of internalization of tumor necrosis factor- α receptors
- E. Stabilization of lysosomal membranes

▼ Explanation

- Answer is A (Decreased synthesis of interleukins)
 - Q asks for mechanism of Cyclosporine:
 - Cyclosporin *inhibits Cyclophilin* → *decreases* intracellular calcineurin → *decreases* IL-2 transcription
 - HY Side-effects you must know:
 1. Hypertension
 2. Hyperkalemia 2ry to Nephrotoxicity
 3. Hypertrichosis
 4. Gingival Hyperplasia
 - IL-2 is basically a cytokine that **stimulates proliferation of B-cells and T-cells**, so in patients with liver transplantation we need to suppress the immune system *to prevent graft-vs-host reaction.*



SUPER HY TO KNOW THE DIFFERENCE!

- Sirolimus = **NO** decrease in IL-2 transcription & **NO** hyperkalemia (Nephrotoxicity)
- Tacrolimus & Cyclosporin = Decrease in IL-2 transcription & hyperkalemia (Nephrotoxicity)



What are other related drugs I need to know?

Okay, so 2 drugs are **calcineurin inhibitors** which **decrease IL-2 transcription**

1. Cyclosporin

- inhibits **Cyclophilin** → inhibits calcineurin → decreases IL-2 transcription

2. Tacrolimus

- inhibits **FK506** → decreases IL-2 transcription
- Side-effects:
 - T2DM
 - Hyperkalemia 2ry to Nephrotoxicity

One other drug **decreases responsiveness** (**NOT** transcription) of IL-2

1. Sirolimus

- blocks **mTOR** → decreases RESPONSIVENESS of IL-2
- Side-effects:
 - Dyslipidemia

Q6

A 45-year-old man comes to the physician because of intermittent bloody diarrhea and abdominal pain during the past month. Sigmoidoscopy and rectal biopsy specimens show inflammatory bowel disease. A trial of a monoclonal antibody preparation is begun. The antibody in the preparation is most likely to be directed against which of the following components?

- A. Bradykinin
- B. C3a
- C. Class I MHC antigens
- D. Fibrin
- E. Prostaglandin E₂

F. Tumor necrosis factor

▼ Explanation

- **Answer is F (Tumor necrosis factor)**
 - **IMP Clues**
 - Intermittent bloody diarrhea and abdominal pain + Sigmoidoscopy and rectal biopsy show inflammatory bowel disease (yep, IBD and sounds like UC specifically)
 - Trial of monoclonal antibody preparation is begun (The monoclonal antibody drugs used in IBD are the TNF-alpha monoclonal antibodies)
 - **TNF-alpha Blockers**
 - **Adalimumab - Infliximab - Certolizumab Pegol - Golimumab - Etanercept**
 - Note how all of the above drugs end in “-mab” as they are all monoclonal antibodies **EXCEPT Etanercept**
 - This is because **etanercept** is the odd one out → **TNF-alpha recombinant receptor**
 - Etanercept can bind to and mop up soluble TNF-alpha floating around in the plasma.
 - Commonly used for **IBD & Rheumatoid arthritis** if they are non-responsive to NSAIDs & Steroids.
 - TNF-alpha is a **proinflammatory cytokine** produced by **macrophages** and is HY as fuck.
 - HY Functions assessed on the USMLE are:
 1. **Septic Shock** (TNF-alpha activates **NO Synthase** → **increases NO** → **vasodilation & hypotension**)
 2. **Cachexia** (TNF-alpha is the **cachexic factor** that causes weight loss in patients with malignancies)
 3. **Maintains Granulomas** (**INF-gamma FORMS granulomas**, however, **TNF-alpha is known to maintain granulomas**)

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

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

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

▼ Answer
TNF-alpha - Infliximab is TNF-alpha monoclonal antibody

- TNF-alpha maintains granulomas.
- Infliximab inhibits TNF-alpha → reactivation of TB

Q7

A 78-year-old man dies of chronic congestive heart failure. Examination at autopsy shows chronic passive congestion of the lungs, hypoxic changes in the brain, and hydropic change of the renal tubular epithelial cells. Which of the following is the most likely cause of the hydropic change?

- A. Ca^{2+} release from mitochondrial stores
- B. Failure of the Na^{+} - K^{+} pump
- C. Increased intracellular H^{+} concentration
- D. Interference with protein synthesis
- E. Loss of plasma membrane integrity

▼ Explanation

- **Answer is B (Failure of the Na^{+} - K^{+} pump)**
 - Na/K ATPases are one of the most energy (ATP) demanding channels in our bodies, this makes them very liable to hypoxia.
 - **Hypoxia = decreased Oxygen = decrease aerobic respiration = decreased Oxidative phosphorylation = decreased ATP production**
 - **Na/K ATPases use ATP** because they move molecules **against** their **concentration gradient**
 - Normally, Na is more outside the cell so naturally Na moves passively to the inside, while K is more on the inside so moves passively to the outside.
 - **So, normally Na in & K out**
 - **Na/K ATPases though moves them in the opposite direction, against the concentration gradient ⇒ Na out & K in**
 - **If hypoxia occurs, Na/K ATPases dysfunction occurs → Can't do their job → Na move in & K moves out.**
 - This causes **Water to follow Na in ⇒ Cellular Swelling** (can be referred to as “hydropic changes”)

? Patient has an episode of AFib. Which part of the kidney would most likely be affected the most?

▼ Answer
Proximal Tubules - as they carry the highest concentration of Na/K ATPases ⇒ **Acute Tubular Necrosis**

- USMLE can refer to it as “PCT” or “tubules”
- If you want to be super accurate, it is the **proximal straight tubules** that are affected the most

Q8

A 37-year-old man who is HIV positive comes to the physician because of a 3-week history of severe pain in his legs and pain, numbness, and tingling in his feet. He is receiving antiretroviral therapy. On physical examination, the soles of the feet are tender to palpation. Sensation to pinprick is decreased over his calves and feet. Which of the following drugs is most appropriate for long-term relief of his pain?

- A. Acetaminophen
- B. Hydrocodone
- C. Methadone
- D. Naproxen
- E. Nortriptyline

▼ Explanation

• Answer is E (Nortriptyline)

◦ IMP Clues

- Severe pain in his legs and pain, numbness, and tingling in his feet + soles of the feet are tender to palpation. Sensation to pinprick is decreased over his calves and feet (Neuropathy)
- He is receiving antiretroviral therapy (some NRTIs classically cause peripheral neuropathy)

• Dx → NRTIs-induced Peripheral Neuropathy

- Didanosine, Stavudine, and Zalcitabine are the NRTIs known for causing peripheral neuropathy
- On the USMLE neuropathy treatments are:
 - TCAs (Amitriptyline & Nortriptyline)
 - MOA → Blocks reuptake of serotonin & norepinephrine
 - Gabapentin
 - MOA → Blocks calcium channels



What is unique regarding Nortriptyline?

▼ Answer

Classically given to the **elderly** due to **weak anti-cholinergic side effects** in comparison to normal TCAs



What are the TCA HY side effects?

▼ Answer

1. CCC → **Coma Convulsions, Cardiopathy (QT prolongation)**
2. TCAs (with H1 blockers & D2 antagonists) all cause the following **triad**:
 - a. **Anti-alpha 1**
 - b. **Anti-cholinergic**
 - c. **anti-H1**



What is the HY side effect of Didanosine?

▼ Answer

Pancreatitis

Q9

A 62-year-old man comes to the physician for a follow-up examination. Two weeks ago, he was discharged from the hospital after sustaining an acute myocardial infarction. He smokes 2 packs of cigarettes and drinks four 12-oz beers daily. His diet mostly consists of cured meats and fast food. He does not exercise. The patient tells the physician, "I know that I need to make some changes in how I live so that my heart can be healthier. I just don't have the willpower to quit smoking and drinking and all that stuff right now." Which of the following best describes this patient's stage of behavioral change?

- A. Precontemplation
- B. Contemplation
- C. Preparation
- D. Action
- E. Maintenance

▼ Explanation

• Answer is B (Contemplation)

- Patient **KNOWS** that smoking is **NOT** healthy and admits to it by saying, "*I know that I need to make some changes in how I live so that my heart can be healthier. I just don't have the willpower to quit smoking and drinking and all that stuff right now.*"
 - He **KNOWS** that smoking is wrong, but he is hesitant about taking the decision to quit. This is Contemplation.

▼ Other Choices

- **Choice A → Precontemplation** is when the patient sees **that there is nothing wrong with smoking** and **he doesn't want to stop**.
- **Choice C → Preparation** is when a patient starts reading about pros and cons & maybe goes to therapy to learn about quitting **(BUT HE HASN'T QUIT YET)**
- **Choice D → Action** is when the patient takes **ACTION** & actually **STOPS smoking**
- **Choice E → Maintenance** is when the patient maintains cessation of smoking,

Q10

A 12-year-old boy is brought to the physician for further evaluation because of three episodes of meningococcal bacteremia during the past 4 years. He has had no other significant infections. Physical examination shows no abnormalities. The most likely cause of these recurrent meningococcal infections is a deficiency of which of the following?

- A. CD4+ T lymphocytes
- B. IgA
- C. Neutrophils
- D. Protein tyrosine kinase
- E. Terminal components of complement

▼ **Explanation**

- **Answer is E (Terminal components of complement)**
 - **IMP Clues**
 - Three episodes of meningococcal bacteremia (Isolated recurrent N.meningitides infection)
 - No other significant infections (This sentence here excludes all the other choices)
- **Dx → C5-C9 Complements Deficiency**
 - In normal circumstances, N.meningitides is most effectively killed by MAC.
 - **C5-C9 Complements activation → Formation of MAC (Membrane Attack Complex) → Forms pores in bacteria membranes → Lysis & Death.**
 - N.meningitides is **most susceptible to MAC**
 - If **Terminal components of complement system (C5-C9)** are **deficient**
 - ⇒ Patients are susceptible to **recurrent Neisseria infections**.

? Who else is susceptible to meningococcemia?

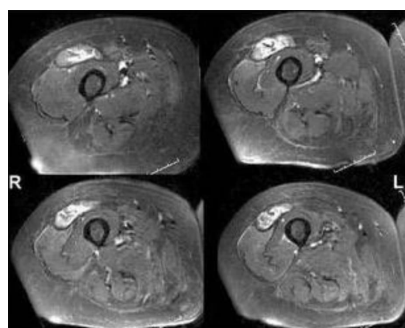
▼ **Answer**

Patients with no spleen.

- **OPSI** (patients who get their spleen removed are at risk of developing sepsis caused by **capsulated organisms**, **most commonly Streptococcus pneumoniae**. Other HY capsulated organisms are *N.meningitides*, *H.influenza*, and *E.coli*)
- **Autosplenectomy** (recurrent infarctions caused by sickled RBCs in Sickle Cel Anemia patients)

Q11

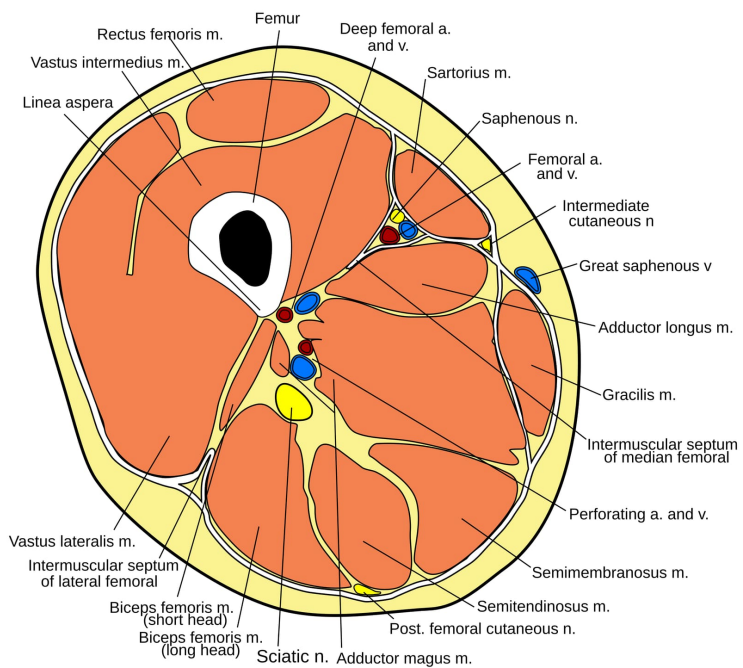
A 33-year-old man comes to the physician because of a 3-week history of pain in his right thigh, especially when walking. There is no history of trauma. Physical examination shows mild swelling but no erythema. The MRI shown depicts a tumor (white on T2-weighted signal) in an anterolateral muscle of the thigh. Which of the following muscles is infiltrated with this tumor?



- A. Adductor brevis
- B. Biceps femoris
- C. Gracilis
- D. Rectus femoris
- E. Vastus intermedius

▼ **Explanation**

- **Answer is D (Rectus femoris)**
 - Q says “Anterolateral muscle of the thigh” + MRI shows a mass on the far anterior muscle.
 - So, let’s exclude:
 - **Choice A** → **Adductor Brevis: *medial*** aspect of thigh “Inner Thigh”
 - **Choice B** → **Biceps Femoris: *posterior*** aspect of thigh “Hamstrings”
 - **Choice C** → **Gracilis: *medial*** aspect of the thigh “Inner Thigh”
 - **Choice D** → **Rectus Femoris: most anterior aspect of the thigh “the answer”**
 - **Choice E** → **Vastus Intermedius: *deep anterior*** aspect of the thigh



Q12

An investigator is conducting a randomized, double-blind, placebo-controlled clinical trial of a new medication for the treatment of mild insomnia in adults. A total of 2000 participants are enrolled in the study and randomized to one of two groups: 1000 participants receive the new medication (Group 1), and 1000 participants receive a placebo that appears identical to the medication (Group 2). Participants in both groups are instructed to take one pill 30 minutes before bedtime each day and to keep a sleep diary. After 1 month, each participant is interviewed, and the daily sleep diaries are reviewed. At follow-up, it is determined that 200 participants in Group 1 and 50 participants in Group 2 did not take the pill as directed. In accordance with intention-to-treat analysis, how should the data pertaining to all individuals who did not adhere to the instructions be treated?

- A. Analyze all nonadherent participants according to the group of the study to which each was randomized
- B. Exclude all nonadherent participants from analysis
- C. Exclude only nonadherent participants in Group 1 from analysis
- D. Exclude only nonadherent participants in Group 2 from analysis
- E. Perform separate analyses of the 250 nonadherent participants and the 1750 adherent participants

▼ Explanation

- **Answer is A (Analyze all nonadherent participants according to the group of the study to which each was randomized)**
 - You see all of this on your STEP Exam, and you start freaking out, reading all the details. Chill.
 - Last sentence says “*with intention-to-treat analysis,*” so without reading anything else the answer is **Choice A**
 - **Intention-to-Treat Analysis is simply a way of sorting the nonadherent participants to their original groups that they were randomized in.**
 - Q says 1000 participants receive the new medication (Group 1), and 1000 participants receive a placebo.
 - We intended to have 1000 participants in each group, so in a intention-to-treat analysis → **We count the participants in the original distribution we intended.**

Q13

An investigator is studying patients with West Nile virus infection. During a 5-year period, data are collected on 25 patients diagnosed with this condition as confirmed by testing at the Centers for Disease Control and Prevention. Demographic information on the patients is reported (age, gender, and ethnicity), as well as information about likely sources of infection. Which of the following best describes this study design?

- A. Case series
- B. Case-control study
- C. Cohort study
- D. Correlational study
- E. Cross-sectional study

▼ Explanation

- **Answer is A (Case-series)**

- Studying Patients with West Nile virus infection in 25 patients for a 5-year period + reporting demographic information (age, gender, race) and the likely source of infection.
 - This is classic **Case-Series Study**
 - Basically, we find **patients (more than one)** with a specific disease and observe them for a period of time & try to answer Qs about epidemiology, symptoms, signs, source of infection, or even mechanism of disease.
- If we did the same to 1 patient ONLY ⇒ **Case-Report Study**.

▼ Other Choices

- **Choice B → Case-Control** studies are where we compared 2 groups, one with the disease (case) and another group without the disease (control) and try and find the risk factors that lead to this disease.
 - In case-control studies, we measure the **Odds Ratio**
- **Choice C → Cohort studies** are when we compared to groups based on presence/absence of a risk factor, then seeing if the risk factor leads to the disease.
 - In cohort studies, we measure the **Relative Risk**
- **Choice D → Correlation studies** determine whether 2+ variables are correlated or not.
- **Choice E → Cross-sectional** studies take a “snapshot” of the current population, there is no following up or looking back into records.
 - In cross-sectional studies, we measure the **incidence & prevalence**.

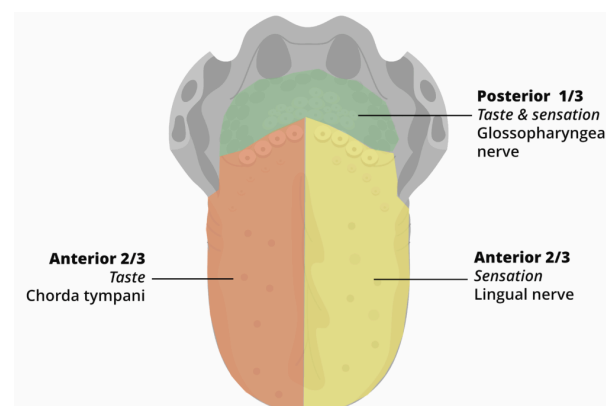
Q14

A 20-year-old man comes to the physician stating that food has lost its flavor ever since he fell down a flight of stairs and hit his head 1 week ago. He says that he feels fine otherwise. Physical examination shows no abnormalities. Neurologic examination is most likely to show damage to which of the following cranial nerves?

- A. Olfactory
- B. Trigeminal
- C. Facial
- D. Glossopharyngeal
- E. Vagus

▼ Explanation

- **Answer is C (Facial)**
 - Let's discuss the tongue's sensory supply
 - **Anterior 2/3 of tongue:**
 - **Taste** → **Chorda Tympani of Facial nerve**
 - **Sensation** → **Lingual nerve of Trigeminal nerve**
 - **Posterior 1/3 of tongue:**
 - **BOTH taste & sensation** → **Glossopharyngeal nerve**



- Q says "food has lost its flavor ever since he fell down a flight of stairs and hit his head" which suggests **a fracture that caused nerve damage**.
 - **Petrous Temporal Bone Fracture** → **damages Chorda Tympani, causing loss of taste & flavor**.

▼ Other Choices

- **Choice A** → Cribriform plate fracture can cause disruption of olfactory nerve. This causes affection of smell sensation, which can affect flavor of food, however, Q says "Physical examination shows no abnormalities," which excludes anosmia.
- **Choice B** → Loss of sensation **NOT** taste of anterior 2/3 of tongue. Additionally, affection of Trigeminal nerve would cause loss of face sensations.
- **Choice D** → Yes, glossopharyngeal nerve would cause loss of sensation & taste of posterior 1/3 of tongue, however, glossopharyngeal nerve injury are relatively uncommon.
- **Choice E** → **Vagus nerve** gives taste sensation to the epiglottis & the Palatoglossal muscle. Irrelevant here.

Q15

A 56-year-old man with a 20-year history of chronic back pain undergoes operative placement of an electrode in his midbrain for pain management. Previous physical and neurologic examinations showed no abnormalities. When the implant is activated, the patient reports a marked decrease in pain. Administration of which of the following substances would most likely result in the return of this patient's pain?

- A. β -Endorphin
- B. Enkephalin
- C. Morphine
- D. Naloxone
- E. Oxycodone

▼ Explanation

- Answer is D (Naloxone)
 - Garbage USMLE Q. Patient has a device that when stimulates the midbrain causes decrease of pain.
 - Midbrain stimulation *activates* pathways that secrete endogenous opioids (*β -Endorphins and Enkephalins*) → acts on opioid *receptors* → inhibits pain signaling to the CNS and by that decrease pain sensation.
 - What would result in the return of the pain sensation?
 - Blocking the opioid receptors
 - → this causes **NO pain inhibition signaling** → sensations are perceived by the CNS & sensed as "pain"
 - What block opioid receptors?
 - Naloxone (Choice D)

Q16

A 30-year-old woman develops serum sickness following parenteral administration of penicillin. A plasma sample is found to contain a mediator that stimulates histamine release from mast cells. Which of the following mediators was most likely found in this patient's plasma?

- A. C1
- B. C3a
- C. C4
- D. C5b
- E. C5-C9

▼ Explanation

- Answer is B (C3a)
 - Q says that "a plasma sample is found to contain a mediator that stimulates histamine release from mast cells"
 - This Q assesses a simple concept:
 - *Anaphylatoxins (C3a, C4a, C5a)* are complements that trigger degranulation of mast cells.
 - The way I remember them is "*-a*" at the end is for "*anaphylatoxins*"

? Serum Sickness is what type of hypersensitivity reaction?
▼ Answer
Type 3 Hypersensitivity Reaction

▼ Other Choices

- Choice A → C1q *deficiency* is associated with SLE [asked on NBMEs]
- Choice C → C4 is *decreased* in Cryoglobulinemia & is *normal* in SLE & PSGN
- Choices D & E → Terminal Complements (C5b-C9) *deficiency* causes inability to form MAC, causing *recurrent Neisseria infection*

Q17

A previously healthy 55-year-old man has recently been diagnosed with hypertension. He has not received any therapy. Laboratory studies show mild hypokalemia, metabolic alkalosis, and increased plasma renin activity (PRA) and aldosterone concentration. Following administration of an angiotensin-converting enzyme inhibitor, PRA increases further. Which of the following is the most likely cause of the hypertension in this patient?

- A. 11 β -Hydroxylase deficiency

- B. Cushing syndrome
- C. Essential hypertension
- D. Primary aldosteronism
- E. Renal artery stenosis

▼ Explanation

- Answer is E (Renal artery stenosis)
 - IMP Clues
 - Previously healthy 55-year-old man has been recently diagnosed with HTN (new-onset HTN is a red flag, so look for causes of secondary HTN)
 - Mild Hypokalemia, metabolic alkalosis, increased plasma renin and aldosterone (this is 2ry hyperaldosteronism, caused by increased renin → increased aldosterone → increase K & H secretion + Na reabsorption)
 - Following administration of ACE inhibitor, PRA increases further (ACEi causes decreased in decreased GFR, causing worsening of renal function. This is an expected complication of RAS, Renal atherosclerosis, and FMD)
- Dx → Renal Artery Stenosis
 - Basically, this patient has **RAS** (most probable cause for a man at that age is **atherosclerosis**), which causes **decreased** flow to the kidney.
 - **Decreased RPF is detected by the JGA in the cortex → increased renin production → increased aldosterone & AT-2 production**
 - Increased Aldosterone → **hypokalemia & metabolic alkalosis**
 - Increased AT-2 → **hypertension**
 - **The intake of ACEi/ARBs causes decreased constriction of the efferent renal arterioles → decreased GFR, causing renin levels to rise.**
 - This sentence is super HY. USMLE will give yap nonsense to you, then mention that **creatinine/renin levels increased after giving ACEi/ARBs**, and the **answer will be RAS or FMD**

?

55M + new onset severe HTN + bruit is heard lateral to umbilicus. What is expected to be seen is Captopril Renal Radionuclide Scan is used?

▼ Answer

Decreased Perfusion

- **Captopril renal radionuclide scan** essentially assesses the renal perfusion before vs after captopril.
 - We know that if the patient has RAS & an ACEi is given, we get **worsening of renal function / decreased perfusion**. This is essentially what we have here.

?

Where would the highest level of renin in the patient’s kidney be found?

▼ Answer

Cortex - renin is produced by the JGA, which is found in the cortex

▼ Other Choices

- Choice A → **11β-Hydroxylase deficiency** would present as symptoms of **increased aldosterone** (hypokalemia & metabolic alkalosis) as well as **increased androgens** (ambiguous genitalia) since birth, as it is a metabolic disorder.
- Choice B → **HY Cushing’s Syndrome features** that are nearly found in all Qs are **osteoporosis, purple striae, and central obesity**. None of them here.
- Choice C → **New-onset HTN with increased renin is secondary HTN**, not primary/essential/idiopathic HTN.
- Choice D → **Primary Aldosteronism** would cause **decreased renin levels** as increased aldosterone causes increased Na & water reabsorption → increase renal perfusion → decreased renin.

Q18

A 32-year-old man comes to the physician because of a 3-month history of swelling and tenderness of both breasts. He has been receiving thyroid hormone and corticosteroid replacement therapy since undergoing surgical removal of a pituitary adenoma 2 years ago. He began human chorionic gonadotropin (hCG) injections 4 months ago. Which of the following is the most likely binding site and action of hCG that is causing the development of gynecomastia in this patient?

Choices	Tissue	Effect
A	Adrenal gland	17-hydroxyprogesterone synthesis
B	Breast	direct stimulation
C	Liver	testosterone metabolism
D	Pituitary gland	prolactin secretion
E	Testicle	estradiol production

▼ Explanation

- Answer is E
 - IMP Clues
 - Man with 3-month hx of swelling & tenderness of both breasts + began hCG injections 4 months ago (Patient got gynecomastia & there is hx of hCG injection, which causes gynecomastia)

- Q asks what is the binding site & action of hCG that causes gynecomastia?
 - b-hCG, FSH, LH, and TSH share the same alpha subunit, **however LH and hCG are the most similar.**

“This is why in females undergoing ovulation induction, a hCG injection is given to simulate an LH surge to induce ovulation.”

 - **b-hCG binds to LH receptors on Leydig cells in the *testicles* → this causes Leydig cells of the testicles to increase testosterone production → *increase testosterone is then aromatized via aromatase enzyme into Estradiol* → increased estradiol production stimulates growth of breast glandular tissue → gynecomastia**
 - This is why Choriocarcinoma (germ cell testicular tumor in males) is a cause of gynecomastia. Choriocarcinoma produces b-hCG.



What is the 2nd messenger for b-hCG signaling?

▼ Answer

cAMP

- FSH, LH, b-HCG, and TSH all use cAMP as a 2nd messenger for signaling.



HY Causes of Gynecomastia on the USMLE

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

Q19

A 55-year-old man with severe emphysema comes to the physician for evaluation of shortness of breath. Which of the following findings are most likely on examination of the lungs?

Choices	Percussion	Tactile Fremitus	Expiratory Phase
A	Hyperresonant	Decreased	Normal
B	Hyperresonant	Decreased	Prolonged
C	Hyperresonant	Increased	Normal
D	Hyperresonant	Increased	Prolonged
E	Resonant	Decreased	Normal
F	Resonant	Decreased	Prolonged
G	Resonant	Increased	Normal
H	Resonant	Increased	Prolonged

▼ Explanation

- Answer is B
 - Patient has severe emphysema, which is loss of the elastic fibers within the lungs, causing dilation of air spaces.
 - **More Air Trapping & Less Air Exiting (Obstructive Lung Disease)**
 - More air trapping ⇒ **Hyperresonance**
 - More air trapping ⇒ **decreased TVF** (vibrations are transmitted better in solids, here is their MORE AIR, so decreased vibrations transmission)
 - Less air exiting & more air trapping ⇒ **Prolonged Expiratory Phase**



What are the 2 HY causes of emphysema on the USMLE?

▼ Answer

1. **Smoking**
 - **Older** Age
 - **Centriacinar/Centrilobular** Emphysema
2. **Alpha-1-Antitrypsin Deficiency**
 - **Younger** Age
 - **Panacinar/Panlobular** Emphysema


Smoking is the biggest risk factor for COPD

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

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

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


Expected PFTs in this patient:

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

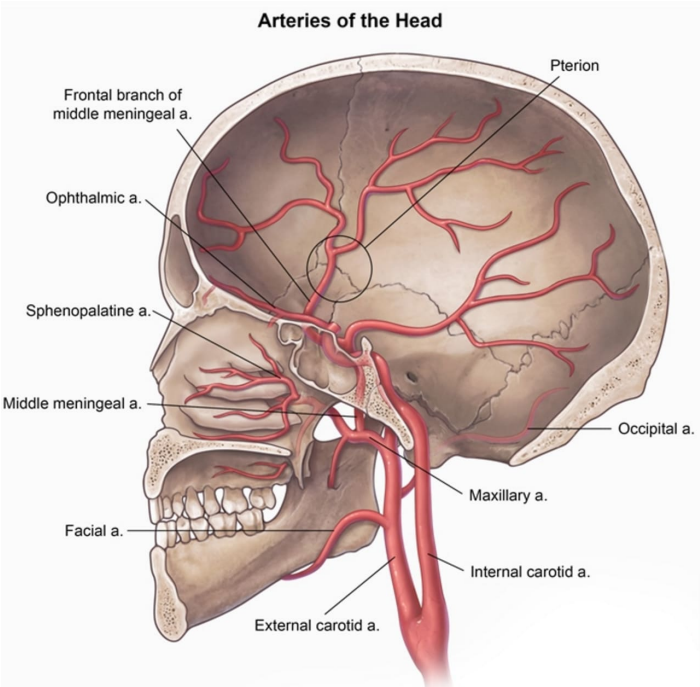
Q20

A 32-year-old woman is brought to the emergency department 20 minutes after she became confused and lost consciousness. Four hours ago, she fell 5 feet from a ladder and struck the right side of her head on the edge of her desk. She felt well enough to continue working. She is unresponsive to painful stimuli. Physical examination shows edema over the right anterior temple. The right pupil is dilated and poorly reactive. The left pupil is normal. Which of the following is the most likely diagnosis?

- A. Arterial laceration
- B. Cavernous sinus thrombosis
- C. Concussion
- D. Ruptured aneurysm
- E. Tearing of bridging veins

▼ Explanation

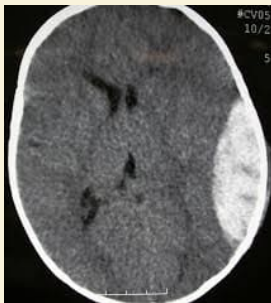
- Answer is A (Arterial laceration)**
 - IMP Clues**
 - Fell from a ladder and struck the right side of her head on the edge of her desk + Edema over the right anterior temple (This is the classical site for pterion injury, causing laceration of Middle Meningeal Artery)
 - She felt well enough to continue working + now she is unresponsive to painful stimuli + confused + lost consciousness (Lucid interval is very characteristic of Epidural hemorrhage)
 - Right pupil is dilated and poorly reactive (arterial blood accumulation causes increased ICP → uncal herniation → Oculomotor nerve compression causing dilated, poorly reactive pupil. EMERGENCY)
- Dx → Epidural Hemorrhage**
 - Trauma to side of the head (**at site of pterion**) is dangerous as **the pterion overlies the middle meningeal artery (MMA)**.
 - Laceration of this artery, causes accumulation of blood above the dura (Epidural Hemorrhage)**
 - Epidural hemorrhage is characterized by **lucid interval**, which is a period of time where the patient is fine/regains consciousness between the initial incident and being comatosed.
 - Initial accumulation of blood is not significant enough to cause symptoms, but as the patient continues “his work/day,” blood accumulates more and more causing compression of brain matter, with possible **uncal herniation** → **ipsilateral Oculomotor nerve palsy** (*dilated, poorly reactive pupil*) and **contralateral hemiparesis**.
 - Herniation could progress to **brainstem compression** → **loss of consciousness, posturing and death**.



? Which of the following is an epidural hematoma?
A)



B)



C)



D)



▼ Answer

B → Epidural Hematoma

Other Choices

- A → SAH (HY cause is *aneurysm rupture*)
- C → ICH (HY causes are *HTN & Amyloid Angiopathy in Alzheimer Disease*)
- D → Subdural Hemorrhage (due to *rupture of bridging veins*; HY causes are *Shaken Baby Syndrome, Alcoholism, falls in the elderly, and anti-coagulants use*)

Q21

A 5-year-old boy is brought to the physician for a follow-up examination 1 week after being diagnosed with a genetic defect that has affected his ability to reabsorb substances in the proximal tubule. Serum studies are most likely to show which of the following findings at this time?

- A. Hyperalbuminemia
- B. Hyperglycemia
- C. Hypermagnesemia
- D. Hypokalemia
- E. Hyponatremia
- F. Hypophosphatemia

▼ Explanation

- Answer is F (Hypophosphatemia)
 - IMP Clues
 - Genetic defect that has affected his ability to reabsorb substances in the proximal tubules (This is Fanconi Syndrome)

- Q asks for expected serum studies
- **Dx → Fanconi Syndrome**
 - **It is the inability of the PCT to reabsorb what it normally reabsorbs → *decreased* reabsorption of amino acids, glucose, phosphate, and bicarb.**
 - Caused by ingestion of **expired tetracyclines**
 - *USMLE might ask you for type of RTA caused by Fanconi Syndrome*
 - Decreased **Reabsorption of HCO₃** ⇒ **Type 2 Renal Tubular Acidosis**
 - RTA Type 2 Findings:
 - **Hypokalemia**
 - **Metabolic Acidosis**
 - **Urine pH starts alkaline (>5.5) but as HCO₃ gets depleted → acidic urine (<5.5)**

? Child with dehydration + decreased muscle tone + bowing of legs + crystals in corneas + serum studies shows hypophosphatemia, hypokalemia, and non-anion gap metabolic acidosis + urine pH is 5 + glucosuria + phosphaturia + aminoaciduria. What is Diagnosis?

▼ **Answer**

Cystinosis

- Cystinosis is an **AR** disease, characterized by a **defect in Cystinosis**, a lysosomal cystine transporter.
- Clinical Features = **Crystals in the cornea + Fanconi Syndrome**

“USMLE can ask for the diagnosis or ask for one of the above labs/urine findings.”

Q22

A 24-year-old man comes to the emergency department because of an 8-hour history of abdominal pain, nausea, and vomiting. He takes no medications. He has a family history of pancreatitis and hyperlipidemia. His temperature is 37°C (98.6°F), pulse is 110/min, and blood pressure is 125/88 mm Hg. Abdominal examination shows mild distention and diffuse tenderness with no rebound tenderness; bowel sounds are decreased. Serum studies show a glucose concentration of 90 mg/dL, triglyceride concentration of 3500 mg/dL, and lipase concentration of 400 U/L (N=14-280); the serum appears milky. The most likely cause of this patient's condition is a deficiency of which of the following?

- A. Apo B-100
- B. Apo E
- C. Hormone-sensitive lipase
- D. LDL receptor
- E. Lipoprotein lipase

▼ **Explanation**

- **Answer is E (Lipoprotein lipase)**
 - **IMP Clues**
 - Family hx of pancreatitis and hyperlipidemia (So he has family hx of either hyperchylomicronemia or hypertriglyceridemia)
 - Abdominal pain, nausea, and vomiting + mild distention + diffuse tenderness + bowel sounds are decreased + lipase concentration of 400 (This is pancreatitis, most likely due to high TAG)
 - Triglyceride concentration of 3500 mg/dL (high TAGs, the cause of pancreatitis) + serum appears milky (this is pathognomonic for hyperchylomicronemia)

- Dx → Hyperchylomicronemia (Type 1 Familial Dyslipidemia)
 - Deficiency of **LPL** or **ApoC-2**
 - Labs: **high** chylomicrons, **high** TAGs, and **high** cholesterol
 - **Turbid creamy plasma**, **pancreatitis**, and **xanthomas**
 - If TAGs >1000mg/dl, they cause pancreatitis (increased fats in pancreas → inflammation)



How does Insulin affect LPL?

▼ Answer

Insulin increases the activity of LPL

- Increased LPL activity causes clearing of lipids from blood stream into Adipose tissue. This promotes storage of fat (Anabolic effect)

If you want to be SUPER-SPECIFIC

Insulin **increases** activity if LPL in **FAT** cells

Insulin **decreases** activity of LPL in **Muscle** cells.

- This causes decreased utilization of fat & maximizes storage.
- This also favors glucose uptake by the muscles after feeding



Familial Dyslipidemias Rapid Review

📋 **"1LP, 2LD, B adds V, 3 is E, 4 gets More"**

1. **Type 1 (Hyperchylomicronemia)**

📋 **"1LP"**

- Deficiency: **LPL** or **Apo-C2**
- **high** Chylomicrons, **high** TAGs, **high** cholesterol
- **Turbid Creamy Plasma → Pancreatitis**

2. **Type 2 (Hypercholesterolemia)**

a. 📋 **"2LD" (Type 2A)**

- Deficiency: **LDL receptor** or **Apo-B100**
- **high** Cholesterol
- **Xanthelasma & Achilles Tendon Xanthomas**

b. 📋 **"B adds V" (Type 2B)**

- **high** Cholesterol + **VLDL**

3. **Type 3 (Dysbetalipoproteinemia)**

📋 **"3 is E"**

- Deficiency: **Apo-E**
- **Decreased** reuptake of remnants → **Increased** chylomicrons & **VLDL**
- **Palmer Xanthoma**

4. **Type 4 (Hypertriglyceridemia)**

📋 **"4 gets More"**

- **VLDL overproduction**
- **high** VLDL, **high** TAGs
- **Pancreatitis**

▼ Other Choices

- **Choices A & D → Hypercholesterolemia (Type 2 Familial Dyslipidemia)** discussed above.
- **Choice B → Dysbetalipoproteinemia (Type 3 Familial Dyslipidemia)** discussed above.
- **Choice C → HSL deficiency** would present inability of hormones to liberate TAGs from adipocytes
 - Hormones include **epinephrine**, **glucagon**, and **cortisol**

Q23

A 15-year-old girl is brought to the physician by her mother because of a 1-day history of a rash on her face, arms, and legs. She first noticed the rash 5 hours after she spent time at the beach on a sunny day. She has been receiving antibiotic therapy for acne. Physical examination shows diffuse erythema and mild edema over the face and extremities. Which of the following antibiotics is the most likely cause of these findings?

- A. Azithromycin
- B. Cephalexin
- C. Ciprofloxacin
- D. Doxycycline
- E. Linezolid

▼ Explanation

- **Answer is D (Doxycycline)**
 - **IMP Clues**
 - 1-day hx of rash on her face, arms, and legs 5 hours after she spent time at the beach on a sunny day (Exceedingly obvious that this is photosensitivity)

- She has been receiving antibiotic therapy for acne (Then one of these drugs is the cause)
- Q asks for which antibiotic caused these findings?
 - Sequence of acne ttt in most patients: **Topical Retinoids** → **Topical Benzoyl Peroxide** → **Topical Clindamycin** → **Oral Tetracycline** → **Oral Isotretinoin**
 - **Doxycycline (Choice D)** is a tetracycline
- Additionally, knowing that **tetracyclines are buzzy for “photosensitivity following antibiotic intake”** is HY.
 - MOA of tetracyclines → **Inhibits 30S ribosomal subunit**, which prevents aminoacyl-tRNA from binding to the A site (can be referred to as **“Inhibits protein synthesis”** on the USMLE)
 - HY Notes you must know:
 - **Binds to bone/teeth and causes deformities/discoloration** (this makes it **contraindicated in pregnant women and children below 8 years of age**) **[asked on NBME]**
 - **Chelates calcium** (this causes **impaired drug absorption if taken with milk**, as they form insoluble complexes) **[asked on NBME]**
 - **Photosensitivity**
 - **Demeclocycline** is a tetracycline that **causes nephrogenic DI**, hence can be **used in patients with SIADH**.

? What other acne ttt drug is contraindicated in pregnancy?

▼ Answer

ORAL Isotretinoin - This is why girls on oral isotretinoin must also be on contraception.

- Isotretinoin binds to **RXR Receptors** (Retinoid X Receptors), which is *nuclear receptor* that **regulates transcription factors of HOX gene, which plays a role in organization of the embryo in the craniocaudal direction**.
- Excessive isotretinoin intake → excessive RXR stimulation → abnormal signaling to HOX gene (and other regulators) → **abnormal embryogenesis (Teratogenic effect)**

▼ Other Choices

- **Choice A** → **Azithromycin** **inhibits 50S ribosomal subunit** - 23s RNA of peptidyl transferase cavity; does not block peptidyl transferase; blocks tunnel that channels nascent peptides away from peptidyl transferase center
- **Choice B** → **Cephalexin** is first-generation cephalosporin used to treat MSSA.
- **Choice C** → **Ciprofloxacin** is a fluoroquinolone that **inhibits DNA Gyrase (*prokaryotic* topoisomerase 2 & 4)**
 - HY side effect is **Cartilage Damage (Tendinopathy, usually Achillis)**
- **Choice E** → **Linezolid** **inhibits 50S ribosomal subunit**; 23S rRNA nucleotides; prevents formation of initiation complex
 - HY side effects are **High risk of serotonin syndrome, Optic neuritis, and Thrombocytopenia**

Q24

A 20-year-old man is brought to the physician by his mother because of bizarre behavior for 6 months. Although he had always been a good student, he failed all his classes at college last term. He no longer showers or shaves, and his appearance has become disheveled and unkempt. He appears distracted at the beginning of the interview and then begins talking nonstop to unseen people in the corner of the examining room. His mother looks upset and says, "It seems as if he's hearing voices all the time now. He's really scaring our family." Which of the following initial responses by the physician is most appropriate?

- A. "He must be schizophrenic. Does schizophrenia run in your husband's family or yours?"
- B. "He needs to take a shower. Have you tried sitting down with him and talking to him about taking better care of himself?"
- C. "How frightening for you to see your son like this. Do you have any idea about what might be causing his behavior?"
- D. "I am concerned he might be on drugs. Do you know anything about the friends he is hanging out with now?"
- E. "Was he under any unusual stress at home or at school or did he have any problems with a girlfriend when all of this started?"

▼ Explanation

- **Answer is C ("How frightening for you to see your son like this. Do you have any idea about what might be causing his behavior?")**
 - In any ethics Q, you must **start by acknowledging the patient's emotions or empathize with them**.
 - Then you need to **ask open ended Qs**, so that you can discover the patient's feelings, worries, and questions. The patient is who should lead the conversation, not you.

▼ Other Choices

- **Choice A** → No acknowledgment. No empathy. Just jumping to conclusions/diagnosis.

- **Choice B** → No acknowledgment. No empathy. Rude too.
- **Choice D** → No acknowledgment. No empathy. Just jumping to conclusions/diagnosis.
- **Choice E** → No acknowledgment. No empathy.

Q25

A 35-year-old man comes to the physician because of a 6-month history of burning abdominal pain that occurs 1 to 2 hours after he eats. He also has had black stools for 2 days. Use of over-the-counter antacids and histamine-2 (H₂)-receptor blocking agents has not been effective in relieving his symptoms. He is sweating profusely and has light-headedness when he stands. His blood pressure is 105/70 mm Hg while sitting. Physical examination shows epigastric tenderness. A CT scan of the abdomen shows a 1-cm mass in the pancreas. Immunohistochemical labeling of neoplastic cells in a biopsy specimen is most likely to involve the use of antibodies directed to which of the following substances?

- A. Amylase
- B. Gastrin
- C. Glucagon
- D. Human pancreatic polypeptide
- E. Insulin
- F. Lipase
- G. Serotonin
- H. Somatostatin
- I. Vasoactive intestinal polypeptide

▼ Explanation

• Answer is B (Gastrin)

◦ IMP Clues

- Burning abdominal pain after he eats (sounds like a Gastric Ulcer)
- Had black stools for 2 days (bleeding gastric ulcer → blood oxidized → Melena, aka black stool)
- Use of OTC antacids & H₂-blockers has not been effective (Red flag to investigate a deeper cause)
- He is sweating profusely and has light-headedness when he stands + His blood pressure is 105/70 mm Hg while sitting (Hypotensive from the bleeding +/- anemic)
- CT scan of the abdomen shows a 1-cm mass in the pancreas (Pancreatic mass + PU disease is ZES)

• Dx → Gastrinoma (Zollinger Ellison Syndrome)

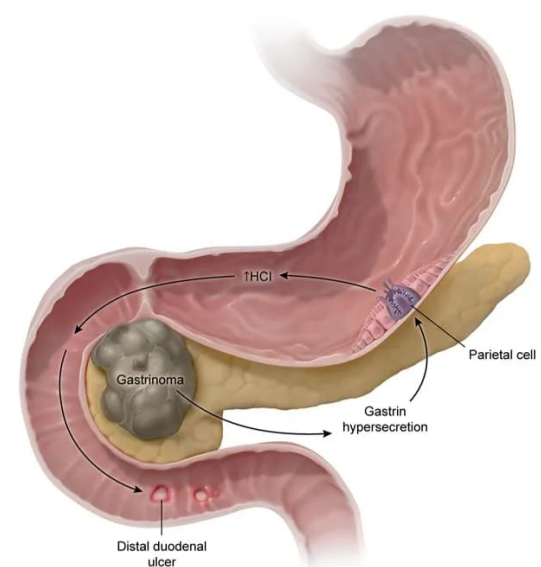
- **Neuroendocrine pancreatic tumor** that is characterized by **excess gastrin secretion**
- **Most likely site of Gastrinoma** → **HEAD of pancreas**

◦ Symptoms include:

- **recurrent duodenal & jejunal ulcers** *resistant to treatment*
- **abdominal pain**
- **diarrhea +/- bloody or melena**

◦ Diagnosis

- CT scan shows **pancreatic mass**
- **Gastrin levels** *remain elevated / increase* after **secretin administration**



? The presence of a gastrinoma is associated with a mutation in?

- A) Tumor Suppressor Gene
- B) Proto-Oncogene
- C) Transcription Factor
- D) RNA Polymerase
- E) DNA Polymerase

▼ Answer

Tumor Suppressor Gene

- **MEN 1** presents as a triad of **Pancreatic tumor, Pituitary Adenoma, and Parathyroid adenoma.**
- Caused by mutation of **Menin**, a tumor suppressor gene on chromosome 11

Q26

A previously healthy 16-year-old girl is brought to the physician by her 18-year-old sister because of a 2-day history of a thick, yellow vaginal discharge and burning with urination. She does not want her parents to know that she is sexually active. Her temperature is 37°C (98.6°F), pulse is 80/min, and blood pressure is 110/70 mm Hg. Examination shows a mucopurulent discharge at the cervical os and friability of the cervix. The uterus is small, firm, and nontender. There are no adnexal masses or external vaginal lesions. A Gram stain of the discharge shows gram-negative diplococci in pairs and greater than 30 leukocytes/hpf. Urinalysis is within normal limits. Testing for *Neisseria gonorrhoeae* and *Chlamydia trachomatis* is ordered. Which of the following is the most appropriate course of action?

- A. Do not prescribe antibiotics until testing results are available
- B. Obtain written consent from a parent before prescribing antibiotics
- C. Obtain written consent from her sister before prescribing antibiotics
- D. Prescribe antibiotics and notify her parents
- E. Prescribe antibiotics without notifying her parents

▼ Explanation

- **Answer is E (Prescribe antibiotics without notifying her parents)**
 - Teenagers have the right to be treated from STDs without the consent of the parents.
 - **3 Things on the USMLE DON'T require parental consent ⇒ Sex, Drugs, Emergencies**
 - Just make sure to *encourage healthy minor-guardian relationship & communication.*

Q27

A 45-year-old woman who is intubated and mechanically ventilated develops fungemia with *Candida albicans* during a prolonged hospital stay. Treatment with caspofungin is started. Which of the following features of the causal organism will most likely be targeted by this drug?

- A. Fungal RNA polymerase
- B. β -Glucan carbohydrates in the cell wall
- C. Lanosterol in the cytoplasmic membrane
- D. N-glycosidases involved in capsule synthesis
- E. Porin proteins in the outer membrane

▼ Explanation

- **Answer is B (β -Glucan carbohydrates in the cell wall)**
 - Q asks what will be targeted by Caspofungin? Straightforward pharmacology Q.
 - **Caspofungin is an echinocandin antifungal which inhibits 1,3,B-D-glucan → inhibits fungal *cell wall* synthesis**
 - Used for **disseminated fungal infections** (like Amphotericin B)

▼ Other Choices

- **Choice A** → Nothing like that exists
- **Choice C** → Can refer to either **Azoles (they inhibit the formation of lanosterol)** OR Amphotericin B & Nystatin (they form bind to ergosterol & form pores)
- **Choice D** → Nothing like that exists.
- **Choice E** → Nothing like that exists for fungi.

Q28

A 27-year-old man comes to the physician because of weakness of his left hand for 3 weeks. He is a professional athlete and rides a bicycle for 8 to 10 hours daily. He has been unable to grasp the handlebar with his normal strength, making it difficult to train for a full day. He has no pain or numbness. Physical examination shows mild weakness with abduction and adduction of the fingers. He is unable to hold a piece of paper between the thumb and the side of the index finger (Froment sign). Sensation is intact. The most likely cause of these findings is compression of which of the following structures?

- A. Deep branch of the ulnar nerve at the hook of the hamate bone
- B. Long tendons coursing through the carpal tunnel
- C. Median nerve caused by dislocation of the lunate bone
- D. Recurrent branch of the median nerve in the palm
- E. Ulnar nerve as it courses through the flexor carpi ulnaris muscle

▼ Explanation

- **Answer is A (Deep branch of the ulnar nerve at the hook of the hamate bone)**

◦ IMP Clues

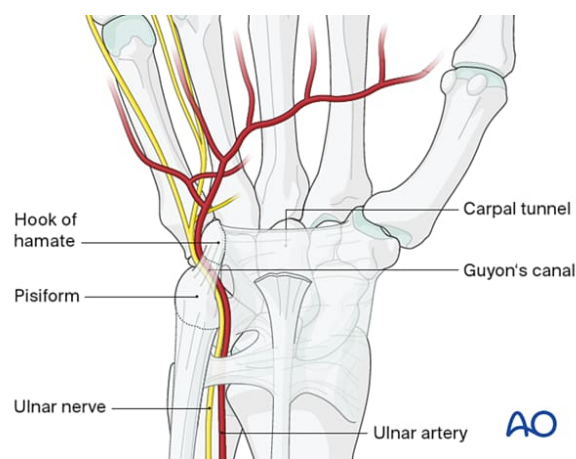
- Rides a bicycle for 8-10 hours daily (Remember what we said about nerve damage in bikers?)
- He has no pain or numbness (The sensory division is not affected)
- Mild weakness with abduction and adduction of the fingers (the interossei muscles) + he is unable to hold a piece of paper between the thumb and the side of the index finger (Froment sign) (weakness of thumb adduction)

◦ Dx → Ulnar Nerve (motor-branch) Injury

- Patient is a professional athlete and **rides the bicycle for 8-10 hours daily**.
 - The **ulnar aspect of the hands** usually rests on the handlebars of the bicycle, which on **prolonged pressure** → pushes on **hook of hamate bone** → **compresses the ulnar nerve in the Guyon's canal**
 - Hence this is sometimes names as **"Handlebar palsy"**

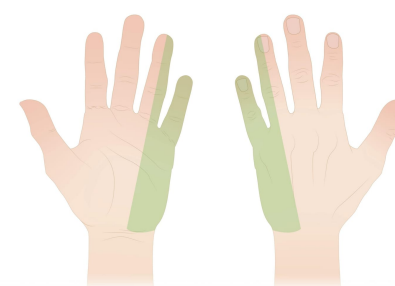
"The Q mentions that the patient's symptoms are pure motor symptoms. You don't need to know the individual branches of the ulnar nerve, just know that there are different motor/sensation deficits possible depending on the affected individual branches."

- "Mild weakness with abduction and adduction of the fingers" is due to **weakness of the interossei muscles** which are supplied by the **ulnar nerve**
- "Unable to hold a piece of paper between the thumb and the side of the index finger (Froment sign)" is due to **weakness of Adductor Pollicis muscle**, which is responsible for **thumb adduction**, supplied by the **ulnar nerve**.



• Ulnar Nerve

◦ Sensation:

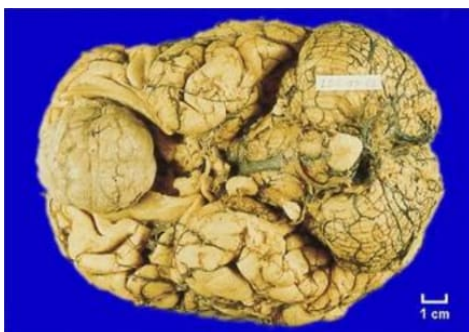


◦ Motor:

1. Flexion of ulnar fingers (medial half of FDP)
2. Abduction & Adduction of fingers (interossei muscles)
3. Thumb adduction (Adductor Pollicis)

Q29

A 65-year-old woman dies 6 months after the onset of severe headaches. Her brain as seen at autopsy is shown in the photograph. Which of the following is the most likely cell of origin of this neoplasm?



- A. Astrocyte
- B. Endothelial
- C. Melanocyte
- D. Meningeal
- E. Squamous epithelial

▼ Explanation

- **Answer is D (Meningeal)**

- Picture shows an **external mass** that appears to have the **same "covering"** of the brain.

- Dx → Meningioma

[📄] Mnemonic: “Men have problems with PSA”

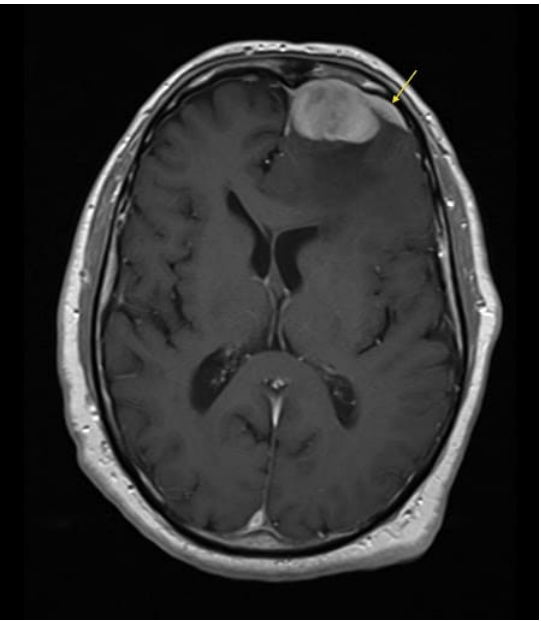
- Meningioma
- Psammoma Bodies (Seen on biopsy)
- Spindle Cells (Seen on biopsy)
- Arachnoid origin *[asked on NBME]*

- The rise from **meninges** so they are always near the surface
- Meningiomas **enhance** (appear white) on imaging & have these “**dural**” **tails** (yellow arrow).

? What conditions are associated with meningiomas?

▼ Answer

MEN1 - NF2- NF1



Q30

A study is conducted to identify healthy women at risk for cardiovascular disease. Because atherosclerosis is an inflammatory process, the concentration of plasma C-reactive protein (CRP), a marker of inflammation, is measured. The plasma CRP concentration is increased in women who subsequently develop coronary artery disease. Which of the following is the most likely site of C-reactive protein biosynthesis?

- A. Bone marrow
- B. Heart
- C. Liver
- D. Spleen
- E. Thymus gland

▼ Explanation

- Answer is C (Liver)
 - Q asks where the site of CRP synthesis is?
 - Answer is Liver. Simple.
 - Acute phase reactants are **produced by the liver** and are **regulated by cytokines (IL-6, IL-1, TNF-alpha)**

| “Knowing which is which is very important and is assessed on the USMLE & NBMEs.”

Positive APRs

1. **CRP** & ESR
2. **Fibrinogen & Ferritin**
3. **Hepcidin**

Negative APRs

1. Albumin
2. Prealbumin (Transthyretin)
3. **Transferrin**

Q31

A 58-year-old man is brought to the emergency department because he has had severe chest pain radiating to the back for the past 30 minutes. X-rays of the chest do not show widening of the aorta. Aortic angiography shows an extra lumen in the media of the proximal aorta. Which of the following is the most likely cause of this finding?

- A. Diabetes mellitus
- B. Fibromuscular hyperplasia
- C. Hypertension
- D. Hypertrophic cardiomyopathy
- E. Syphilis

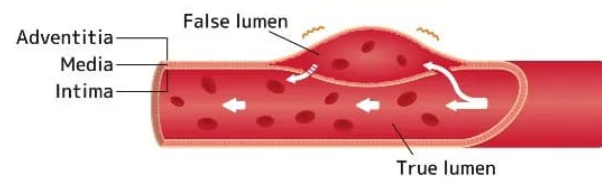
▼ Explanation

- Answer is C (Hypertension)
 - IMP Clues
 - Severe chest pain radiating to the back (Classic Aortic Dissection description)

- CXR do not show widening of the aorta (Nonspecific really, I have seen widening of the aorta in aneurysms, dissection, and rupture. However, my guess is that they include it to exclude dissecting aneurysms, which can be caused by choice E)
- Aortic angiography shows an extra lumen in the media of the proximal aorta (Diagnostic; a false lumen is seen)

◦ **Dx → Acute Aortic Dissection**

- **Aortic Dissection is tear in the intimal layer of the aortic wall, causing blood to flow between → splitting apart the tunica media and intima, creating a “false lumen.”**
- Most HY risk factor on the USMLE is → **Hypertension**.
 - Other HY risk factors include **cocaine & Connective Tissue Diseases (Marfan Syndrome & Ehlers-Danlos)**



▪ Presentations:

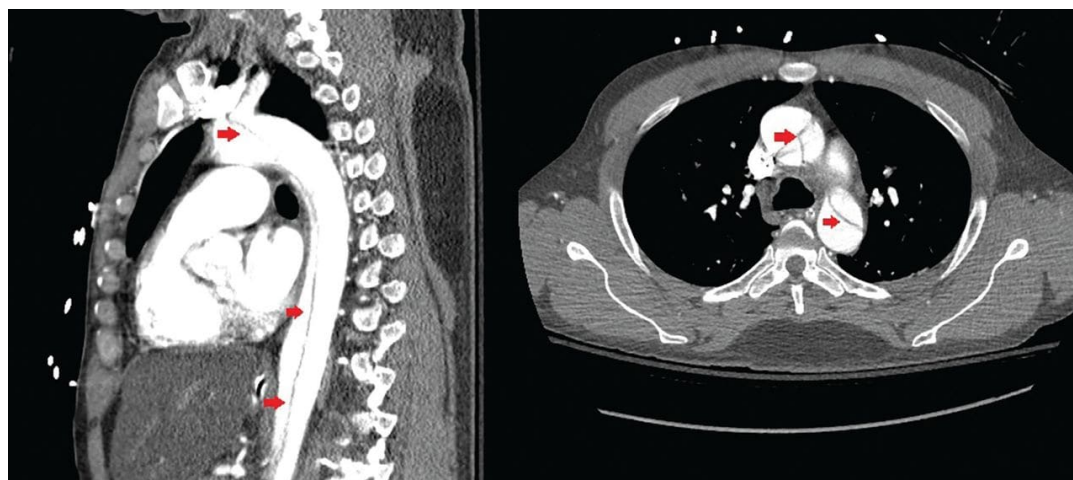
- **Unequal blood pressure between both arms + diminished pulse** (blood pressure is **LOWER in affected arm**)
 - This differentiation is made on a Q on the NBMEs, where *Q* has normal/high blood pressure in the right arm and low blood pressure in the left arm. The *Q* then asks **what does the dissection spare/affect?**
 - In this example here, the **spared artery is the brachiocephalic trunk** (which gives the right subclavian artery), so blood pressure is normal/high

? What drug is beneficial to patients having an aortic dissection?

▼ **Answer**

Beta Blockers

- **Aortic Regurgitation** (if dissection extends to **Aortic Root/Valve**)
- **Stroke** (if dissection extends to **Carotids**)
- **MI** (if dissection extends to **coronary arteries**)
- **Horner Syndrome** (if dissection extends to the **sympathetic chain**) **[unusual but seen on NBME]**



Q32

A 51-year-old man develops diaphoresis, tachycardia, and a blood pressure of 155/100 mm Hg 24 hours after undergoing an abdominal operation. Two hours later, he has a generalized tonic-clonic seizure. Which of the following is most likely responsible for these adverse effects in this patient?

- A. Acute renal failure
- B. Alcohol withdrawal
- C. Anaphylactic reaction
- D. Narcotic pain medication
- E. Sepsis from a gram-positive organism

▼ **Explanation**

- **Answer is B (Alcohol withdrawal)**
 - **IMP Clues**

- Diaphoresis, tachycardia, and blood pressure of 155/100 mmHg (Sympathetic overactivity)
- 24 hours after undergoing abdominal operation (This means that these symptoms developed 24 hours post-op. Patients are usually prepped a day or more before an operation, so his time in the hospital is probably much more)
- Generalized tonic-clonic seizures (Sympathetic overstimulation + Seizures in a patient who is hospitalized for some time is buzzy for withdrawal on the USMLE)

• **Dx → Alcohol Withdrawal**

- **12-48hrs (Alcoholic Hallucinosi**s): Tactile (bug crawling on skin) or Visuals (bugs crawling on walls) Hallucinations
- **48-96hrs (Delirium Tremens): HTN, Tachycardia**, Tremulousness, **seizures**, diaphoresis, and restlessness

“USMLE doesn’t really care about strict timing of these, and honestly the do overlap. So, just know that acute cessation of drinking (USMLE loves surgery/hospitalization as an example) + HTN & Tachycardia + seizures is Alcohol withdrawal.”

▼ **Other Choices**

You can get to the answer by exclusion if you’re confused.

- **Choice A → Acute Renal Failure** presents as Anuria/Oliguria + Increased BUN/Cr + hyperkalemia, hypocalcemia, hyperphosphatemia, and 2ry hyperparathyroidism.
- **Choice C → Anaphylaxis** presents minutes after exposure, and causes hypotension, bronchospasm, angioedema +/- urticaria. Due to mast cell degranulation.
- **Choice D → Narcotic side effects** are sedation, hypotension, bradycardia, bradypnea, and pinpoint pupils (miosis).
- **Choice E → Sepsis** presents as hypotension and fever (sometimes hypothermia).

Q33

A 55-year-old man comes to the physician because of a 2-month history of decreased appetite; he also has had a 9-kg (20-lb) weight loss and an intermittent rash during this period. Physical examination shows necrolytic migratory erythema over the axillae and groin. Laboratory studies show a serum glucose concentration of 280 mg/dL and plasma glucagon concentration of 1500 pg/mL (N=20-100). A CT scan of the abdomen shows a mass at the head of the pancreas. Which of the following processes is most likely occurring in this patient's liver?

- A. Decreased activity of carnitine acetyltransferase
- B. Glycogen synthesis
- C. Increased activity of acetyl-CoA carboxylase
- D. Inhibition of ketogenesis
- E. Partial oxidation of fatty acids

▼ **Explanation**

• **Answer is E (Partial Oxidation of fatty acids)**

◦ **IMP Clues**

- Decreased appetite + weight loss (buzzy for malignancy)
- Intermittent rash + necrolytic migratory erythema over the axillae and groin + serum glucose 280 + plasma glucagon is 1500 + CT scan shows a mass at head of pancreas (They handed you the diagnosis)

• **Dx → Glucagonoma**

- **Neuroendocrine pancreatic tumor**, originating from **alpha-cells islets**
- Presentation
 - **Necrolytic Migratory Erythema**
 - **Hyperglycemia**
 - **Hyperglucagonemia**
 - Glucagon is a *catabolic hormone* (opposite of insulin), so it promotes **protein catabolism**, **glycogenolysis**, **gluconeogenesis**, and **lipolysis** (referred to here as “**Oxidation of fatty acids**”)
- Diagnosis
 - **CT/MRI scan shows pancreatic mass**
 - **Glucagon serum concentration (>500pg/mL is diagnostic)**



What is the second messenger of glucagon?

▼ **Answer**

Increases cAMP



What drug toxicity does glucagon treat?

▼ **Answer**

Beta Blocker

- **BB decrease cAMP**
- **Glucagon is used as it increases cAMP**

▼ **Other Choices**

- **Choice A → Carnitine acetyltransferase** carries long chain FAs into the mitochondria for oxidation. Glucagon **INCREASES** oxidation, so its activity is **INCREASED** not decreased.

- **Choice B** → Glucagon is catabolic, so **glycogen synthesis is decrease & glycogen breakdown (glycogenolysis) is increased**.
- **Choice C** → **Acetyl-CoA carboxylase** is the rate-limiting enzyme of fatty acid **synthesis**. **Glucagon stimulates fatty acid oxidation**.
- **Choice D** → **Ketogenesis** occurs in the **fasting** state. Glucagon is a fasting-state hormone, so ketogenesis is **INCREASED**

Q34

A previously healthy 37-year-old woman comes to the physician because of a 6-month history of fatigue; she has had an 18-kg (40-lb) weight gain during this period. Her temperature is 37.6°C (99.7°F), pulse is 85/min, respirations are 12/min, and blood pressure is 190/95 mm Hg. Physical examination shows a round face and truncal obesity. There are purple striae over the abdomen and flank and ecchymoses over the forearms and lower extremities. Pelvic examination shows no abnormalities. Her plasma adrenocorticotrophic hormone (ACTH) concentration is less than 5 pg/mL (N<120). Her serum cortisol concentration does not become suppressed following administration of low and high doses of dexamethasone. Which of the following is the most likely cause of these findings?

- A. Ectopic ACTH production
- B. Pituitary basophilic adenoma
- C. Tumor of the adrenal zona fasciculata
- D. Tumor of the adrenal zona glomerulosa
- E. Tumor of the adrenal zona reticularis

▼ Explanation

- **Answer is C (Tumor of the adrenal zona fasciculata)**

◦ IMP Clues

- Fatigue + weight gain + BP is 190/95 mmHg + round face + truncal obesity + purple stria + ecchymoses (Features of Cushing's)
- Pelvic examination shows no abnormalities (Excludes ACTH-secreting ovarian tumors)
- ACTH is low (Primary Hypercortisolism, originating from the adrenal gland itself) + Dexamethasone suppression test no change (not needed, but okay. Further confirmation of the diagnosis)

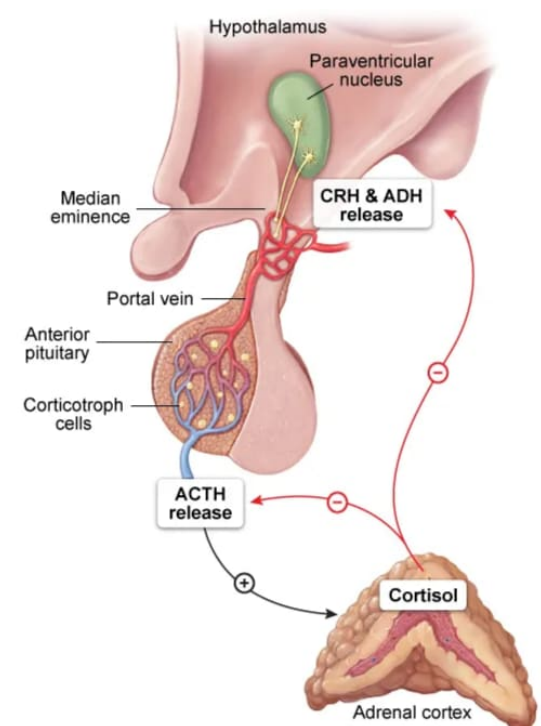
- **Dx → Adrenal Gland Adenoma**

- Tumor of the adrenal **Zona Fasciculata**, the layer that produces **glucocorticoids**.
- **Increased** production of glucocorticoids → **negative** feedback on **ACTH (pituitary) and CRH (hypothalamus)** ⇒ **Primary Hypercortisolism**
- CT scan of the abdomen would reveal an **enlarged adrenal (the secreting one)**, while the **other one would be atrophied**.
 - **Low ACTH** causes **atrophy of the non-secreting adrenal gland**.



Features of Cushing's Syndrome:

- **Central Obesity, Moon Facies, Buffalo Hump, and Thin Extremities** (Cortisol **increases lipolysis** and causes **fat redistribution** that favors trunk, face, and upper back with thin limbs)
- **Proximal Muscle Weakness** (due to **increased protein catabolism**, which is then used in **hepatic gluconeogenesis**)
- **Glucose Intolerance, Diabetes Miletus, and Weight Gain** (Caused by **increased hepatic gluconeogenesis, lipolysis, and hyperinsulinemia**)
- **Red/Purple Striae & Ecchymoses** (due to cortisol **inhibition of fibroblast proliferation & collagen synthesis**, causing **thinning of the dermis & capillary fragility**)
- **Hypertension** (due to **permissiveness**, causing potentiation of catecholamines effects on alpha-1 receptors **[asked on NBME]** & due to **mineralocorticoid receptor activity**, acting like aldosterone causing salt and water retention → increased blood volume)
- **Osteoporosis** (due to **inhibition of osteoblastic activity**, causing less bone mineralization and more bone resorption) **[asked on NBME]**
- **Increased Infection Risk** (due to **inhibition of PLA2 activity** decreasing LTs/PGs + **inhibition of neutrophils migration + inhibition of IL-2 production**, causing reduced T-cells activation and proliferation → Lymphopenia)



▼ Other Choices

- **Choice A** → **Ectopic ACTH production** would cause high ACTH, high cortisol. Most HY source is small cell lung cancer.
- **Choice B** → **Pituitary basophilic adenoma** would also cause high ACTH, and high Cortisol. However, dexamethasone suppression test (high dos) would decrease cortisol concentration.

- **Choice D** → **Tumor of the adrenal zona glomerulosa** would cause Conn's Disease, primary hyperaldosteronism.
- **Choice E** → **Tumor of the adrenal zona reticularis** would cause high androgen levels.

Q35

A 60-year-old man has a round, semitransparent nodule on his nose. Examination of tissue obtained on biopsy shows small basophilic cells forming tumor islands surrounded by clear spaces and extending across the basement membrane. Which of the following is the most likely diagnosis?

- A. Actinic keratosis
- B. Basal cell carcinoma
- C. Compound nevus
- D. Junctional nevus
- E. Melanoma
- F. Seborrheic keratosis

▼ Explanation

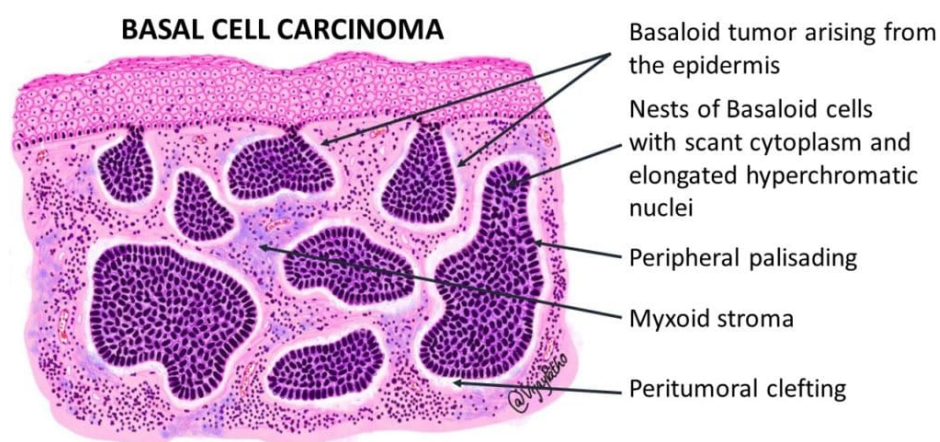
• Answer is B (Basal cell carcinoma)

◦ IMP Clues

- Round, semitransparent nodule on his nose (semitransparent is buzzy for BCC and nose for sun-exposed areas)
- Biopsy shows small basophilic cells forming tumor islands surrounded by clear spaces and extending across the basement membrane

• Dx → Basal Cell Carcinoma (BCC)

- Gross: **Pearly / slightly translucent** mass with **telangiectasia** (classically rolled edges)
- Origin: **Basal layer of EPIDERMIS (NOT DERMIS)** [asked on NBME]
- Biopsy: **Purple / dark blue cells with peripheral palisading and cleft formation** (Classic description you learn everywhere)
 - Let's rephrase this using the words the Q mentioned:
 - "Basophilic cells" = **purple/dark blue cells**
 - "Tumor Islands" = **Peripheral palisading**
 - "Surrounded by clear spaces" = **Cleft formation**
 - Extending across basement membrane = just means that it invaded the basement membrane, so malignant
- Sites: **Sun-exposed areas** (Nose, Ears, Face)
- Outcome: **Local growth with tissue destruction** (rarely metastasizes) [asked on NBME]



▼ Other Choices

• Choice A → Actinic Keratosis

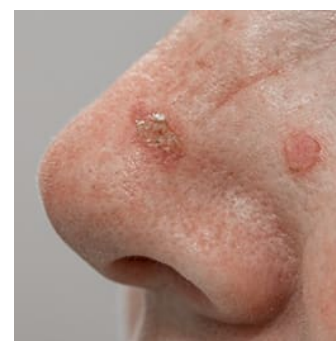
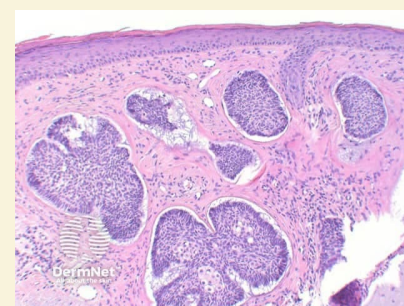
- also named on the USMLE as "Solar Keratosis"
- **Scaly / rough** lesions with a "sandpaper feel" on **sun exposed areas**, usually found on farmers / construction workers / fishermen

Basal Cell Carcinoma:

Gross BCC:



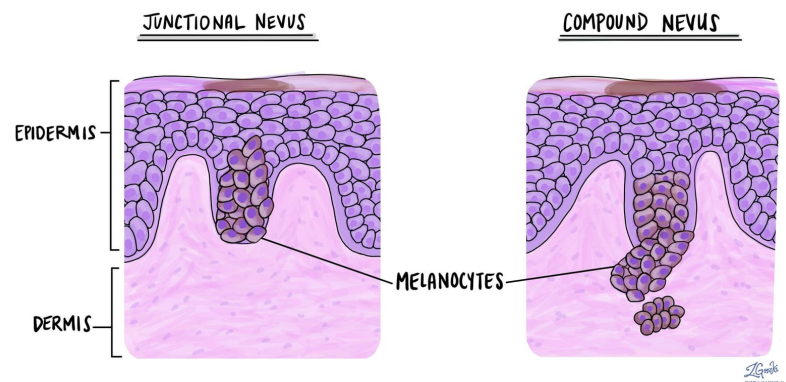
Microscopic BCC:



? What are people with Actinic Keratosis at risk of developing?

▼ Answer
SCC of skin.

- **Choice C → Compound Nevus** is a **benign proliferation of melanocytes** (no irregularity, asymmetry, or multiple colors) located in **both the epidermis & dermis** (hence the "compound" in name)
 - Growths **stop** at 40-50s. **If progression → check for melanoma.**
- **Choice D → Junctional Nevus** is a **benign proliferation of melanocytes** located at the **junction of the epidermis & dermis** (hence the junctional in name)
 - Usually **progresses** into compound nevus
- **Choice E → Melanoma**
 - Malignancy of **Melanocytes**, which are from **neural crest origin** (positive for **S-100, HBM-45, and vimentin**) *[asked on NBME]*
 - Biopsy shows **atypical melanocytes**, sometimes they say **"atypical pigmented cells."**
 - Associated with **BRAF V600E mutation** (BRAF is a **proto-oncogene**, which codes for **serine-threonine kinase**)
 - **Vemurafenib** is a BRAF serine-threonine kinase **inhibitor** used for **metastatic melanoma positive for BRAF**
 - Types: **Superficial, Nodular, Lentigo maligna, and Acral Lentiginous**



? African American with melanoma. What is the most likely type & site?

- ▼ Answer
- Acral Lentiginous Melanoma** - It is the most common type of melanoma in African Americans
- Most common sites → **Palms/soles/nail beds.**
 - Why? **Decreased Melanin in these areas.**

- **Choice F → Seborrheic Keratosis**
 - Old patient + **sun exposure**
 - **Greasy waxy skin growths** that appear as if they can be **"peeled off"** or **"about to fall"**
 - Associated with **Leser-Trelat sign**: sudden eruption of seborrheic keratosis 2ry to **visceral malignancy**



Q36

A 6-month-old girl is brought to the emergency department by her parents because of vomiting for 6 hours. She has been feeding poorly for 1 day because of an upper respiratory tract infection. Her temperature is 37°C (98.6°F), pulse is 100/min, respirations are 18/min, and blood pressure is 88/58 mm Hg. Physical examination shows lethargy and a clear nasal discharge. Laboratory studies show:

Serum	
Ammonia	increased
Citrulline	decreased
Glutamine	increased
Urine orotic acid	increased

This patient most likely has a deficiency of which of the following enzyme activities?

- A. Arginase
- B. Argininosuccinase
- C. Argininosuccinate synthetase
- D. Carbamoyl phosphate synthetase
- E. Ornithine transcarbamylase

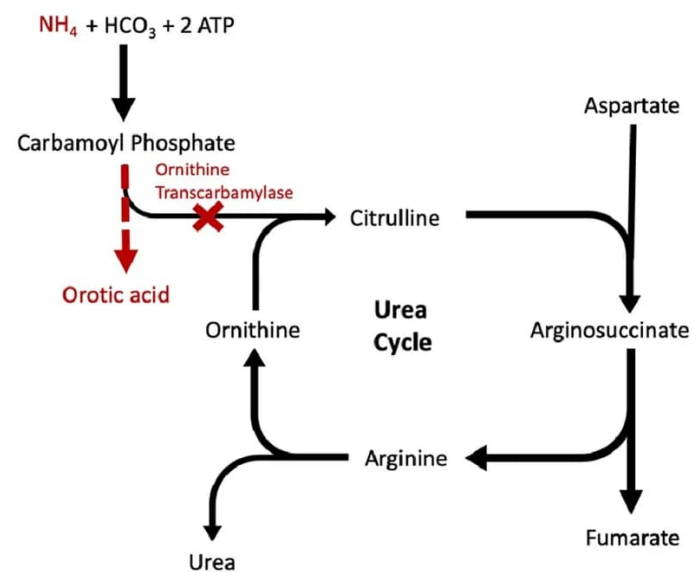
▼ Explanation

- **Answer is E (Ornithine transcarbamylase)**
 - **IMP Clues**
 - High ammonia & Orotic Acid

- Low Citrulline

◦ **Dx → Ornithine transcarbamylase (OTC) Deficiency**

- If you're clueless, I'd advise you to see Dirty Medicine's video about Urea Cycle
- Urea Cycle's aim → **conversion of ammonia to urea, which is the excreted by the kidney.**
 - The rate-limiting enzyme is **CPS I** (converts $\text{NH}_4 \rightarrow \text{Carbamoyl Phosphate}$)
- **OTC** is an enzyme that combines **Carbamoyl Phosphate + Ornithine → Citrulline.**
 - In the labs provided, we have **low citrulline**. So, previous enzyme is deficient (OTC)
 - This causes **accumulation of Ammonia and Carbamoyl Phosphate**
 - Carbamoyl Phosphate is then shunted to form **Orotic Acid**
 - **Hyperammonemia → neurotoxicity**
 - Body tries to convert **ammonia + glutamate → glutamine** (hence it is increased in given labs)
 - However, this causes **depletion of glutamate**, which is needed for **TCA (glutamate → α-KG)**
 - **dysfunction of TCA → less ATP → Neurotoxicity & Brain edema**
- **Result:**
 - **Lethargy, poor feeding, vomiting, coma, and death**



Q37

A physician is assigned to a search and rescue team attempting to locate and recover the victim of a light plane crash with only the pilot onboard. The plane crashed in a remote mountainous region of Alaska and has been missing for more than 2 weeks. A search helicopter detected what was believed to be a signal from the area of the downed plane and has picked up the pilot. The pilot has only minor injuries but has complications of exposure and has lost a considerable amount of weight. While the pilot was able to locate a good water supply, he had no food during his period of isolation. The pilot most likely has which of the following conditions at this time?

- A. Decreased nitrogen retention
- B. Increased nitrogen retention
- C. Negative nitrogen balance
- D. Normal nitrogen balance
- E. Positive nitrogen balance

▼ **Explanation**

- **Answer is C (Negative nitrogen balance)**
 - “The plane crashed in a remote mountainous region of Alaska and has been missing of more than 2 weeks + he has lost a considerable amount of weight + he had no food during this period”
 - Basically, he's been **starving for like 2 weeks** with no food, so **catabolism is more than anabolism in this patient.**
 - **Catabolism > Anabolism ⇒ Negative Nitrogen Balance**
 - **Anabolism > Catabolism ⇒ Positive Nitrogen Balance**

Q38

A 62-year-old woman comes to the physician because of a 3-year history of a mild cough that has produced purulent sputum for the past 2 weeks. She has smoked 2 packs of cigarettes daily for the past 42 years. She drinks 3 to 6 beers daily. Findings on physical examination show swelling of the metatarsals, metacarpals, and proximal phalanges. X-rays of the affected bones show new bone formation. There is also arthritis of adjacent joints and clubbing of the digits. Which of the following is the most likely underlying disease?

- A. Ankylosing spondylitis
- B. Bronchogenic carcinoma
- C. Congenital cyanotic cardiac disease
- D. Hepatic cirrhosis
- E. Interstitial pulmonary fibrosis
- F. Rheumatoid arthritis
- G. Systemic sclerosis (scleroderma)

▼ Explanation

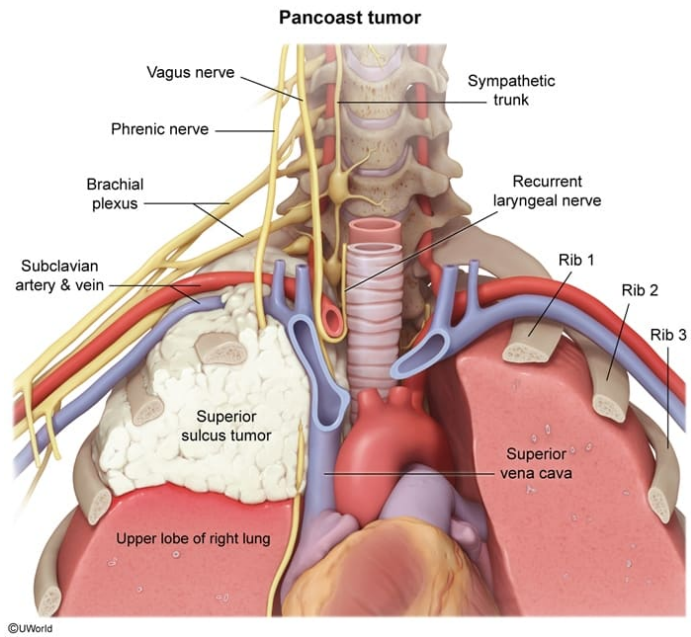
- **Answer is B (Bronchogenic carcinoma)**
 - **IMP Clues**
 - 2 pack history of cigarettes daily for the past 42 years (Smoking is usually associated with lung cancer, some types more than others)
 - Swelling of metatarsals, metacarpals, and proximal phalanges + X-rays of the affected bone show new bone formation + clubbing of the digits (HY association with adenocarcinoma)
- **Dx → Adenocarcinoma of the Lung (Bronchogenic Carcinoma)**
 - **It is the most common lung tumor**
 - Site → **peripheral** (can present as **apical** lesion → **Pancoast tumor** or **SVC Syndrome** or **Brachiocephalic Syndrome**)
 - **WEAKLY** associated with smoking (associated with **radon exposure** though)

USMLE gives you a vignette with a **man that lives in a basement** and asks **what is he most at risk of developing**; answer is **"Bronchogenic Carcinoma"**

 - Adenocarcinoma of the Lungs due to **Radon Exposure** (*radon is a radioactive gas produced by the decaying of uranium, naturally found in soil & rocks*)
 - Risk is high in **people living in basements, poorly ventilated lower floors, and underground miners**
 - HY Paraneoplastic Syndromes:
 - **Hypertrophic Osteoarthropathy** (**clubbing + joint pain + new bone formation**, due to **fibrovascular proliferation**)
 - **Hypercoagulability** (can present as **thrombosis** or **migratory thrombophlebitis** [Trousseau sign]) *[asked on NBME]*
 - **Dermatomyositis** (*violaceous eyelids rash + Shawl distribution rash + Gottron's papules + proximal muscle weakness*)



Dermatomyositis is also seen as a **HY paraneoplastic syndrome secondary to Ovarian cancer**.



Q39

A 48-year-old man is brought to the emergency department 12 hours after taking a massive overdose of ferrous sulfate. Serum sodium and potassium concentrations are within the reference range. Which of the following sets of serum concentrations is most consistent with this overdose?

Choices	Cl ⁻ (mEq/L)	HCO ₃ ⁻ (mEq/L)
A	76	52
B	96	8
C	96	28
D	106	32

▼ Explanation

- **Answer is B**
 - Patient here ingested a **massive dose of ferrous sulfate, which is basically iron**.
 - Q then asks you what are the expected serum concentration of chloride & bicarbonate?
 - Well, we know that **Iron OD is a cause of high-anion gap metabolic acidosis** (The **"I"** in **MUDPILES**)
 - **High anion gap** = **[Na] - [Cl + HCO3] = 13 or more**
 - So, basically the lower the sum of Cl & HCO3, the higher the anion gap.
 - **Choice B (96 + 8 = 104) is the lowest** of all the choices

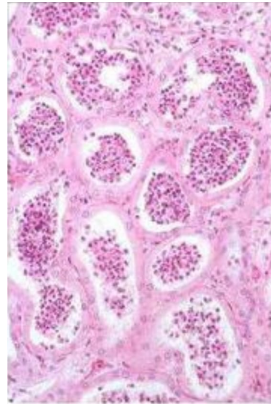


Causes of high anion gap: "MUDPILES"

- **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)

Q40

A 28-year-old woman at 32 weeks' gestation comes to the physician because of a 4-day history of fever and back pain. She says that during this time she also has been crying frequently. Her temperature is 38°C (100.4°F). Physical examination shows costophrenic angle tenderness. The photomicrograph shown represents her disease. Which of the following mechanisms is the most likely cause?



- A. Chorioamnionitis
- B. Endometritis
- C. Glomerulonephritis
- D. Hematogenous infection
- E. Obstructive uropathy
- F. Pelvic inflammatory disease

▼ **Explanation**

- **Answer is E (Obstructive Uropathy)**

- **IMP Clues**

- 32 weeks' gestation (We're expecting pregnancy related conditions)
 - Fever + back pain + costophrenic angle tenderness (Pyelonephritis)

- **Dx → Obstructive Uropathy**

- In the **third trimester**, the **uterus gets larger in size → compresses ureters**. In addition, the **progesterone in pregnancy causes relaxation of the ureters**.
 - Both of these factors cause **urinary stasis, bacterial overgrowth, and ascending infections** ⇒ **Pyelonephritis**
 - Can also cause **hydronephrosis** due to obstruction.

Q41

A 23-year-old woman comes to the physician for a follow-up examination. She underwent a median sternotomy for repair of an atrial septal defect 3 months ago. She is otherwise healthy. Her last visit 6 weeks ago showed a well-healing surgical incision. Physical examination today shows expansion of scar tissue to 6 mm beyond the edges of the original incision. An abnormality in which of the following processes is the most likely cause of these findings?

- A. Collagen synthesis
- B. Epithelial proliferation
- C. Fibrin deposition
- D. Granulation tissue formation
- E. Neovascularization
- F. Neutrophil infiltration

▼ **Explanation**

- **Answer is A (Collagen Synthesis)**

- **IMP Clues**

- Expansion of scar tissue to 6mm beyond the edges of the original incision (BEYOND is the keyword here, as it hints to keloids)

- **Dx → Keloid**

- 2 HY conditions related to wound healing you need to differentiate:

- 1. **Keloids**

- **Increased collagen synthesis (Type 3 & Type 1 collagen) in disorganized organization**
 - This causes the excessive scar tissue to extend **BEYOND the wound borders + keeps growing overtime**
 - Incidence is increased in people with **darker skin & Recurrence is high**

- 2. **Hypertrophic Scar**

- **Increased collagen synthesis (Type 3 collagen), which causes it to be parallel in organization**
 - This causes the scar tissue to be **CONFINED to the wound borders + flatten overtime.**

? Patient underwent a surgery 6 weeks ago. Scar site is healing well and negative for any signs of infection. She asks you when can she expect her normal skin to return to normal strength?

▼ **Answer**
NEVER - 80% of tensile strength is regained after ~3 months; after that little-to-none is regained.

- No specific predisposition & recurrence is unlikely

? The patient in this Q most likely has overactivity of which cytokine?

▼ Answer

TGF-Beta - Excess TGF-B is associated with hypertrophic scars & keloids

Wound Healing Rapid Review:

1. 3 mins - 3 hours

- **Homeostasis** (Vasoconstriction & Fibrin clot formation)

2. 3 hours - 3 days

- **Inflammation** (Vasodilation, increased vascular permeability, neutrophils chemotaxis, macrophages influx)

3. 3 days - 3 weeks

- **Proliferation** (Angiogenesis, Formation of Type 3 collagen granulation tissue, Re-epithelization)

4. 3 weeks - 3 months

- **Remodeling** (Type 3 collagen is converted to Type 1 collagen which increases tensile strength of wound)

? What molecule is responsible for fibroblast migration to wound healing site?

▼ Answer

Fibronectin

Q42

A 52-year-old man is brought to the emergency department because of a 4-hour history of a severe headache, anxiety, sweating, and palpitations. He has a 2-year history of hypertension well controlled with clonidine and hydrochlorothiazide, but he ran out of his prescriptions 3 days ago. His pulse is 120/min, and blood pressure is 170/110 mm Hg. Physical examination shows diaphoresis. Which of the following effects is most likely to follow an injection of propranolol in this patient?

- A. Decreased total peripheral resistance and decreased cardiac output
- B. Decreased total peripheral resistance and increased cardiac output
- C. Increased total peripheral resistance and decreased cardiac output
- D. Increased total peripheral resistance and increased cardiac output
- E. No change in total peripheral resistance or cardiac output

▼ Explanation

- Answer is C (Increased total peripheral resistance and decreased cardiac output)
 - Patient got an injection of **propranolol**, a **NON-SELECTIVE Beta Blocker**
 - **Blocking of B1 Receptor** → **decreases Cardiac Output**
 - **Blocking of B2 Receptor** → **increases Total Peripheral Resistance**

SELECTIVE vs NON-SELECTIVE BETA BLOCKERS: For beta blockers ending with “-olol”:

- Starts with **A** → **M**: **SELECTIVE BETA BLOCKER** (B1 selective)
- Starts with **N** → **Z**: **NON-SELECTIVE BETA BLOCKER**

Beta 1 Receptors vs B2 Receptors Rapid Review:

1. **B1 Receptors** are found in the **heart** & the **kidney**

- a. In the **heart**, B1 stimulation causes increased cAMP → Protein Kinase A → increased calcium influx → **increased Cardiac Output**
- b. In the **kidney**, B1 stimulation causes **increased renin production**

2. **B2 Receptors** are found in the **lungs**, **peripheral arterioles**, and the **uterus**

- a. In the **lungs**, B2 stimulation causes smooth muscle relaxation → **bronchodilation**
- b. In the **uterus**, B2 stimulation causes smooth muscle relaxation → **uterus relaxation/stops contraction (tocolytic)**
- c. In the **peripheral arterioles**, B2 stimulation causes smooth muscle relaxation → **vasodilation & decreased total peripheral resistance**

Q43

A 45-year-old man is undergoing a surgical procedure. Which of the following maneuvers by the anesthesiologist would result in an increase in intracranial pressure?

- A. Decreasing airway pressures

- B. Decreasing fractional inspired oxygen (FiO₂)
- C. Decreasing respiratory rate
- D. Increasing airway pressures
- E. Increasing FiO₂
- F. Increasing respiratory rate

▼ Explanation

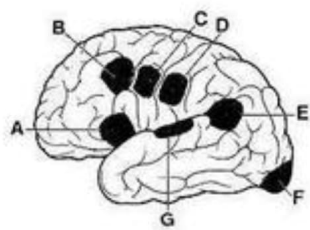
- **Answer is C (Decreasing respiratory rate)**
 - This concept is very HY and is on every NBME.
 - How does CO2 levels regulate cerebral flow?
 - **Decreased RR** → *decreased* CO2 wash-out → **increase CO2 levels** → brain thinks it is "*hypoxic*" → **increases cerebral flow** (CO2 is a vasodilator of vascular endothelium) → **increases ICP**
 - **Increased RR** → *increased* CO2 wash-out → **decreased CO2 levels** → brain thinks it is "*fine*" → **decreases cerebral flow** → **decreases ICP**

How is this concept tested?

- **Q will ask you directly how can anesthesiologist increase ICP?** Answer is **decrease RR**.
- **Q will give you a man with cerebral edema, and will ask you what should the anesthesiologist do?** Answer is **increase RR**.
- **Q can ask what how does REM sleep affect cerebral flow?** Answer is **increases cerebral flow**. REM sleep causes decreased RR.

Q44

Immediately after a cerebral infarction, a 62-year-old right-handed man has decreased fluency of spontaneous speech, with phrase lengths of less than four to five words. His comprehension is normal. Neurologic examination shows weakness of the lower two thirds of the face on the right. This patient most likely has a lesion in which of the following labeled areas in the drawing of the brain?



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

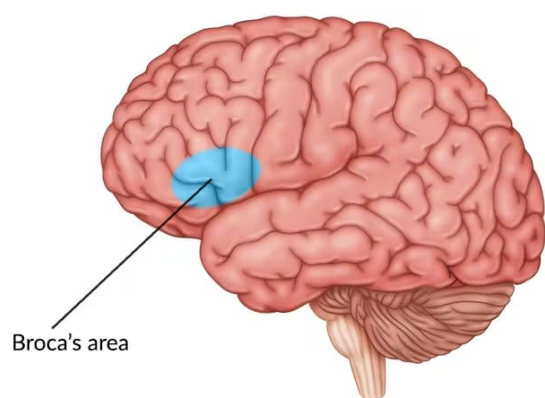
▼ Explanation

- **Answer is A**
 - **IMP Clues**
 - Decreased fluency of spontaneous speech (Aphasia)
 - Phrase lengths of less than four to five words (Brocha's aphasia)
 - Comprehension is normal (Also a feature of Broca's Aphasia)
- **Dx → Broca's Aphasia**
 - Affection of the dominant **inferior frontal gyrus (Broca's area)** causes **Broca's Aphasia**
 - **NON-FLUENT** aphasia with **impaired repetition**
 - **Comprehension is normal**, so the patient appears "*frustrated*" that he understands you but can't articulate fluently

?
Patient had a stroke then developed decreased fluency of speech & repetition. His comprehension is normal, however. What is the site of stroke?

▼ Answer
LEFT Middle Cerebral Artery (MCA)

- The dominant lobe is the left lobe on the USMLE. If the Q, however, that the patient is left-handed → dominant lobe is the right lobe. If not mentioned, assume that the left lobe is the dominant one



? Patient had a stroke then developed decreased fluency of speech. His repetition & comprehension are found to be normal. What is this patient's diagnosis?

▼ Answer

Transcortical Motor Aphasia

- If a stroke sounds like Broca's, but then you find that the repetition is normal. choose transcortical motor aphasia

▼ Other Choices

- **Choice B** → **Premotor Cortex lesion** would present as impaired planning of motor actions of the contralateral side.
- **Choice C** → **Primary Motor Cortex lesion** would present as contralateral weakness, paralysis, and hyperreflexia specifically in the upper limb as the lesion site is more lateral.
- **Choice D** → **Primary Sensory Cortex lesion** would present as contralateral loss of sensation specifically in the upper limb as the lesion site is more lateral.
- **Choice E** → **Wernicke's Area lesion** would cause **Wernicke's Aphasia**
 - Affection of the **dominant superior temporal gyrus, supplied by the MCA**
 - **FLUENT** aphasia with **impaired repetition**, meaning that the patient says a bunch of random words. He's fluent, but he doesn't make sense (referred to as **word salad**)
 - **Comprehension is impaired**
- **Choice F** → **Occipital Lobe lesion** would present as contralateral homonymous hemianopia, if the lesion was a "vascular lesion" of the PCA, there would be macular sparing as it has dual blood supply.
- **Choice G** → **Primary Auditory Cortex lesion** would cause incomplete hearing loss, more noticeable on the contralateral side.

? Patient had a stroke then developed impaired comprehension. His repetition is normal, but when asked a few Qs, he started saying his grocery list. What is this patient's diagnosis?

▼ Answer

Transcortical Sensory Aphasia

- If a stroke sounds like Wernicke's, but then you find that the repetition is normal. choose transcortical sensory aphasia

Q45

A 45-year-old man comes to the office for counseling prior to a bariatric operation for weight loss. He was recently diagnosed as prediabetic. He is 170 cm (5 ft 7 in) tall and weighs 116 kg (256 lb); BMI is 40 kg/m². Physical examination shows no other abnormalities. In addition to recommending that the patient follow a balanced diet postoperatively, it is most appropriate for the patient to avoid ingesting excessive amounts of which of the following?

- A. Gluten-containing foods
- B. Green leafy vegetables
- C. Nuts
- D. Protein
- E. Starchy foods

▼ Explanation

- **Answer is E (Starchy Foods)**
 - Patient will be undergoing bariatric surgery, so counseling about lifestyle modifications & post-op recommendations is important.
 - One of the most common post-bariatric surgery complications is **Dumping Syndrome**
 - **Basically, the removal of part of stomach + pylorus, causes the food to be "dumped" directly into small intestines (without the stomach digestion & the pyloric sphincter regulations)**
 - This causes one of two things:
 1. **Early Dumping Syndrome (mins after):** Rapid emptying of the food (hyperosmolar chyme) into the intestines causes rapid shifting of fluids from the plasma into the GI tract lumen ⇒ **Diarrhea, abdominal pain, hypotension, tachycardia, flushing, and diaphoresis**
 2. **Late Dumping Syndrome (hours after):** Rapid glucose absorption causes excessive insulin release & spiking ⇒ **Hypoglycemia** (Sweating, tremors, palpitations)

- So, to address these complications you must advise the patient to **eat small, low carb meals or add complex carbs & proteins into the meals.** (Choice E)

Q46

A 47-year-old woman comes to the physician because of a 6-month history of increasingly severe cough and shortness of breath. She has had no fever, chills, or muscle aches. She does not smoke. She works as a librarian and is often exposed to dusty books. She lives alone with four parakeets. She became a vegetarian 2 years ago. She is an avid knitter and can spin her own wool. Crackles are heard in the lower lung fields. Laboratory studies show an erythrocyte sedimentation rate of 40 mm/h. A chest x-ray shows areas of reticulogranular changes. Examination of a biopsy specimen of the lung shows interstitial infiltrates of lymphocytes and granulomas. Which of the following is the most likely cause of this patient's condition?

- A. Consumption of soy-based food products
- B. Contact with dust
- C. Contact with parakeets
- D. Vitamin B deficiency
- E. Wool exposure

▼ Explanation

- Answer is C (Contact with parakeets)

- IMP Clues

- 6 months hx of increasingly severe cough and shortness of breath (Chronic cough & dyspnea, so we're thinking lung pathology)
- No fever, chills, or muscle aches (Excludes infections)
- She does not smoke (Excludes COPD)
- Often Exposed to dusty books (dust predisposes the patient to IPF not HP)
- She lives alone with four parakeets (one of the antigens known to cause HP)
- She became a vegetarian 2 years ago (This is just put here by the Q writers to make you think of Vit B12/9 deficiencies but nothing here supports it)
- She is an avid knitter and can spin her own wool (wool predisposes to byssinosis, which is pneumoconiosis)
- Crackles are heard in the lower lung fields + CXR shows area of reticulogranular changes + biopsy shows interstitial infiltrates of lymphocytes and granulomas (Immune-mediated response to an antigen, causing fibrosis)

- Dx → Hypersensitivity Pneumonitis (HP)

- **Type III/IV hypersensitivity reaction to environmental *antigens***, most HY for the USMLE are:
 - **Exposure to hay (Farmer's Lung)**, where the antigen is **thermophilic actinomyces**
 - **Exposure to birds (Bird Fancier's Lung)**, where the antigen is **bird/avian proteins**
- Presence of these antigens in the lung interstitial tissue, causes type 3/4 HS reaction
 - **Early Changes (Type III HS)** → Immune complexes deposition in the lungs → activation of complements → neutrophils & macrophages activation
 - **Late Changes (Type IV HS)** → CD4 activation → Th1 → INF-gamma activation of macrophages → **non-caseating granuloma formation**
 - Lymphocytes & macrophages produces inflammatory cytokines → lung epithelial damage → increased fibroblast activity → increased collagen deposition → fibrosis & thickening of alveoli
 - **Fibrosis = Restrictive PFTs pattern & reticulonodular/reticulogranular appearance on CXR**

Q47

A 65-year-old woman with cardiovascular disease is found to have multiple, small, cholesterol gallstones. She is considered a poor candidate for cholecystectomy. The most appropriate treatment for this patient is a drug that would cause which of the following biliary changes?

- A. Decreased free sodium
- B. Decreased lecithin
- C. Decreased phospholipids
- D. Increased bile salt
- E. Increased mucus

▼ Explanation

- Answer is D (Increased bile salt)

- **Cholesterol stone** are caused by an **imbalance** between **Cholesterol (insoluble)** and **Bile salts (soluble)** and **phospholipids/lecithin (soluble)**.
- In obese or dyslipidemia patients, the **increased levels of cholesterol** in bile causes an imbalance in the ratios ⇒ **Insoluble Cholesterol Stone Formation**

- Ursodiol (a drug used in patients with gallstones) is a type of bile acid that is highly soluble → **increases** bile solubility and flow & **decreases** synthesis and absorption of cholesterol
 - How does it do all of that?
 - Ursodiol (ursodeoxycholic acid) is **more hydrophilic** than other bile acids → Less efficient in forming cholesterol-containing micelles → **decreased** cholesterol absorption
 - Downregulates **HMG-CoA Reductase** activity → **decreased** cholesterol synthesis
 - **Increases the bile salts** (as it is a bile salt) in the bile → **more** solubility and **better** flow

Q48

An investigator wishes to determine the effectiveness of a new preparation of candy containing citric acid (Substance X) as a therapy for Sjogren syndrome. Both Substance X and a placebo, which does not contain citric acid, are administered to healthy volunteers. It is found that Substance X produces twice as much saliva as the placebo does. However, analysis of the ionic composition of the saliva shows that the saliva of the placebo group contains half as much sodium chloride as that from the Substance X group. In contrast, the concentration of bicarbonate is approximately the same in both groups. Which of the following best explains these findings?

- A. Citric acid decreases water absorption by the salivary ducts
- B. Citric acid stimulates secretin release, thereby increasing ionic secretion
- C. Citric acid stimulates turnover of the $\text{Na}^+ - \text{K}^+ - \text{Cl}^-$ cotransporter
- D. Ductal ion reabsorption is more efficient at low flow rates
- E. Salivary ducts are impermeable to bicarbonate

▼ **Explanation**

- **Answer is D (Ductal ion reabsorption is more efficient at low flow rates)**
 - Q asks why does the saliva of volunteers taking the placebo have half as much chloride when compared with the saliva of the volunteers taking Substance X?

1. First, we need to understand the mechanism of saliva secretion:

- Saliva is secreted by the **salivary glands**, which are made up of **acini & ducts**
 - **Acini** → **Secretes "primary" saliva**, which is derived from plasma hence having the **same concentration of electrolytes (isotonic to plasma)**
 - also includes digestive enzymes like **salivary amylase & lipase**
 - **Ducts** → **Modifies "primary" saliva** by:
 - **Reabsorption of Na & Cl**
 - **Secretion of K & HCO_3**

Note that ducts are impermeable to water, hence movement of solutes is what facilitates change in tonicity.

- Net Result → **hypotonic saliva (less Na & Cl, and more K and HCO_3)**

2. How saliva secretion composition differs according to the speed of flow:

- **Low Flow** ⇒ **More** contact time in ducts (**MORE** reabsorption of Na and Cl & **MORE** secretion of K & HCO_3)
 - So, Low Flow ⇒ **HIGH** concentration of Potassium, but **LOW** concentrations of Na, Cl, and HCO_3
- **High Flow** ⇒ **Less** contact time in ducts (**LESS** reabsorption of Na and Cl & **LESS** secretion of K)
 - High Flow ⇒ **LOW** concentration of Potassium, but **HIGH** concentrations of Na, Cl, and HCO_3

Notice how I didn't say less secretion of HCO_3 , HCO_3 is the **ONLY EXCEPTION.**

- HCO_3 is needed to buffer food and acids, so ingestion of food/acids causes **high flow saliva WITH HIGH HCO_3** .
- This is caused by the **parasympathetic system** causing **active HCO_3 secretion**

- So back to our Q, why does normal saliva have lower Cl than saliva stimulated by citric acid?

- **Normal saliva = lower flow rate = more duct contact time = more reabsorption of Cl ("Ductal ion reabsorption is more efficient at low flow rates") (Choice D)**

Q49

A 25-year-old woman is brought to the emergency department after collapsing in the intensive care unit where she works as a nurse. Coworkers report that she had appeared fine all morning, but shortly after lunch she became pale and diaphoretic and then collapsed. She has a history of several episodes of confusion and autonomic symptoms associated with hypoglycemia that occurred at various times of day without apparent precipitants. She is unresponsive. Her temperature is 37.1°C (98.8°F),

pulse is 96/min, respirations are 18/min, and blood pressure is 100/60 mm Hg. An initial fingerstick shows a blood glucose concentration less than 20 mg/dL. A bolus of 50% dextrose is administered. Laboratory studies now show:

Glucose	32 mg/dL
Plasma free insulin	70 µU/mL (N=5-35)
C-peptide	< 0.075 nmol/L (N=0.3-1.29)
Proinsulin	< 1 pmol/L (N=1.5-13.4)

Which of the following is the most likely diagnosis?

- A. Factitious disorder
- B. Fructose intolerance
- C. Glycogen storage disease
- D. Insulin autoimmune hypoglycemia
- E. Insulinoma
- F. Non-β cell pancreatic tumor
- G. Reactive hypoglycemia

▼ Explanation

- Answer is A (Factitious disorder)
 - IMP Clues
 - She works as a nurse (on the USMLE, this line repeats so much & it usually means that the “patient” is a healthcare professional and understands medications and has access to them, making it more likely to be factitious)
 - She appeared fine all morning but became pale & diaphoretic and collapsed (sudden onset) + history of several episodes of confusion and autonomic symptoms associated with hypoglycemia without precipitant (basically, sudden recurrent attacks of hypoglycemia)
 - Initial fingerstick shows a blood glucose concentration less than 20mg/dl (severe hypoglycemia)
 - Plasma insulin is high (could be either exogenous intake or an insulinoma)
 - C-peptide & Proinsulin are low (this is the keyword we need; c-peptide & insulin are secreted together. This mean that an isolated increase in insulin is likely due to exogenous insulin intake)
 - Dx → Factitious Disorder
 - To understand this, you need to know how insulin is produced: (it will be quick & concise I promise)
 - Preproinsulin is produced → proinsulin → insulin + c-peptide
 - This means high endogenous production of insulin, would be accompanied with high proinsulin and c-peptide levels (like an insulinoma)
 - Here, we have HIGH Insulin + LOW c-peptide and LOW proinsulin. This means that the insulin is not produced endogenously ⇒ EXOGENOUS INSULIN INTAKE
 - This is consistent with her being a nurse, having access to insulin at the hospital. Also, woman are more likely to have factitious disorders.

Q50

A 23-year-old woman sustains significant blood loss in a motor vehicle collision. She is given 3 units of blood and has an uneventful recovery. Four weeks later, she becomes jaundiced. She is afebrile. Laboratory evaluation shows anemia and reticulocytosis; there is no evidence of infection. Which of the following additional studies is likely to be most useful in establishing the diagnosis?

- A. Direct antiglobulin test
- B. Hemoglobin electrophoresis
- C. Serum conjugated bilirubin concentration
- D. Serum ferritin concentration
- E. Serum transferrin concentration
- F. Serum erythropoietin concentration

▼ Explanation

- Answer is A (Direct antiglobulin test)
 - IMP Clues
 - She is given 3 units of blood + Four weeks later she becomes jaundiced (Hx of blood transfusion + delayed hemolysis)
 - She is afebrile + no evidence of infection (this excludes blood-transfusion transmitted diseases)
 - Jaundice, anemia, reticulocytosis (Hints to hemolysis)

- **Dx → Delayed Transfusion Reaction**

- **Hemolysis** in a patient **post-transfusion** over a longer period of time usually **days-weeks** (hence the name "*delayed*")
- **MOA** → **antibodies against donor's minor RBC antigens** (Rh, Kell, Duffy, Kidd)
 - Hence the pathophysiology is immunological antibodies, the diagnosis can be established by **detecting these antibodies via Coomb's test** (aka **Direct Antiglobulin Test**) (Choice A)

Let's Revise the Transfusion Reactions on the USMLE:

1. **Transfusion Related Acute Lung Injury (TRALI):**

- Simply put, **TRALI = ARDS-like state post transfusion**
- Usually, **<6 hours post-transfusion**
- MOA → **Neutrophils in lungs react to cytokines in transfused blood.** Simple.

2. **Transfusion Associated Circulatory Overload (TACO):**

- ARDS-like state **>6 hours post transfusion** [remember, TRALI < 6 hours]. OR
- ARDS-like state **post transfusion** regardless of time in a patient with **hx of cardiovascular disease**
- MOA → **increased hydrostatic pressure** → **volume overloads heart's capacity** → **transudation** in lung

3. **Delayed Transfusion Reaction:**

- Hemolysis in a patient post transfusion over a longer period of time usually **days-weeks** (hence the name "*delayed*")
- MOA → **antibodies against donor's minor RBC antigens** (Rh, Kell, Duffy, Kidd) [**so Coomb's +ve**]

4. **Hemolytic ABO mismatch:**

- Fever + chills +/- other symptoms of severe hemolysis within **minutes of transfusion**
- MOA → **antibodies against donor's RBC A/B antigens** [**so Coomb's +ve**]

5. **Febrile Non-hemolytic Transfusion Reaction (FNHTR):**

- Fever + chills within **hours of transfusion**
- MOA → **Donor's WBCs releasing cytokines when they react with antibodies in recipient's plasma** [so Coomb's -ve]



Okay I know that all of this seems overwhelming. Let's do a quick simplified revision:

- Do we have **ARDS-like symptoms & signs post-transfusion**?
 - Yes? look at time frame
 - **< 6 hours** → **TRALI**
 - **> 6 hours** → **TACO**
- Do we have **ARDS-like symptoms & signs post-transfusion in a patient with hx of cardiac disease**?
 - Yes? → **TACO (REGARDLESS OF TIME)**
- Do we have **Fever + chills post transfusion**?
 - Yes? look at time frame
 - Within **minutes** → **ABO mismatch** (present with signs of severe hemolysis + Coomb's **positive**)
 - Within **hours** → **FNHTR** (NO hemolysis, hence the name, + Coomb's **negative**)
 - Within **days to weeks** → **Delayed Transfusion reaction** (present with signs of hemolysis + Coomb's **positive**)

Easy? Yes.



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