



NBME EXPLANATIONS

NBME 21 Block 4

from CrackNBME

21-Block 4

Q1

A 60-year-old man is brought to the emergency department after being thrown from his car and striking a guardrail in a high-speed automobile collision. He was the unrestrained driver. Physical examination shows blood at the urethral meatus and fractures of the pelvis and the left femur. A Foley catheter is unable to be inserted. Which of the following is the most likely explanation?

- A. Hypospadias
- B. Prostatic hypertrophy
- C. Ruptured bladder
- D. Urethral disruption
- E. Urethral stricture

▼ Explanation

• Answer is D (Urethral Disruption)

◦ IMP Clues:

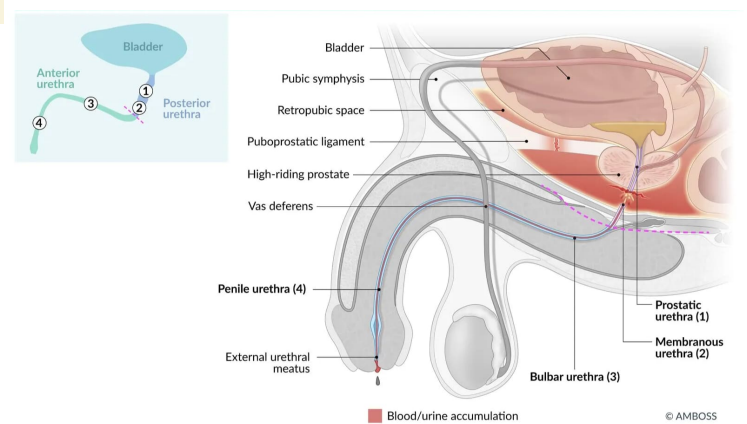
- Blood at the urethral meatus (urinary system injury, probably urethral)
- Fracture pelvis (This keyword is actually important for localization of the injury)
- Foley catheter is unable to be inserted (Well, yah because it is injured & full of blood)

• Dx → Posterior Urethral Injury

- Pelvic Fracture & Instrumentation (forced catheterization) exerts a shearing force on the Fixed Parts of the urethra (*Membranous Urethra*)

- This causes injury & disruption of the **bulbomembranous junction (site of junction of fixed membranous & mobile bulbar urethra)**

- This causes **bleeding at the meatus & urethral obstruction** causing **inability to void urine**.
- The prostate "**rides-high**" due to separation of below support of the urethra & accumulation of blood in the retropubic space
 - A "**high-riding prostate**" is a **specific finding of posterior urethral injuries**
- Catheterization is actually **contraindicated** due to risk of further damaging the urethra



? What types of Injuries cause Anterior Urethral Injury?

▼ Answer

Saddle Injuries or Perineal Blunt injury - This causes disruption of the anterior urethra (most commonly the bulbar urethra)

▼ Other Choices

- **Choice A → Hypospadias** is the opening of the urethral meatus on the ventral aspect of the penis. It is a **congenital deformity** & not related to pelvic fractures.
- **Choice B → BPH** would not cause blood at the urethral meatus, nor is it related to pelvic fractures.

? Remember what hormone causes BPH?

▼ Answer

DHT - so treatment is **Finasteride** (*5-alpha reductase inhibitor*)

Testosterone is converted to Dihydrotestosterone via *5-alpha reductase*

• Choice C → Ruptured Bladder

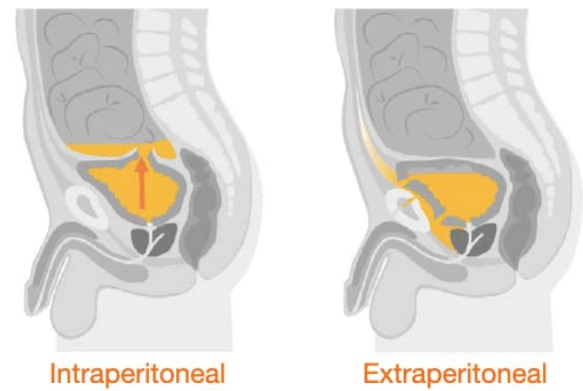
- 2 Types of injuries you need to know → **Intraperitoneal & Extraperitoneal**

1. Intraperitoneal injuries

- Usually caused by **blunt trauma** to the pelvic area.
- This causes rupture of bladder into the **peritoneal space**, which can progress to **peritonitis**
- Patient will present with **hematuria or inability to void urine**. *No blood at meatus.*

2. Extraperitoneal Injuries

- Usually caused by **pelvic fractures** or **penetrating injuries**
- This causes extravasation of blood to the **peri-vesical or retropubic area**
- The pain is **suprapubic** and **localized**
- Patient also presents with **hematuria or inability to void urine. No blood at meatus.**



- **Choice E** → **Stricture** may be a **LONG term** complication of urethral injuries if inadequately managed or may be caused by **radiation to prostate in cases of cancer** or any other causes that causes chronic inflammation, scarring, and fibrosis.

Q2

A 66-year-old man with stage IV colon cancer comes to the physician because of a 3-day history of severe diarrhea after receiving chemotherapy with fluorouracil, leucovorin, and irinotecan. The physician prescribes an opioid antidiarrheal agent with little or no ability to produce central nervous system effects, even when given in relatively high doses. Which of the following agents was most likely prescribed?

- A. Buprenorphine
- B. Codeine
- C. Hydrocodone
- D. Loperamide
- E. Morphine

▼ Explanation

- **Answer is D (Loperamide)**
 - **IMP Clues:**
 - Physician prescribes an opioid anti-diarrheal agent with little or no CNS effects (pretty much, they gave us the MOA of the drug)
 - **Loperamide**
 - **Mu-opioid receptor agonist** with **LOW** addictive potential. Like really low. This is because it **doesn't pass the BBB**. Only works peripherally.
 - Used as an **anti-diarrheal**. Simple

▼ Other Choices

- All of these have high potential for addiction
- **Choice A** → **Buprenorphine** is a weak opioid partial agonist that is helps with detox.

Q3

A 48-year old man is referred for evaluation of possible hypertension. On the basis of ten measurements, the patient's average diastolic blood pressure is 113 mm Hg, and the standard deviation is 8 mm Hg. If four rather than ten measurements of the mean blood pressure are made, which of the following is the expected impact on the size of the 95% confidence interval about the mean blood pressure?

- A. Change, but the direction cannot be predicted
- B. Decrease in width
- C. Increase in width
- D. Remain the same

▼ Explanation

- **Answer is C (Increase in width)**
 - So, you have 10 patients with an average of 113mmHg +/- 8mmHg as SD with confidence interval of 95%.
 - Q asks what would happen to the confidence interval if we only had 4 patients
 - Well, now that we have **less data, our "confidence" decreases**.
 - This makes us increase the range of possible chances

- If we increase our confidence interval, we increase the chance that our data fits in that interval.
- So basically, we have *less* data, so “confidence” in our estimate goes down, requiring a **wider range** to maintain the 95% confidence.

Q4

A 75-year-old woman comes to the physician's office because of poor concentration and decreased energy for the past month. For 6 months, she has been waking up at 4 AM and been unable to get back to sleep. Physical examination shows no abnormalities. Which of the following is the most likely cause of the sleep disturbance in this patient?

- A. Major depressive disorder
- B. Narcolepsy
- C. Paroxysmal nocturnal dyspnea
- D. Periodic leg movements
- E. Sleep apnea

▼ **Explanation**

• **Answer is A (Major Depressive Disorder)**

◦ **IMP Clues:**

- Poor concentration + decreased energy + poor sleep schedule (signs of depression)
- Physical examination shows no abnormalities (this excludes PND & apnea)

◦ **Dx → MDD**

- USMLE doesn't follow the full depression criteria (the 5/9 SIGECAPS)
- **Poor concentration, decreased energy, disturbed sleep +/- weight loss or loss of interest in things the patient used to enjoy** is enough.
- **Elderly are vulnerable for depression**, so I think 1/2 of the vignettes will be an elderly patient & the other half will be mix of middle-aged females & maybe some males.

▼ **Other Choices**

- **Choice B → Narcolepsy** presents as **increased daytime sleepiness, cataplexy (sudden muscle weakness), and sleep disorders (paralysis, hallucinations)**



What is the pathophysiology of Narcolepsy

▼ **Answer**

Deficiency of *Orexin (Hypocretin)* - Treatment of Narcolepsy is by **Modafinil** (promotes release of orexin from hypothalamus)

- **Choice C → PND** is a type of dyspnea that occurs after 3-4 hours of sleep. The patient wakes up suddenly due to shortness of breath that resolves within 15-20 mins.

- **Choice D → Periodic Leg movement** refers to **restless leg syndrome**

- Irresistible urge to move leg while sleeping
- Associated with **IDA**
- If not IDA, then the 2nd most common cause is **Dopamine dysfunction so treated with D2 agonists**



What are Restless Leg Syndrome patients at risk of developing?

▼ **Answer**

Parkinson's Disease - correlated dysfunction of dopamine signaling increases risk of Parkinson's Disease

- **Choice E → Sleep apnea** is usually caused by obesity.
 - Increased fat/tissue in neck causes **poor oxygenation** → **chronic hypoxia** → **pulmonary HTN, Cor pulmonale, depression.**
 - Patients usually have **congested faces**, with **red eyes**, and **edematous under-eyes.**

Q5

A 23-year-old woman develops persistent sneezing each year in the spring. Her sneezing worsens when she works in her garden. A drug with which of the following mechanisms of action is most likely to be effective in treating this patient?

- A. Inhibition of histaminergic (H₂) receptors
- B. Inhibition of phosphodiesterases
- C. Stabilization of lymphocyte membranes

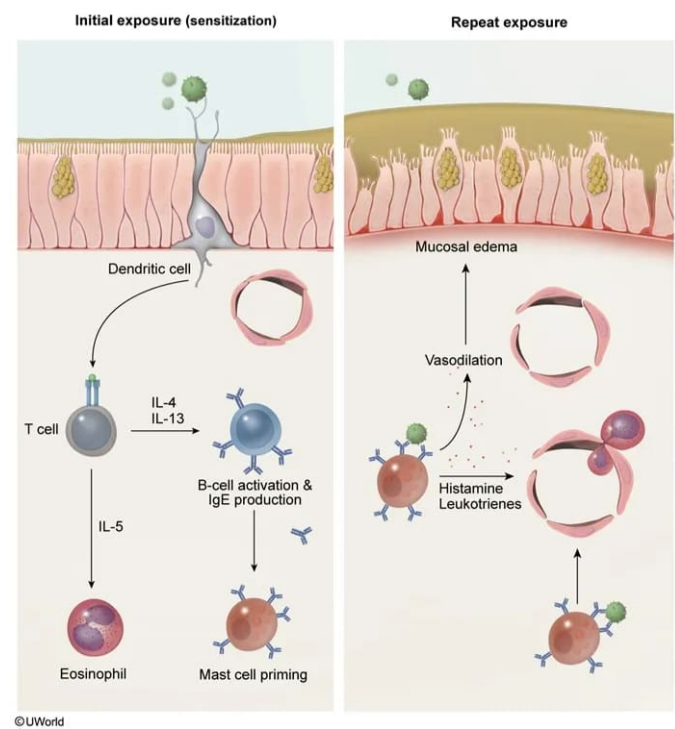
- D. Stabilization of mast cell membranes
- E. Stimulation of β_2 -adrenergic receptors

▼ Explanation

- **Answer is D (Stabilization of mast cell membranes)**
 - **IMP Clues:**
 - Persistent sneezing each year in the spring (sounds like an allergy)
 - Sneezing worsens when she works in her garden (definitely an allergy)
- **Dx → Allergic Rhinitis**
 - Allergies are **IgE-mediated Type 1 Hypersensitivity Reaction**
 - The first time your body gets exposed to an allergen, IgE is made & connects to **mast cells**.
 - The next time you get exposed to that same allergen, it binds to IgE Receptors on mast cells, causing **mast cell degranulation** and liberation of **inflammatory mediators** (most commonly, **Histamine which binds to H1 receptors**).
 - So, what drug can you take to prevent this?
 - **Mast Cell Stabilizers** (Nedocromil, cromolyn sodium)



USMLE can rephrase the re-exposure pathogenesis as **"antigens/allergens cross-link IgE molecule already bound to IgE receptors on mast cells"** or **"aggregation/clustering of High Affinity IgE Receptors on mast cells"** instead of simply using allergen binds to IgE Receptors on mast cells



▼ Other Choices

- **Choice A** → Inhibition of H2 would cause less HCL production in stomach. What you are looking for is H1. Not 2.
- **Choice B** → Many classes of PDE inhibitors on the USMLE.
 - **PDE5 inhibitor** is **Sildenafil (Viagra)** used for **ED & Pulmonary HTN**
 - **Non-selective PDE inhibitor** is **Theophylline** which was used for **Asthma management**
- **Choice C** → Does something like that even exist? Even if it does, garbage for USMLE.
- **Choice E** → **B2 agonists** would cause bronchodilation. This is not an asthma case.



Why has the use of PDE inhibitor Theophylline decreased?

▼ **Answer**
Due to associated **Neurotoxicity & Cardiotoxicity**.

Q6

A female newborn delivered at 26 weeks' gestation is found to have hyaline membrane disease. She is intubated and mechanically ventilated. Her vital signs are continuously monitored, and inspired oxygen is maintained at a level that will sustain an oxygen saturation between 92% and 95%. The primary goal of this treatment is protection of which of the following structures?

A. Basal ganglia

B. Choroid plexus

C. Cochlea

D. Ductus arteriosus

E. Retina

▼ Explanation

- **Answer is E (Retina)**
 - **IMP Clues:**
 - Newborn delivered at 26 weeks has hyaline membrane disease + intubated & mechanically ventilated (okay, so I'm expecting a Q of ventilation complications)
 - Inspired oxygen is maintained at a level between 92% and 95% (Oxygen not 100% to prevent O2 complications, yes O2 complications)
 - **Q here tests why O2 saturation is not > 95%?**

- There are 3 HY complications of high O2 concentration in premature newborns:

1. Retinopathy of Prematurity

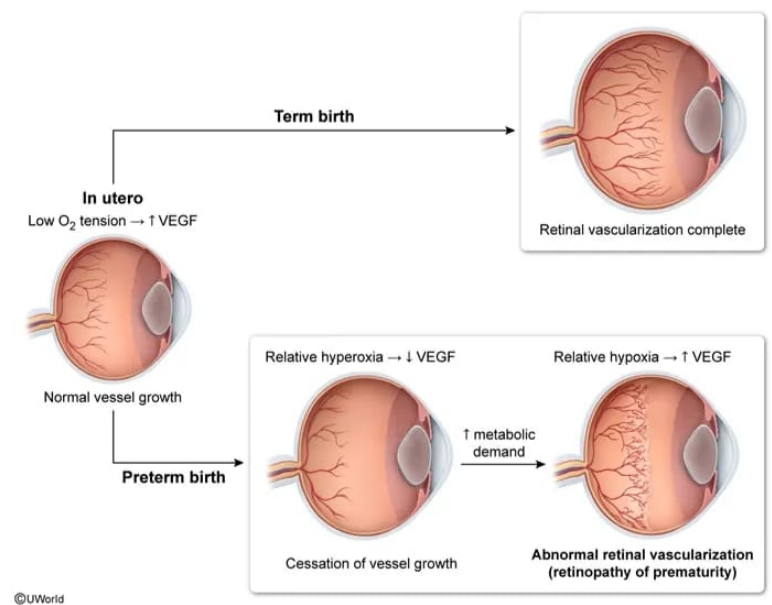
- High O2 saturation → **decreased** VEGF → Retinal vessels don't form & obliterate → when the baby is weaned off the 100% O2 ventilator → *Relative* hypoxia → **increased** VEGF → **Retinal neovascularization** → vessels are malformed and weak → bleeding → **Retinal detachment & blindness (Choice E)**

2. Bronchopulmonary Dysplasia

- High O2 pressure → overstretches the weak immature alveoli → rupture of alveoli & it's supporting (also weak) capillaries → **fibrosis**
- High O2 saturation → **ROS production** → damage to endothelium & capillaries → **fibrosis**

3. Intraventricular Hemorrhage

- Premature newborns have a **highly vascular region in their brain called the germinal matrix**.
- High O2 saturation → *decreased* VEGF → intraventricular vessels don't form & obliterate → when the baby is weaned off the 100% O2 ventilator → *Relative* hypoxia → **increased** VEGF → Intraventricular neovascularization → vessels are malformed and weak → bleeding → **IVH**



Q7

A 35-year-old man with diabetic ketoacidosis has a decrease in plasma glucose concentration from 900 mg/dL to 270 mg/dL during treatment with insulin and volume repletion. Which of the following additional laboratory values is most likely to decrease with the insulin therapy?

- Serum calcium concentration
- Serum potassium concentration
- Serum sodium concentration
- Urinary ammonia excretion
- Urinary potassium excretion

▼ Explanation

- **Answer is B (Serum potassium concentration)**

◦ IMP Clues:

- Patient with DKA that took insulin had plasma glucose concentration decrease from 900 to 270mg/dl (So, the insulin did work)

- Q asks what else would decrease with insulin?

- This is a pass-level Q here. **Insulin moves glucose & potassium inside the cell**
- This is why we always give DKA management is essentially **fluids + insulin + glucose + potassium**.
- How does this happen?
 - **Insulin upregulates Na/K ATPase** → 3Na out for 2K in ⇒ *decreases* serum potassium
 - **Insulin upregulates H/K exchanger** → H out for K in ⇒ *decreases* serum potassium

? Why is DKA associated with hyperkalemia?

▼ Answer

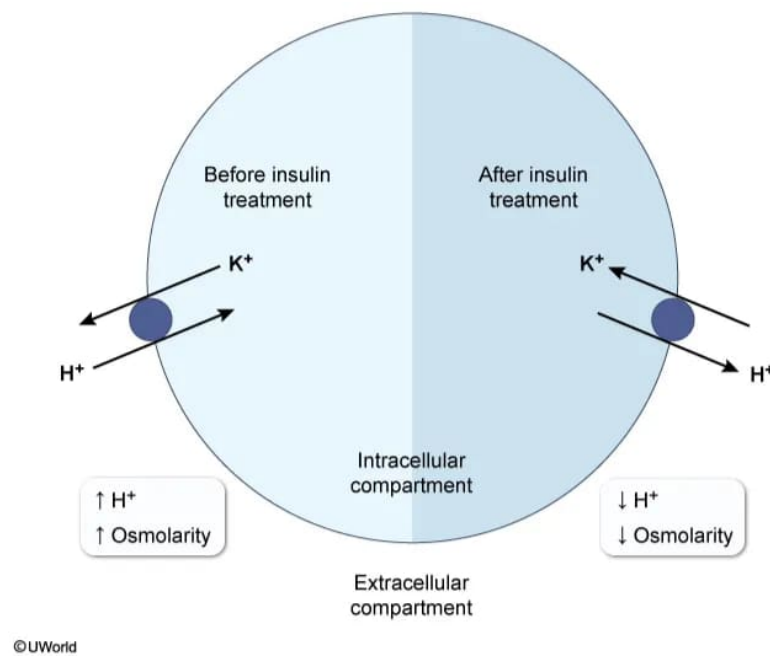
DKA means no Insulin. No insulin causes:

1. Dysfunction of Na/K ATPase

- 3Na stays in and 2K stays out ⇒ hyperkalemia

2. Potassium-Proton Shift

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



Q8

A 7-year-old girl is brought to a clinic in a developing country where lack of adequate good-quality protein has been identified as a critical issue. She is at the 70th percentile for height and 90th percentile for weight. Her vital signs are within normal limits. Physical examination shows no abnormalities. Which of the following amino acids is most critical in the analysis of this child's diet at this time?

- A. Alanine
- B. Aspartic acid
- C. Glycine
- D. Methionine
- E. Tyrosine

▼ Explanation

• Answer is D (Methionine)

- Easy Q that tests your knowledge of **essential amino acids**.
- Q asks which amino acid is most critical in the analysis of this child's diet brought from a developing country with lack of good quality protein? Basically, what amino acid does she need that she cannot make?
- **Methionine** is the only essential amino acid in the answer choices.



Essential Amino Acids

use the mnemonic "**PVT TIM HaLL**" (Private Tim Hall)

- **P** → Phenylalanine
- **V** → Valine
- **T** → Threonine
- **T** → Tryptophan (*NOT* Tyrosine)
- **I** → Isoleucine
- **M** → Methionine
- **H** → Histidine
- **L** → Leucine
- **L** → Lysine



Remember the Essential Fatty Acids?

▼ Answer

Linolic Acid (Omega 6) & alpha-linoleic acid (Omega 3)

▼ Other Choices

- None of these are essential.

Q9

A 72-year-old man comes to the physician because of a 2-week history of a nonproductive cough. He has non-Hodgkin lymphoma treated with a variety of antineoplastic drugs. Physical examination shows hyperpigmentation around the elbows. A chest x-ray shows diffuse infiltrates. Which of the following drugs is the most likely cause of this patient's symptoms?

- A. Bleomycin
- B. Carboplatin
- C. Chlorambucil
- D. Prednisone
- E. Vincristine

▼ Explanation

- Answer is A (Bleomycin)
 - IMP Clues:
 - Nonproductive cough (most likely not infective etiology)
 - Non-Hodgkin lymphoma treated with a variety of antineoplastic drugs (will probably test us on some drug)
 - Hyperpigmentation around the elbows (potential side effect of the drugs)
 - Diffuse Infiltrates on CXR (lungs are affected, perhaps from the drug?)
- Dx → Drug-Induced Pulmonary Fibrosis
 - Bleomycin is one of the drugs used in the treatment regimen of lymphoma
 - MOA: Causes Free Radicals formation which causes DNA damage
 - Side Effects:
 - Pulmonary Fibrosis (Most HY)
 - Hyperpigmentation

? What are the HY drugs that cause pulmonary fibrosis on the USMLE?

- ▼ Answer
1. Bleomycin
 2. Busulfan
 3. Methotrexate
 4. Amiodarone
 5. Nitrofurantoin

▼ Other Choices

- Choice A → Carboplatin
 - DNA Cross-linking agent (from the family of Cisplatin)
 - Side effects → Neurotoxic, Ototoxic, and Nephrotoxic

? Patient had Cisplatin toxicity. What is the antidote?

- ▼ Answer
- Normal Saline followed by Amifostine

- Choice C → An alkylating agent you won't get tested on
- Choice D → HY side effects of prednisone are osteoporosis, striae, avascular necrosis, DM, and the classic cushingoid appearance
- Choice E → Vincristine is a microtubule inhibitor.
 - Side effect → Neurotoxicity

? Remember the other microtubule inhibitors?

- ▼ Answer
- Vincristine
 - Vinblastine
 - Colchicine
 - Griseofulvin
 - -bendazoles

Taxanes (Paclitaxel & Docetaxel) are microtubule stabilizers

Q10

A 26-year-old man with HIV infection comes to the physician because of a 3-day history of generalized reddening skin involving the palms, arms, legs, and soles. A rapid plasma reagin (RPR) test result is positive. Treatment with which of the following antibiotics is most likely to eradicate the causal organism?

- A. Acyclovir
- B. Aztreonam
- C. Caspofungin
- D. Fluconazole
- E. Nystatin
- F. Oseltamivir
- G. Penicillin

▼ Explanation

• Answer is G (Penicillin)

◦ IMP Clues:

- Generalized Reddening skin involving palms, arms, legs, and soles (Remember the DD of rashes involving palms & soles? I told you it's HY AFF)
- Rapid Plasma Reagin (RPR) test results positive (this narrows our DD to syphilis)

• Dx → Secondary Syphilis Rash

- Q asks what antibiotic is most likely to eradicate syphilis. **Penicillin.**
 - **MOA: B-lactam, which binds to & inhibits PBP-1 (inhibits peptidoglycan cross-linking) which inhibits cell wall synthesis.**
- Penicillin is so effective at treating syphilis that if a patient is allergic to penicillin, we desensitize him and still give him penicillin. It is *THAT* effective.

? What other HY causes of rashes that involve the palms & soles on the USMLE?

▼ Answer

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



? What complication can rise during ttt of Syphilis with Penicillin?

▼ Answer

Jarisch-Herxheimer Reaction

- **Rapid release of cell wall components/organism products ⇒ LPS-like reaction ⇒ Fever, chills, hypotension**
- **HY to know that this reaction can also happen in other spirochetes infection, like *Lyme Disease*, and not just unique to syphilis [asked on NBME]**

▼ Other Choices

- **Choice A** → Used for HSV & VZV
 - **Acyclovir MOA ⇒ Inhibits HSV/VZV DNA polymerase**
- **Choice B** → Used for gram negative infections. Can be used in people with penicillin allergy
 - **Aztreonam MOA ⇒ Monobactam- Binds to & inhibits PBP-3 (inhibits peptidoglycan cross-linking) which inhibits cell wall synthesis.**
- **Choice C** → Antifungal that is usually used in disseminated fungal infections of fungemia
 - **Caspofungin MOA ⇒ Inhibits 1,3,B-D-glucan which inhibits fungal cell wall synthesis**
- **Choice D** → Antifungal that is used for most fungal infections
 - **Fluconazole MOA ⇒ Inhibits 14-demethylase, which inhibits ergosterol synthesis (fungal plasma membrane)**
- **Choice E** → Nystatin is either used orally for oral candidiasis or topically for vaginal candidiasis
 - **Nystatin MOA ⇒ Ionophore - Binds to ergosterol (fungal plasma membrane) and causes holes**

- **Choice F** → Used for influenza.
 - **Oseltamivir MOA** ⇒ Neuraminidase inhibitor which prevents virion release from the cell

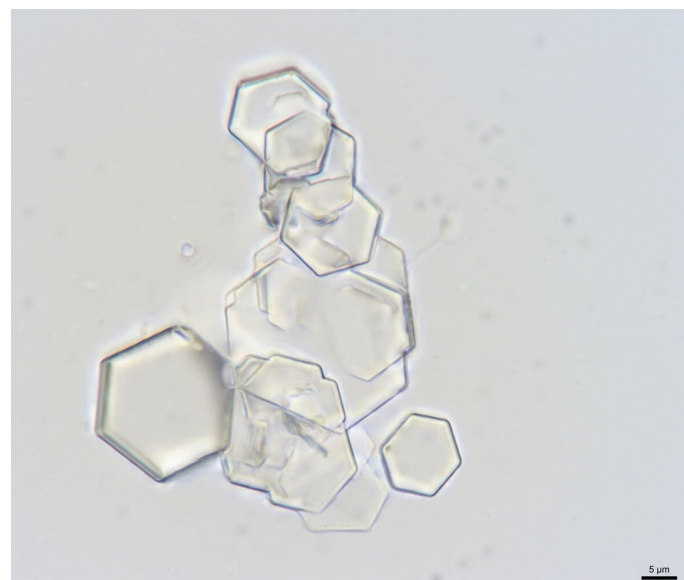
Q11

A 30-year-old man has had intermittent severe lower abdominal pain, right flank tenderness, and hematuria for 1 day. His brother has a history of recurrent renal calculi. The patient's urine turns cherry red when tested with nitroprusside. Hexagonal crystals are present in the urinary sediment. Which of the following substances is most likely to be found in an increased concentration in this patient's urine?

- A. Calcium
- B. Copper
- C. Cysteine
- D. Tyrosine
- E. Uric acid

▼ **Explanation**

- **Answer is C (Cysteine)**
 - **IMP Clues:**
 - Intermittent severe lower abdominal pain + flank pain + hematuria (get that DD going)
 - Brother has history of recurrent renal calculi (something hereditary)
 - Urine turns cherry red with nitroprusside + urine sediment shows hexagonal crystals (seals the deal, this is classic diagnosis of Cystinuria)
- **Dx → Cystinuria**
 - **AR disorder; Dysfunction of PCT transporter that reabsorbs Cysteine, Ornithine, Lysine, Arginine (COLA)**
 - Failure of reabsorption causes accumulation of cystine in urine → **Cystine Stones (Hexagonal Shaped)**
 - **Young Children or Middle Age** patients that present with **recurrent renal stones**
 - Diagnosed by a **positive urine cyanide nitroprusside test**
 - Cysteine is reduced in urine & -SH is produced.
 - -SH binds to cyanide → purple color



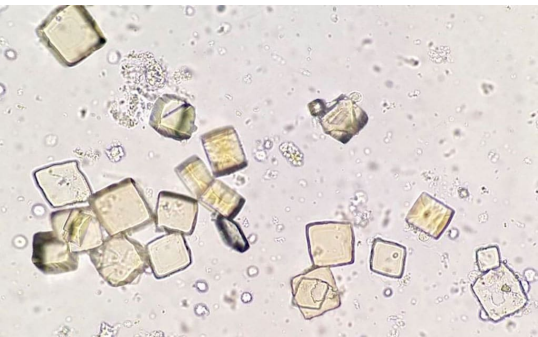
▼ **Other Choices**

- **Choice A** → **Calcium** in urine can present as either
 - **Calcium Oxalate** Crystals (**Crohn's disease, hypercalcemia**) in **acidic urine**
 - **Calcium phosphate** crystals in **alkaline urine**



Calcium Oxalate: Envelope shaped

- **Choice B** → Increased Copper in urine is a feature of **Wilson's disease**
 - **Young patient with Parkinson-like symptoms is Wilson's until proven otherwise.**
- **Choice D** → Isolated Tyrosine in urine is probably found in **tyrosinemia**
- **Choice E** → **Uric acid** can present as **Rhomboid Crystals** in **Gout or Tumor lysis syndrome** in **acidic urine**
 - **Remember that gout has needle-shaped stones in joints & rhomboid shaped crystals in urine.**



Rhomboid shaped Uric acid crystals

Q12

A 32-year-old woman comes to the physician because her sister recently died of melanoma. Other first-degree family members have been similarly affected, and other family members also have large pigmented skin lesions. Which of the following lesions is most likely on both sun-exposed and nonsun-exposed areas of this patient's skin?

- A. Acanthosis nigricans
- B. Basal cell carcinoma
- C. Blue nevi
- D. Dysplastic nevi
- E. Pigmented seborrheic keratosis

▼ Explanation

- Answer is D (Dysplastic Nevi)
 - IMP Clues:
 - Sister died from melanoma + other family members have been similarly affected (seems like something hereditary)
 - Other members have large pigmented skin lesions (okay so a lesion that CAN progress to melanoma)
 - Both sun-exposed & nonsun-exposed areas (very helpful for exclusion)
 - Dx → Familial Dysplastic Nevi Syndrome
 - AD condition characterized by the presence of multiple dysplastic nevi with high malignant potential (100% lifetime risk of developing melanoma).
 - Found on Both sun-exposed & nonsun-exposed areas.

▼ Other Choices

- Choice A → Acanthosis Nigricans is found on both sun-exposed & nonsun-exposed areas, yes. However, it is associated with insulin resistance & obesity. It can sometime be associated with gastric cancer. [asked on NBME] No melanomas though.
- Choice B → BCC is found in sun-exposed areas & it is usually pearly translucent papule.
- Choice C → Garbage so don't bother. It's a benign pigmented lesion that is stable in size & character.
- Choice E → Seborrheic Keratosis are waxy plaques with a "stuck on" appearance. The are found on both sun-exposed & nonsun-exposed areas. Their sudden eruption is associated with GI adenocarcinoma (Leser-Trelat Sign)

Q13

A 53-year-old woman who underwent an operation for breast cancer begins taking tamoxifen. Which of the following best represents the effects of tamoxifen on estrogen receptors in breast and uterine tissue in this woman?

Choices	Breast	Uterus
A	Agonist	Agonist
B	Antagonist	Antagonist
C	Antagonist	Partial agonist
D	Partial agonist	Antagonist
E	Partial agonist	Partial agonist

▼ Explanation

- Answer is C
 - Q asks for MOA of tamoxifen.

- **Tamoxifen** is a **Selective Estrogen Receptor Modulator (SERM)** which acts on:
 - **Breast** as an **antagonist** (hence, used for ER & PR positive breast cancer)
 - **Uterus** as a partial **agonist** (hence, the increased risk of endometrial hyperplasia & cancer)
 - **Bone** as a partial **agonist** (hence, decreases osteoporosis; however, benefit less than risk)
 - **Associated with *increased rate of thromboembolism***
- **Raloxifene** is also a **SERM** which acts on:
 - **Breast** as an **antagonist**
 - **Uterus** as an **antagonist** (hence, NO risk of endometrial cancer)
 - **Bone** as a partial **agonist** (decreases risk of osteoporosis)
 - **Risk of Thromboembolism is found to be *lower than Tamoxifen***

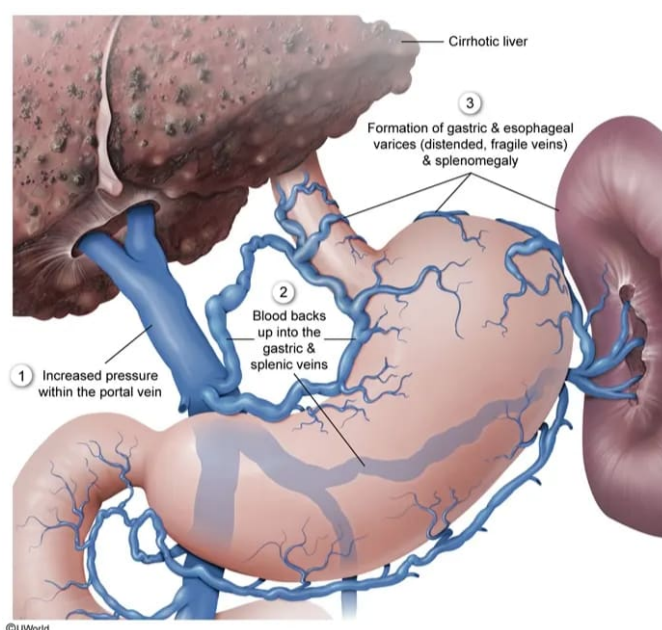
Q14

A 66-year-old woman with pancreatic cancer comes to the office because of a 2-day history of black, tarry stools. Physical examination shows pallor and diaphoresis. Upper endoscopy shows gastric varices. A CT scan of the abdomen shows thrombosis of the splenic vein. Which of the following veins is most likely the source of bleeding in this patient?

- A. Esophageal
- B. Left gastric
- C. Right gastric
- D. Right gastroepiploic
- E. Short gastric

▼ **Explanation**

- **Answer is E (Short gastric)**
 - **IMP Clues:**
 - Black tarry stools (Upper GI bleeding)
 - Pallor & Diaphoresis (patient is shocked)
 - Endoscopy shows gastric varices (the source of bleeding)
 - CT scan of the abdomen shows thrombosed splenic vein (caused by the pancreatic cancer, which caused the gastric varices)
- **Dx → Bleeding gastric varices**
 - The thrombosed splenic vein caused the pressure to increase in all its tributaries. One of them is the short gastric veins which supply the fundus of the stomach.



Concept Overview:

- 1. Patient has Upper GI bleeding caused by **esophageal** varices.**
 - a. What is source of bleeding → **Esophageal branches**
 - b. What vessel is thrombosed → **Left Gastric vein**
- 2. Patient has Upper GI bleeding caused by **gastric** varices.**
 - a. What is source of bleeding → **short gastric veins**
 - b. What vessel is thrombosed → **Splenic vein**
- 3. Patient with portal HTN**
 - a. TIPS is placed between what vessels → **Portal & Hepatic vein**
 - b. If a shunt is needed to bypass the PV, between what vessels should the shunt be placed → **Choose a systemic vein (Renal vein, which drains into IVC) + Related Portal circulation vein (Splenic vein)**

This is all you need to know regarding this concept. Trust me. I know my shit.

? Exact same Q but endoscopy shows Esophageal Bleeding. What is the thrombosed vessel?

▼ **Answer**
Left Gastric Vein

Q15

An undernourished 70-year-old man has fever, night sweats, and a productive cough. X-ray of the chest shows a cavitary lesion in the right lung. Numerous acid-fast bacilli are seen on microscopic examination of sputum. Which of the following cytokines plays the dominant role in the inflammatory response in this patient's lung?

- A. Granulocyte-macrophage colony-stimulating factor (GM-CSF)
- B. Interferon- α
- C. Interferon- γ
- D. Interleukin-4 (IL-4)
- E. IL-5

▼ Explanation

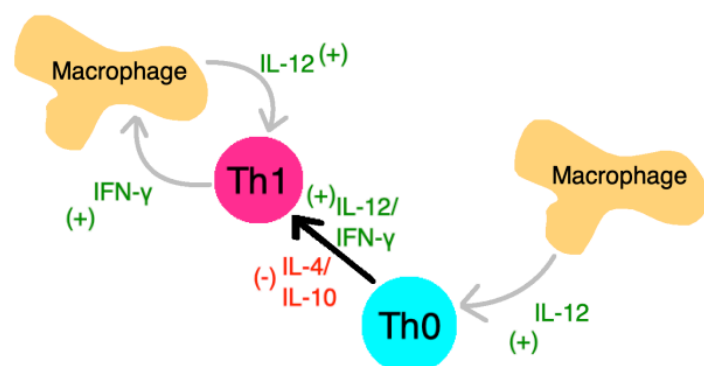
• Answer is C (Interferon-gamma)

◦ IMP Clues:

- Fever, night sweats, and productive cough (classic TB Triad)
- CXR shows cavitary lesions in the right lung + Numerous acid-fast bacilli seen on sputum examination (confirm TB)

• Dx → Tuberculosis Infection

- Q basically asks what cytokine plays the dominant role in the pathophysiology of TB.
- Pathophysiology of TB is predominantly all about the **granuloma formation** (the cavitary lesion). **A caseating granuloma.**
- Okay so what cytokine forms these granulomas?
 - **Interferon-gamma.**
 - Let's recap as this cycle is so HY:
 1. **Th1** is stimulated to release **INF-gamma**.
 2. **INF-gamma** activates **macrophages**.
 3. **Macrophages** form the **granulomas**.
 4. Both **IL-12** & **INF-gamma** further stimulate conversion of **Th0** to **Th1**.



HY Related Concepts:

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



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

▼ Answer

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



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

▼ Answer

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

▼ Other Choices

- **Choice A** → **GM-CSF** stimulates the formation of macrophages & other granulocytes from their progenitor cells. It is primarily used in **neutropenics**.
- **Choice B** → **INF-alpha** *maintains* granulomas, not form them.
- **Choice D** → **IL-4 (with IL-10)** stimulates the transformation of Th0 into Th2, which go on and stimulate B-cells to form antibodies.
- **Choice E** → **IL-5** is involved in eosinophils maturation. IL-5 monoclonal antibodies are actually used for severe intractable asthma associated with eosinophilia.

? What are the HY IL-5 Monoclonal antibodies??

▼ Answer

Benlizumab, Reslizumab, and Mepolizumab

("Ben Really like Maple syrup")

Q16

A previously healthy 4-week-old male newborn is brought to the emergency department because of persistent nonbilious projectile vomiting after eating. Physical examination shows visible abdominal peristalsis and a 2-cm, firm, ovoid mass in the right upper quadrant. Which of the following is the most likely diagnosis?

- A. Duodenal atresia
- B. Hepatoblastoma
- C. Pancreas divisum
- D. Pyloric stenosis
- E. Reflux esophagitis

▼ Explanation

• Answer is D (Pyloric Stenosis)

◦ IMP Clues:

- Non-bilious projectile vomiting (non-bilious means level of obstruction is above duodenum & projectile is a buzzy for pyloric stenosis)
- Visible abdominal peristalsis (a clinical finding of obstruction)
- 2-cm firm, ovoid mass in RUQ (location of pylorus)

• Dx → CHPS (Congenital Hypertrophic Pyloric Stenosis)

- Pylorus is congenitally thickened, causing an obstruction.
- Obstruction causes **nonbilious projectile vomiting**, leaving the child *dehydrated & hungry*.

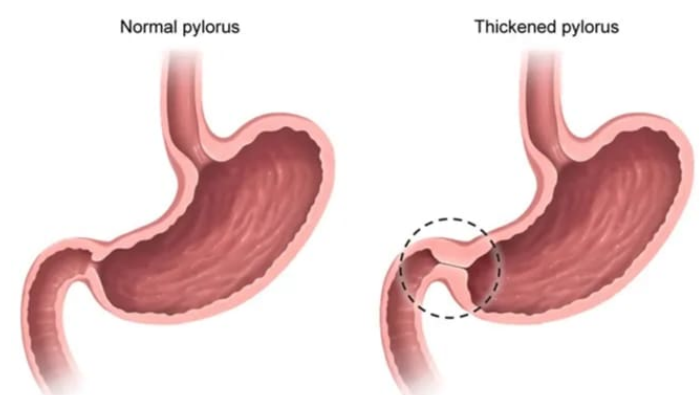
◦ USMLE tests the concept of Pyloric Stenosis by:

1. Asking for a diagnosis

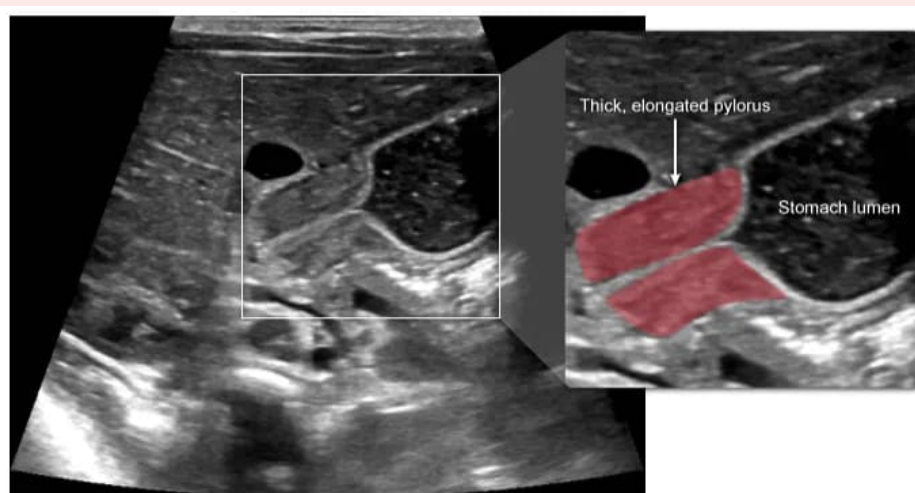
- They give you **non-bilious vomiting + olive-like abdominal mass +/- abdominal peristalsis**.
- Dx is → CHPS

2. Asking for expected arrows:

- They give you an arrows Q asking for **K, Cl, Na, HCO₃, PCO₂, and pH**
- Answer is → **low K, low Cl, normal/low Na, high HCO₃, high Pco₂, high pH**
- Vomiting causes **hypokalemic hypochloremic metabolic alkalosis**



USMLE can decide to give you an ultrasound like they do in STEP 2 for Pyloric Stenosis, showing a thickened elongated pyloric muscle:



? Vomiting vs Diarrhea
Arrows: K, Cl, Na, HCO₃, PCO₂, and pH

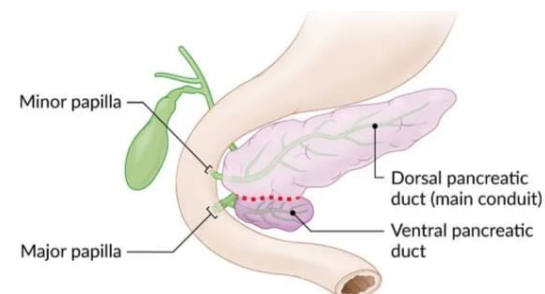
▼ Answer

Vomiting	Diarrhea
low K	low K
low Cl	normal Cl
normal/low Na	normal/low Na
high HCO ₃	low HCO ₃ ,
high PCO ₂	low Pco ₂ ,
high pH	low pH
"Hypokalemic Hypochloremic Metabolic Alkalosis"	"Non-Anion Gap Metabolic Acidosis"

▼ Other Choices

• Choice A → Duodenal Atresia

- Atresia of duodenum caused by **failure of duodenal recanalization** [asked on NBME]
 - Causes duodenal obstruction, which causes:
 - **Bilious vomiting** (as the atretic level is below the *ampulla of Vater*)
 - **Abdominal Distention & decreased stool formation**
 - **Polyhydramnios** (infant can't swallow amniotic fluid)
 - Associated with **Down Syndrome & Double-bubble Sign on AXR.**
- **Choice B → Hepatoblastoma** is a pediatric tumor which has nothing to do this vignette. He's trying to get you to see ohh an URQ mass where the liver is. No.
 - **Choice C → Pancreatic divisum** is LY for STEP1. But I like GI, so I'm going to explain it concisely.
 - Pancreas has 2 ducts (major & minor pancreatic ducts). These 2 ducts rise from different embryonal sites & fuse together.
 - Failure of fusion is pancreatic divisum.
 - Most people are asymptomatic; however, some do experience pancreatitis. Not a cause of vomiting here.
 - **Choice E → Reflux Esophagitis** is GERD. GERD is *not* bilious yes, but it is also *non-projectile*. Also, you will not find the signs of obstruction.



- Fused pancreatic buds, unfused ducts
- ↑ Risk of chronic abdominal pain/pancreatitis, but usually asymptomatic



What would biopsy of reflux esophagitis reveal?

▼ **Answer**

Basal zone hyperplasia with eosinophilic infiltration

Q17

A test has been developed to screen for human papillomavirus infections of the uterine cervix. If the prevalence of the disease increases by 50%, which of the following features of the test will increase?

- A. False-negative rate
- B. False-positive rate
- C. Predictive value of a positive test
- D. Predictive value of a negative test
- E. Sensitivity of the screening test
- F. Specificity of the screening test

▼ **Explanation**

- **Answer is C (Predictive value of a positive test)**
 - Q says if prevalence of the disease increases 50%, what will also increase.
 - First, you must know the diagram on the right/below:
 - Secondly, you must understand that sensitivity & specificity of a test **are not** affected by changes in prevalence. So directly, you see a Q with prevalence, you exclude sensitivity & specificity.
 - Thirdly, increase in prevalence = increase in TP = increase in PPV (TP is in PPV formula)
 - If we have a population of 1000 (200 diseases & 800 healthy)
 - We also have a screening test with 90% sensitivity & specificity
 - TP = 180
 - FN = 20
 - FP = 80
 - TN = 720
 - $PPV = TP / (TP + FP) = 180 / (180 + 80) = 180 / 260 = \sim 69\%$
 - $NPV = TN / (FN + TN) = 720 / (20 + 720) = 720 / 740 = \sim 97.3\%$
 - Now let's increase the prevalence by 50%
 - 300 diseases & 700 healthy is our new ratio
 - TP = 270
 - FN = 30
 - FP = 70
 - TN = 630

	Disorder	No Disorder
Positive Test Result	True Positive (TP)	False Positive (FP)
Negative Test Result	False Negative (FN)	True Negative (TN)

Sensitivity = $TP / (TP + FN)$
 Specificity = $TN / (TN + FP)$
 PPV = $TP / (TP + FP)$
 NPV = $TN / (FN + TN)$

- $PPV = TP/(TP+FP) = 270/(270+70) = \sim 79\%$ (increased)
- $NPV = TN/(FN+TN) = 630/(30+630) = \sim 95.4\%$ (decreased)

Q18

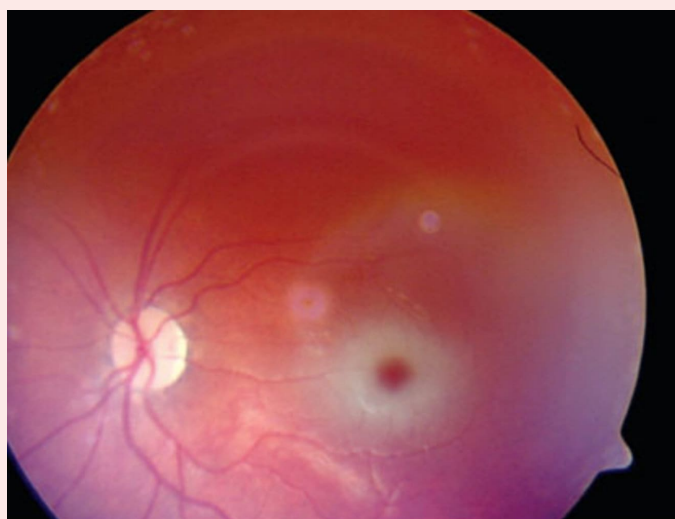
A 6-month-old girl is brought to the physician because her parents think she is weak and has an exaggerated reaction to loud noises. Examination shows muscle weakness, an increased startle reflex, and cherry-red spots on the retinas. The most likely cause of this disorder is accumulation of which of the following lipids in the patient's lysosomes?

- A. Ceramide
- B. Glucocerebroside
- C. GM₁
- D. GM₂
- E. GM₃
- F. Lactosylceramide

▼ Explanation

- **Answer is D (GM2)**
 - **IMP Clues:**
 - Cherry-Red Spots on the retina (only 3 things is cherry red spots on the retina: CRAO, and 2 lysosomal diseases)
 - Q asks which type of lipid is accumulated in patient's lysosomes (so we know it on of the 2 lysosomal diseases)
 - **Dx → Tay-Sachs Disease**
 - Deficiency of **Hexosaminidase A**
 - More common in **Ashkenazi Jewish population**
 - Accumulation of **GM2-Ganglioside**
 - HY Findings are **Cherry-Red Macula, onion-skin lysosomes, and NO Hepatosplenomegaly.**

This is how a Cherry-Red Macula looks like:



Cherry-Red Macula on the USMLE:

1. Tay-Sachs Disease

- Deficiency of **Hexosaminidase A**
- Accumulation of **GM2-Ganglioside**
- HY Findings are **Cherry-Red Macula, onion-skin lysosomes, and NO Hepatosplenomegaly.**

2. Neimann-Pick Disease

- Deficiency of **Sphingomyelinase**
- Accumulation of **Sphingomyelin**
- HY Findings are **Cherry-Red Macula, Foamy cells** (lipid laden macrophages) in bone marrow, and **Hepatosplenomegaly**

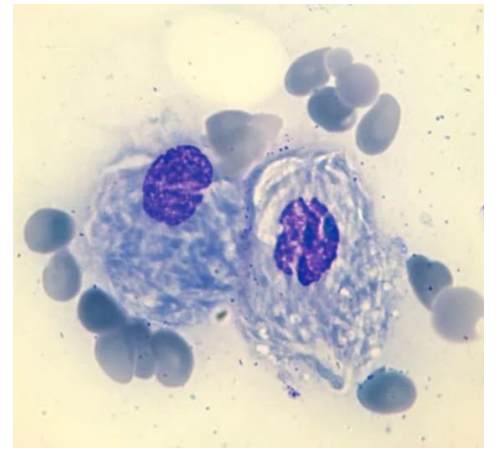
3. Central Retinal Artery Occlusion

- Occlusion of **central retinal artery**
- Due to **stroke, embolism**
- Presents as **SUDDEN PAINLESS** loss of vision in one eye in a patient with risk factors.
- Risk Factors are **Atherosclerosis** (carotid bruit), **AF**, **Thyrotoxicosis**, and **Hypercoagulability.**

▼ Other Choices

- **Choice A → Fabry Disease**
 - Deficiency of **alpha-Galactosidase**
 - Accumulation of **Ceramide Trihexoside**
 - HY Findings are **Hypohidrosis, Angiokeratosis, Renal Failure, and Peripheral Neuropathy**

- **Choice B → Gaucher's Disease**
 - Deficiency of **Glucocerebrosidase**
 - Accumulation of **Glucocerebroside**
 - HY Findings are **Osteoporosis, Avascular necrosis**, and **Gaucher Cells** (tissue paper cytoplasm cells)



- **Remaining Answer choices** are Biochemistry garbage you won't get tested on

Q19

A 36-year-old woman undergoes a total hysterectomy and bilateral salpingo-oophorectomy for extensive endometriosis of the pelvis. Following the operation, she decides that she does not want to begin hormone replacement therapy. Which of the following changes is most likely to occur in the gonadotrophs if this patient refuses this postoperative treatment?

- A. Apoptosis
- B. Atrophy
- C. Hyperplasia
- D. Metaplasia
- E. Necrosis

▼ **Explanation**

- **Answer is C (Hyperplasia)**
 - Patient here removed her ovaries & refused hormonal (Estrogen) therapy.
 - Q asks what would happen to gonadotrophs (cells in pituitary glands that produce FSH & LH)
 - **NO Estrogen → NO feedback inhibition on FSH & LH → Increased secretion on FSH & LH → still NO feedback inhibition (body thinks FSH & LH not enough)**
 - **Gonadotrophs increase in number (Hyperplasia) to secrete more FSH & LH (Choice C)**

Q20

A 56-year-old man undergoes a renal transplant. Five minutes after the graft blood vessels are anastomosed to host vessels, he develops hemorrhage and thrombotic occlusion of the graft vessels. Which of the following is the most likely mediator of this process?

- A. CD4+ T lymphocytes
- B. CD8+ T lymphocytes
- C. IgA plus complement
- D. IgG plus complement
- E. Macrophages
- F. Mast cells

▼ **Explanation**

- **Answer is D (IgG plus complement)**
 - **IMP Clues:**
 - Renal transplant (either rejection Q, virus reactivation, or immunology Qs)
 - 5 mins (timing is everything in these graft rejection Qs)
 - Thrombotic occlusion of graft vessels (V.IMP clue + the timing for the dx)
- **Dx → Hyperacute Graft Rejection**
 - **There are 3 Types of graft rejection:**
 1. **Hyperacute Rejection**
 - Timing → **minutes to hours**

- Etiology → **Type 2 HS** reaction due to **preformed** antibodies to donor antigen
- Pathophysiology → **Complement activation & Neutrophils infiltration** → vessel **ischemia & necrosis** (*fibrinoid necrosis*)

2. **Acute Rejection**

- Timing → **< 6 months**
- Etiology → **Type 4 HS** reaction due to **cell-mediated (CD8)** reaction to **donor MHC** (CD4 antibodies are also involved, but CD8 dominates)
- Pathophysiology → **Lymphocytic infiltration** causing vasculitis

3. **Chronic Rejection**

- Timing → **Months - Years**
- Etiology → **Type 4 HS** reaction due to **mixed cell-mediated/humoral reaction**
- Pathophysiology → **Fibrosis & Vessel obliteration**



Rapid Review Case Scenarios:

1. Patient underwent renal transplant & intra-op **mottling** was found.
 - Dx → **Hyperacute Rejection**
 - Biopsy → **Fibrinoid Necrosis**
2. Patient underwent renal transplant **3 weeks ago** + developed fever, oliguria, and high Creatinine.
 - Dx → **Acute Rejection**
 - Biopsy → **Vasculitis with Lymphocytic Infiltration**
3. Patient underwent lung transplant **1 years ago** + developed SOB, fever, and cough.
 - a. Dx → **Chronic Rejection**
 - b. Biopsy → **Fibrosis & endarteritis obliterans**

Q21

A 4-month-old female infant is brought to the emergency department by her parents because she had a seizure 1 hour ago. She has had diarrhea for the past 3 days. She has consumed nothing but water for the past 24 hours because her parents ran out of formula. She is most likely to have which of the following electrolyte abnormalities?

- A. Hyperchloremia
- B. Hyperglycemia
- C. Hypoglycemia
- D. Hyponatremia
- E. Hyponatremia

▼ **Explanation**

- **Answer is E (Hyponatremia)**
 - **IMP Clues:**
 - Seizures (DD is hypocalcemia or hyponatremia)
 - She had diarrhea (so electrolytes all over the place & dehydrated)
 - Consumed nothing but water because parents ran out of formula (Water in an infant is a big NO)
 - **Dx → Dilutional Hyponatremia**
 - Patient was *dehydrated* & parents ran out of formula, so they gave her *water*.
 - Water is not given to infants because they lack full renal maturation.
 - Water cause **dilutional hyponatremia**, which caused the **seizures**.

Q22

A 28-year-old woman at 18 weeks' gestation has palpitations. Laboratory studies show an increased serum total thyroxine (T₄) concentration. Which of the following tests is best to confirm a diagnosis of hyperthyroidism in this patient?

- A. Fine-needle aspiration biopsy of the thyroid gland
- B. Free T₄
- C. Radioactive iodine uptake
- D. Serum total triiodothyronine (T₃)
- E. Thyroid antibodies

▼ **Explanation**

- **Answer is B (Free T₄)**
 - **IMP Clues:**

- 18 weeks gestation (she's pregnant)
- Has palpitations (okay, get the DD list ready)
- Increased serum total T4 concentration (expected due to pregnancy + might be the cause of palpitations)

◦ **How does pregnancy affect Thyroid Hormones?**

- Well, we know that pregnancy causes elevated estrogen.
- **Estrogen** stimulates the liver to produce **more TBG**
- More TBG causes **Total T4 to increase**
 - **Total T4 = T4 carried by TBG + Free T4**
- **Free T4** is the *effective* chunk. **Free T4 is normal** so **TSH is normal** as well.
- So, in pregnancy, we have **NORMAL Free T4, HIGH Total T4, and NORMAL TSH**

◦ Q asks how do we confirm that the patient has hyperthyroidism?

- If **Free T4** is **high**, then we do have **hyperthyroidism**
- As we said, **Free T4** is the **effective part**. If it is high, then it is what to blame for symptoms of hyperthyroidism.

▼ **Other Choices**

- **Choice A** → You don't put a needle in a person's throat to diagnose high "hyperthyroidism"
 - Needle Aspiration Biopsy is taken if a tumor is suspected.
 - On the USMLE, thyroid tumors are almost always non-secreting. Just a cold hard nodule.
- **Choice C** → Radioactive Iodine on the USMLE is very simple.
 - You will get plenty of Arrow Qs asking about uptake in most thyroid disorders
 - Wanna learn something cool?
 -  **NEVER CHOOSE UP ARROW UNLESS IT IS GRAVE'S DISEASE.**
 - Even if it is Subacute thyroiditis with hyperthyroidism? Nope. Only Graves. Trust me on this.
- **Choice D** → Total T3 will not help. Is the increased Total due to increased TBG? Or is it due to increased Free T3? Or both? I'd have to measure the Free part to make sure.
- **Choice E** → You check for thyroid antibodies after you establish the diagnosis of hypo/hyperthyroidism not before. You measure the antibodies to find the etiology: is it Graves? is it Hashimoto's? Not is it hypo or hyperthyroidism.

Q23

An 80-year-old woman cannot concentrate her urine above 450 mOsmol/kg H₂O. She accumulates 450 mOsmol/day of solute, which must be excreted by the kidneys. She loses 900 mL of water insensibly and 100 mL of water in sweat and feces. Which of the following best represents the minimum volume of water that this woman must ingest in food and drink daily (in L) to prevent an increase in plasma osmolality?

- A. 0.5
- B. 1.0
- C. 1.5
- D. 2.0
- E. 2.5

▼ **Explanation**

- **Answer is D (2.0)**
 - **IMP Clues:**
 - Woman cannot concentrate her urine above 450mOsmol/Kg H₂O (okay so the maximum she can concentrate her urine is 450 solutes in 1kg of water)
 - She accumulates 450 mOsmol/day of solutes (okay so we need that 450 out to maintain balance)
 - She losses 900ml insensibly & 100ml in sweat & feces (okay another 1L total needs to be replaced)
 - Q wants the *minimum* volume that needs to be ingested to **maintain same plasma osmolality**.
 - Okay so same plasma osmolality, **we need the ingested to equal the excreted**.
 - What's the excreted?
 - **900ml insensible water loss + 100ml in feces & sweat = 1L**
 - **450mOsmol/day = 1L**
 - The maximum her kidney can concentrate is 450mOsmol/kg

- Kg of water = Liter of water
- so, for every 1L of urine, 450mOsmol can be excreted.
- This is convenient & easy to calculate because what needs to be excreted per day (450mOsmol/day) is equal to her maximum concentrating powers. (450mOsmol/Liter)

- **So, what's the total she is excreting? 2L**
- **So how much should she ingest to equal what she's excreting? 2L (Choice D)**

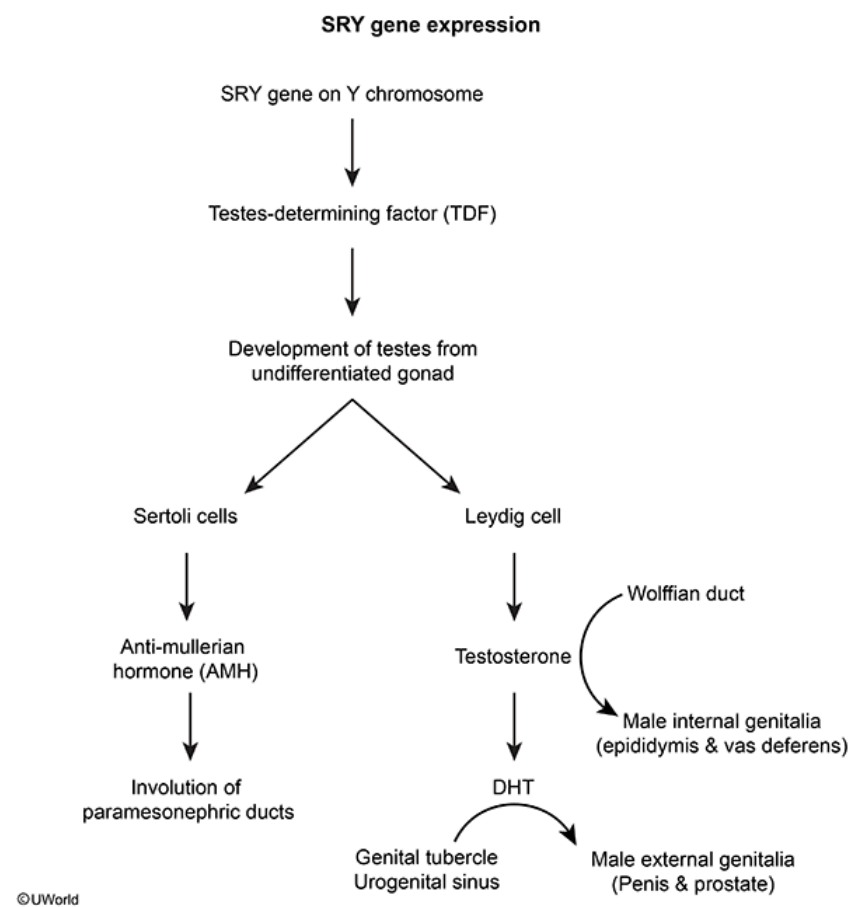
Q24

A newborn has female external genitalia and a 46,XY karyotype. An MRI shows male genital ducts. The most likely cause of this anomaly is a gene mutation resulting in the absence of expression of which of the following hormones or factors?

- A. Antimüllerian hormone
- B. Dihydrotestosterone
- C. Estrogen
- D. Sex-determining region of the Y chromosome (SRY) protein
- E. Testosterone

▼ **Explanation**

- **Answer is B (Dihydrotestosterone)**
 - Okay so **46 XY** → patient has **Y chromosome & SRY gene (Choice D)**
 - MRI shows **male genital ducts (internal genitalia) & No female ducts** → patient as **MIF (Anti-Müllerian hormone) (Choice A)**
 - Has **female external genitalia** → patient has **dysfunctional DHT (receptor or 5-alpha-reductase enzyme deficiency) (Choice B)**
 - **Testosterone & Estrogen** don't affect any of these processes (**Choices C & E**)
- **Dx → 5-alpha Reductase Deficiency**
 - **DHT binds androgen receptors** on the genital tubercle to promote **differentiation into external male genitalia**
 - DHT is absent in males with 5-alpha reductase deficiency, so the genital tubercle **differentiates into female external genitalia**
 - DHT also mediates testicular descent, so the **testes are undescended**
 - **At puberty, physiologic increases in testosterone overcomes the deficiency of 5-alpha reductase, causing virilization of "apparent" females.** They present with:
 - **Hirsutism**
 - **Nodulocystic acne**
 - **Clitoromegaly**
 - **Voice deepening**
 - **Increased muscle mass**



Q25

A 40-year-old woman who had pneumonia due to Streptococcus pneumoniae 6 months ago comes to the physician for a follow-up examination. X-rays of the chest show no abnormalities. Which of the following is produced by the cell type most likely responsible for the restitution of near-normal lung structure?

- A. Factor VIII (antihemophilic factor)
- B. Histamine
- C. P-selectin
- D. Surfactant
- E. Type I collagen

▼ **Explanation**

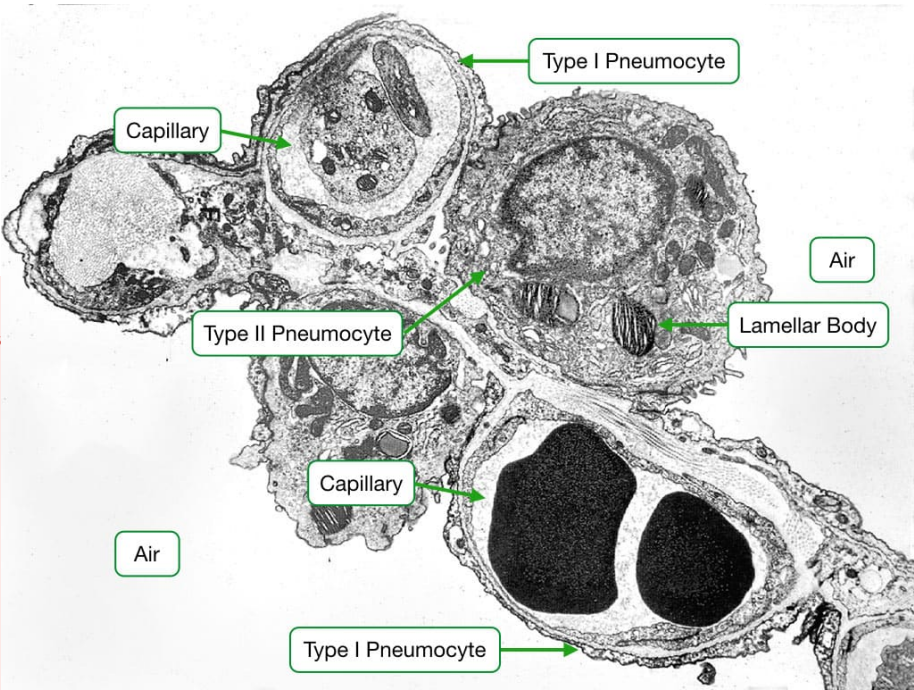
- Answer is D (Surfactant)
 - Q asks what is produced by the same cell that causes lung regeneration
 - I asked you this Q a few blocks back. Its **Type 2 pneumocytes**.
 - What also does **Type 2 pneumocytes** do?
 - **Secrete Surfactant** (Choice D)

What else do you need to know?

Type I pneumocytes ⇒ Cover 95% of the alveolar surface & are involved in **gas exchange**

Type II pneumocytes ⇒ cover 5% of the alveolar surface & are involved in **regeneration of alveolar epithelium & surfactant production (via lamellar bodies)**

- In Post-Inflammatory Fibrosis, **Type II pneumocytes increases**, **fibroblasts increases**, and **Type I pneumocytes decrease**
- Surfactant is made up of lipids, most HY to know is **"Phosphatidylcholine/Lecithin"** [asked on NBME] and the other LY one is phosphatidylglycerol
 - **Lecithin-to-sphingomyelin ration of ≥ 2 indicated maturity of fetal lungs**
 - Function is to **decrease surface tension, prevent alveolar collapse, and increase compliance of alveoli**



▼ Other Choices

- Choice A → **Factor 8** deficiency is Hemophilia A. Nothing to do with lungs.
- Choice B → **Histamine** is one of the inflammatory mediators. Also, irrelevant to lungs.
- Choice C → **P-selectin** (with E-selectin & L-selectin) allow for neutrophil migration & rolling to inflammatory sites.
- Choice E → **Type 1 collagen** is what makes up bones & Late-stage wound healing.

Q26

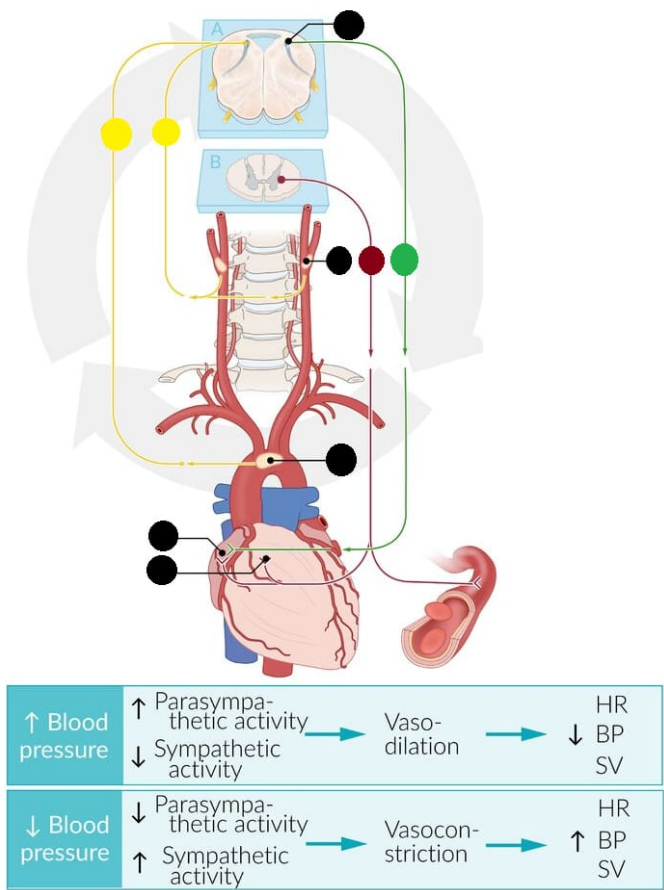
A 34-year-old man is evaluated after becoming light-headed after running 12 miles of a marathon on a hot day. His pulse is 130/min and his blood pressure is 80/60 mm Hg. Which of the following sets of changes in his autonomic nervous system is most likely?

Choices	Number of Impulses From Carotid Baroreceptor	Sympathetic Efferent Activity	Parasympathetic Efferent Activity
A	↑	↑	↑
B	↑	↑	↓
C	↑	↓	↑
D	↓	↑	↓
E	↓	↓	↑
F	↓	↓	↓

▼ Explanation

- Answer is D
 - Patient is hypotensive (BP is 80/60 mmHg)
 - Q asks what arrows are expected.

- Hypotension is a critical state, so sympathetic system is activated
 - How?
 - Carotid baroreceptors detect pressure levels
 - When pressure gets **high**, carotid baroreceptor impulses **increase to activate parasympathetic centers to decrease HR.**
 - When pressure gets **low** (as in this hypotensive patient), **decreased carotid baroreceptor impulses** ⇒ **decreased parasympathetic activity**
 - This is reciprocated by an **increase in Sympathetic Stimulation**, which causes **increased vasoconstriction**, resulting in:
 - **Increased Heart Rate**
 - **Increased Stroke Volume**
 - **Increased Blood Pressure**
 - Bottom line is patient is **hypotensive** ⇒ so **less pressure** in baroreceptors ⇒ **less impulses** from carotid baroreceptors to parasympathetic centers ⇒ **decreased Parasympathetic activity** ⇒ **Increased Sympathetic activity** (Choice D)



Q27

A 30-year-old woman develops "dimness of vision," loss of color vision, and constriction of visual fields 1 month after beginning combination therapy including isoniazid, rifampin, pyrazinamide, ethambutol, and cycloserine for pulmonary tuberculosis. Which of the following drugs is most likely responsible for these adverse effects?

- A. Cycloserine
- B. Ethambutol
- C. Isoniazid
- D. Pyrazinamide
- E. Rifampin

▼ Explanation

- Answer is B (Ethambutol)
 - IMP Clues:
 - Dimness of vision + loss of color vision + constriction of visual fields (okay so ocular symptoms)
 - After beginning TB Drugs (okay so likely a side effect of those drugs)
 - Dx → Drug-induced Optic neuritis
 - Ethambutol is the drug that causes optic neuritis



TB Drugs Rapid Review:

Use the **"RIPE"** mnemonic

1. Rifampin

- **MOA** → Inhibition of **DNA-dependent RNA polymerase**
- **Side Effects** → Hepatotoxicity - Orange body secretion - CYP450 **induction**

2. Isoniazid

- **MOA** → Inhibition of **mycolic acid synthesis**
- **Side Effects** → Hepatotoxicity - Vitamin B6 deficiency - CYP450 **inhibition**

3. Pyrazinamide

- **MOA** → Inhibition of **fatty acid synthase I**
- **Side Effects** → Hepatotoxicity - Hyperuricemia (gout)

4. Ethambutol

- **MOA** → Inhibition of **arabinosyl transferase**
- **Side Effects** → Optic neuritis - Hyperuricemia (gout)

Few Tricks to help you memorize the side effects as they are HY:

"RIP" = Hepatotoxic

- Rifampin - Isoniazid - Pyrazinamide = Hepatotoxic

"PE" = Hyperuricemia & Gout

- Pyrazinamide - Ethambutol = Hyperuricemia & Gout

Isoniazid has 3 "i" & so does Inhibition

- Isoniazid = CYP450 Inhibition

Rifampin has 2 "i" & so does "Induction"

- Rifampin = CYP450 inducion

EthambutOI = Optic neuritis

Q28

A physician prescribes a recently marketed drug for 20 patients. After several months, five patients develop increased serum AST and ALT activities and show clinical symptoms of hepatotoxicity. The physician discontinues the drug for all patients and reports the adverse effects to the FDA. The physician has participated in which of the following phases of clinical drug testing?

- A. Phase 1
- B. Phase 2
- C. Phase 3
- D. Phase 4

▼ Explanation

- **Answer is D (Phase 4)**
 - **IMP Clues:**
 - Recently marketed drug (this is all you need)
 - **If a drug is on the market, this means it already had the FDA approval and is now in stage 4.**
 - USMLE always does this trick. They may give you a 5-line vignette and flood you with unnecessary garbage, while all you need is that "marketed drug". **Boom phase 4.**

▼ Other Choices

- **Choice A** → **Phase 1** mainly tests **safety**, which is tested on **<10 (10¹) healthy or diseases patients**.
- **Choice B** → **Phase 2** mainly tests **Efficacy & Safety**, which is tested on **< 100 (10²) of diseases patients**.
- **Choice C** → **Phase 3** *compares between the new drug & existing treatments* on **100s of people (10³)**

Q29

A 75-year-old woman has the sudden onset of Horner syndrome on the right, dysphagia, and difficulty speaking. Pain and temperature sensations are decreased on the right side of her face and left side of her body. Which of the following arteries is most likely to have been occluded?

- A. Anterior inferior cerebellar

- B. Basilar
- C. Posterior cerebral
- D. Posterior inferior cerebellar
- E. Superior cerebellar

▼ Explanation

- **Answer is D (Posterior Inferior Cerebellar)**

- **IMP Clues:**

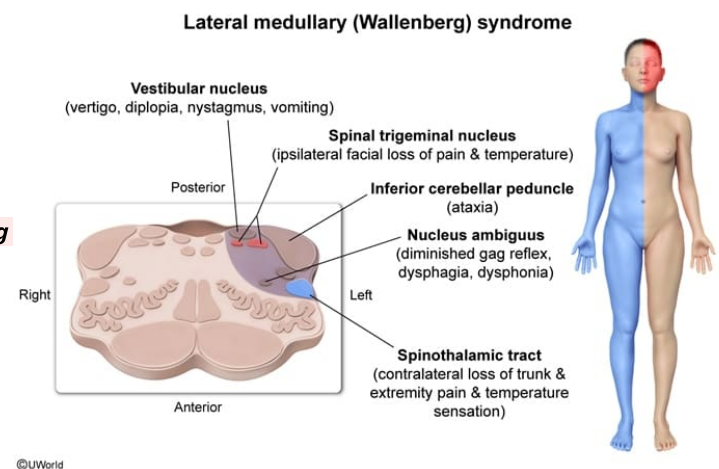
- Sudden onset (sudden onset is usually trauma or embolism)
- Horner syndrome + Dysphagia + Difficulty speaking + decreased pain & temperature on right side of face + left side of body (dysphagia & hoarseness are buzzy for Lateral Medullary Syndrome)

- **Dx → Lateral Medullary Syndrome**

- **Occlusion of Posterior Inferior Cerebellar Artery (PICA)**

- Affection of:

- **Sympathetic Chain → *IPSILATERAL* Horner Syndrome**
- **Cerebellum → *IPSILATERAL* Ataxia**
- **CN X → Hoarseness & Uvula deviation to opposite side *[This here is the buzzy finding in Wallenberg Syndrome]***
- **Trigeminal nucleus → *IPSILATERAL* facial loss of pain & temperature sensation**
- **Spinothalamic tract → *CONTRALATERAL* bodily loss of pain & temperature sensation**



USMLE will give you a similar picture to the one below in a patient with feature of stroke AND HOARSENESS/DYSPHAGIA.

- Q then asks for site of lesion; Choose **Lateral Medulla**, and we know that it is supplied by **Posterior ICA**; so posterior.



▼ Other Choices

- **Choice A → AICA occlusion causes Lateral pontine syndrome**

- Similar presentation to lateral medullary syndrome above. Just substitute the CN X palsy to **CN VII palsy**.
- Horner syndrome + **facial nerve palsy** + decreased pain & temperature on right side of face + left side of body
- Facial nerve palsy presentations:
 - ***Ipsilateral* hyperacusis**
 - ***Ipsilateral* loss of nasolabial fold + facial drooping**
 - ***Ipsilateral* inability to blow (buccinators)**

- **Choice B → Basilar artery occlusion causes Locked-in Syndrome** (sounds cool I know)

- Triad:

- **Quadriplegia** (can't move)
- **Aphonia** (can't talk)
- **Impaired *horizontal* eye movement but intact vertical** (only looks up & down)

- **Choice C → PCA occlusion causes *contralateral* homonymous hemianopia with macular sparing**

- **Choice D → You won't get tested on**

Q30

A 23-year-old man drinks alcohol heavily on a weekend. Which of the following cellular changes is most likely to occur in his liver?

- A. Acute cellular swelling
- B. Agenesis
- C. Apoptosis
- D. Atrophy
- E. Fatty change
- F. Hyperplasia
- G. Hypertrophy
- H. Hypoplasia
- I. Metaplasia

▼ Explanation

- **Answer is E (Fatty Change)**
 - This Q is poorly written. If a man drinks heavily for **one** day, this causes **acute cellular swelling**
 - **Chronic drinking is what causes Fatty changes**, which then **progresses to cell swelling** then **necrosis**.
 - BUT WHAT NBME WANTS IS KING.
 - **Binge drinking is → Fatty change.**

▼ Other Choices

- **Choice A** → We talked about it
- **Choice B** → Agenesis means not formed.
- **Choice C** → Programmed cell death
- **Choice D** → Decrease in size or number
- **Choice F** → Increase in number
- **Choice G** → Increase in size
- **Choice H** → Incomplete development
- **Choice I** → Reversible change from one type of tissue to another type of tissue

Q31

A healthy 32-year-old woman at 35 weeks' gestation is participating in a study of normal pregnancy. During her labor, oxytocin concentrations are noted to increase. Which of the following is the most likely underlying cause of this finding?

- A. Birth canal reflex
- B. Estrogen
- C. Human chorionic gonadotropin
- D. Progesterone
- E. Prolactin
- F. Prostaglandin E₂

▼ Explanation

- **Answer is A (Birth Canal Reflex)**
 - Q asks why does oxytocin *increase* during labor?
 - We all know from our OBGYN rounds that this is **Ferguson Reflex**
 - The descending head of baby **pushes on the cervix**, causing the **cervix to dilate**.
 - This dilation causes **oxytocin levels to rise**.
 - **Oxytocin causes the uterus to contract more, causing the cervix to dilate more & the cycle goes on and on.**



What 2nd Messenger does Oxytocin use?

▼ Answer

Activates Gq → Increases IP3

Q32

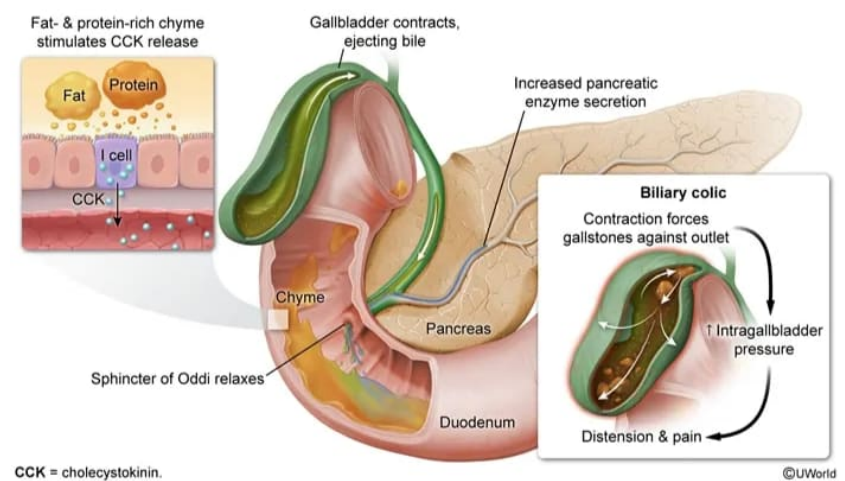
A 56-year-old man undergoes surgical resection of the duodenum after injuring his small intestine in a motor vehicle collision. Which of the following is most likely expected to decrease after this procedure?

- A. Release of cholecystokinin
- B. Release of gastrin
- C. Secretion of intrinsic factor
- D. Secretion of pepsin
- E. Secretion of vasoactive intestinal polypeptide

▼ Explanation

• Answer is A (Release of Cholecystokinin)

- Q says patient removed the duodenum & asks what is expected to decrease:
 - Duodenum has 3 types of Cells that secrete GI-related hormones & peptides
 1. **I-Cells** → secretes **CCK** (the answer here)
 2. **S-Cells** → secretes **Secretin**
 3. **K-Cells** → secretes **GIP**
 - Only of the above choices, **CCK is found (Choice A)**
 - Stimulant of CCK secretion?
 - **Fatty food**
 - Function of CCK?
 - **GB contraction to release bile**
 - **Relaxation of sphincter of Oddi**
 - **Stimulates pancreas secretions (rich in lipase)**



? Patient ate fatty food + felt biliary colic. What hormone / peptide is responsible for that pain?

▼ Answer
CCK

? USMLE shows you a graph of concentrations of different pancreatic secretions. A hormone is then administered which causes the number of total secretions to increase while retaining the same concentrations of enzymes. What hormone was administered?

▼ Answer
Secretin - Increases water & HCO₃ portion of pancreatic secretions

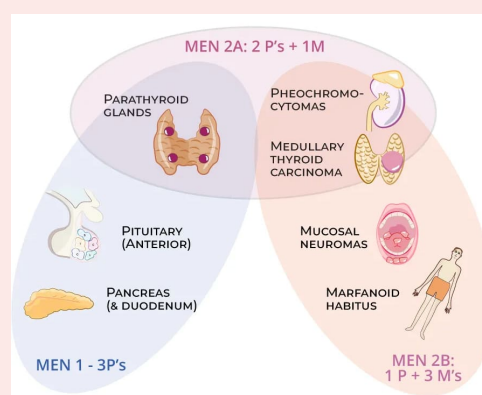
▼ Other Choices + HY Related Notes

- Choice B → **Gastrin** is released from **G-cells** of **stomach antrum** & stimulates **HCL secretion**

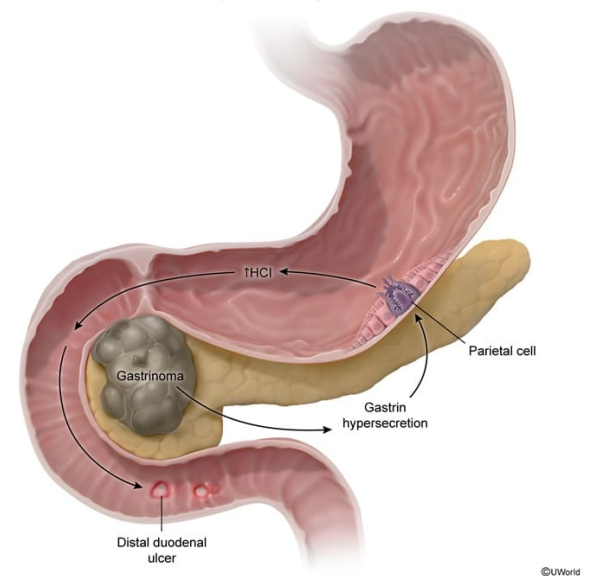
Gastrinoma (Zollinger Ellison Syndrome)

- **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**

Can also be part of MEN 1 Syndrome:



Zollinger-Ellison syndrome



- Choice C → **IF** is released from **parietal cells** of **stomach**
 - Deficiency causes vitamin B12 deficiency
- Choice D → **Pepsinogen** is secreted by **chief cells** of **stomach**
- Choice E → **VIP** is secreted from **enteric neurons**

? What are the features of VIPoma?

▼ Answer

VIPoma on the USMLE can present in 2 ways:

1. WDHA Syndrome

- Watery Diarrhea
- Hypokalemia
- Achlorhydria

2. Flushing + Diarrhea + pancreatic mass on CT

- Dx → **VIPoma**
- Expected electrolyte disturbance → **Hypokalemia**

Q33

A 2-week-old male newborn has a patent ductus arteriosus. Which of the following findings is most likely present in this newborn?

- A. Higher than normal left ventricular cardiac output
- B. Higher than normal peripheral vascular resistance
- C. Higher than normal right ventricular P_{O_2}
- D. Lower than normal pulmonary capillary blood flow
- E. Lower than normal systemic arterial P_{O_2}

▼ Explanation

- Answer is A (Higher than normal left ventricular cardiac output)

- This newborn has **PDA**. Let's review the hemodynamics.

- **Patent Ductus Arteriosus is an opening between the aorta and the pulmonary trunk,**
 - Blood moves out of **LV** → **Aorta** → **PDA** → **Pulmonary trunk** → **LA & LV**.
 - This causes **volume overload (preload)** on the **left side of the heart**.
 - **Increased preload = increased stretch = more powerful contraction [This is Starling's law] = higher Stroke Volume**

$$CO = HR \times SV$$

- **INCREASED SV = Increased CO**

? What's the most HY cause of PDA?

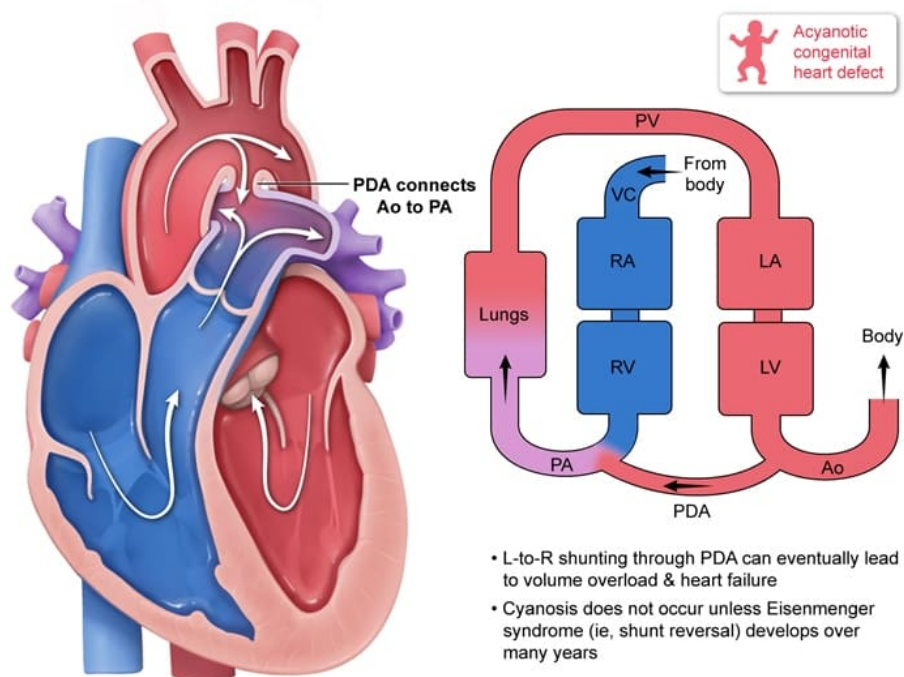
▼ Answer

Congenital Rubella Syndrome



Prostaglandins keep PDA open, while high Oxygen levels cause the PDA to close

Patent ductus arteriosus



Ao = aorta; LA = left atrium; L-to-R = left-to-right; LV = left ventricle; PA = pulmonary artery; PV = pulmonary veins; RA = right atrium; RV = right ventricle; VC = vena cava; PDA = patent ductus arteriosus.

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▼ Other Choices

- **Choice B** → **Peripheral vascular resistance** is influenced by **arterioles**.
 - Arterioles *contract* = **higher BP**
 - Arterioles *relax* = **lower BP**
 - The **increased CO** is actually reciprocated by a **decrease in BP** to maintain the balance
 - **Decreased BP is decreased peripheral vascular resistance**
- **Choice C** → **Higher than normal RV P_{O_2}** ? This is nonsense. The blood is returning to the **Left side of the heart**. The Right side is not involved.

- **Choice D** → **pulmonary blood flow is actually increased**. RV gives to pulmonary trunk and Aorta/LV also give to pulmonary trunk. So *HIGHER* pulmonary blood flow
- **Choice E** → **Lower systemic Po2** would be a result of a pulmonary pathology causing decreased oxygenation → hypoxia

Q34

A 55-year-old woman with a benign nodule in the left lobe of the thyroid gland is undergoing a partial thyroidectomy in the hospital. A branch of the thyrocervical trunk is ligated to interrupt the blood supply of the resected specimen. It is most appropriate to also ligate a direct branch of which of the following arteries in this patient?

- A. Brachiocephalic
- B. Deep cervical
- C. External carotid
- D. Lingual
- E. Vertebral

▼ **Explanation**

- **Answer is C (External Carotid)**
 - Simple Anatomy Q here. Patient undergoes partial thyroidectomy & the surgeon will ligate a branch of thyrocervical trunk supplying the thyroid (inferior thyroid artery) & asks the other artery (superior thyroid artery) that will be ligated in branch of what artery.
 - Let's Discuss Blood Supply of the Thyroid gland + HY Related Notes :)
- **Blood Supply of Thyroid Gland**
 - Thyroid gland is supplied by 2 main arteries: *Superior & Inferior Thyroid arteries*

1. **Superior Thyroid Artery**

- Origin: **Common Carotid** → **External Carotid** → **Superior Thyroid artery**
- HY Related Notes: The **External Laryngeal branch of the Superior Laryngeal Nerve** courses in close proximity to the Superior Thyroid Artery.

? **What is the function of the External laryngeal nerve?**

▼ **Answer**
External Laryngeal nerve controls the cricothyroid muscles.

The *Internal* Laryngeal nerve supplies the mucosa above the vocal cords + secretomotor action.

2. **Inferior Thyroid Artery**

- Origin: **Subclavian artery** → **Thyrocervical trunk** → **Inferior Thyroid artery**
- HY Related Notes: The **Recurrent Laryngeal nerve** courses in close proximity to the Inferior Thyroid Artery.

? **What is the function of the Recurrent laryngeal nerve?**

▼ **Answer**
Recurrent Laryngeal Nerve supplies **all intrinsic laryngeal muscles except cricothyroid** (supplies by external laryngeal nerve) & supplies **sensation (+ secretomotor action)** to mucosa below vocal cords

 Let's Recap

1. **External Branch of Superior Laryngeal Nerve**

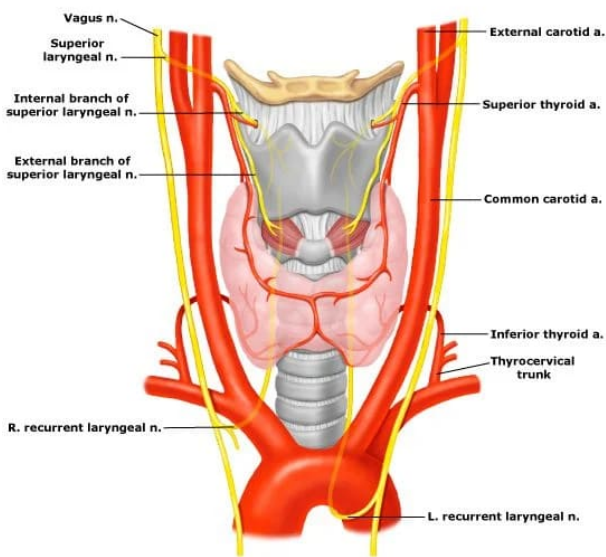
- Motor: **Cricothyroid** muscle
- Sensory: —

2. **Internal Branch of Superior Laryngeal Nerve**

- Motor: —
- Sensory: Mucosa above vocal cords

3. **Recurrent Laryngeal Nerve**

- Motor: **All intrinsic laryngeal muscles (except cricothyroid)**
- Sensory: Mucosa below vocal cords



▼ **Other Choices**

- **Choice A** → Branches off into Right subclavian & Right Common Carotid arteries
- **Choice B** → Supplies Deep compartments of Neck & Back

- **Choice D** → Supplies tongue & floor of mouth
 - **Choice E** → Supplies brainstem & cerebellum
-

Q35

A 28-year-old man comes to the physician for evaluation of infertility. Physical examination shows no abnormalities. His serum concentrations of testosterone, follicle-stimulating hormone, luteinizing hormone, and prolactin are within the reference ranges. Which of the following is most likely to be found in an abnormal concentration on semen analysis?

- A. Fructose
- B. 5 α -Reductase
- C. Selenium
- D. Sodium
- E. Zinc

▼ **Explanation**

- **Answer is A (Fructose)**
 - **IMP Clues:**
 - 28-year-old man (should have no problems)
 - Infertility (okkk, noted)
 - Examination shows no abnormalities (no varicocele or gynecomastia or apparent syndromes)
 - Serum Testosterones, FSH, LH, and PRL are normal (so non-hormonal issue)
 - Okays so patient has **infertility despite normal hormones & examination.**
 - Let's go through the answer choices
 - **Choice A → Fructose.**
 - Fructose is **found in semen** & is what supplies the sperm with **energy** to swim. **If no fructose is present, sperm will not be able to swim.** This might cause fertility.
 - **Choice B → 5-alpha reductase.**
 - **Testosterone is converted to DHT by 5-alpha reductase.**
 - **Boys** with 5-alpha reductase deficiency present as 12-year-old **"appearing girls"** that **developed a phallus & a mustache.**
 - Turns out, 5-alpha reductase is what influences the development of **external genitalia.** When puberty hits, the **massive surge of testosterone overcomes the 5-alpha reductase deficiency.**
 - **Choice C → Selenium** is involved in **anti-oxidation.** Its deficiency is quite uncommon. I don't think you will ever get assessed on selenium on the USMLE.
 - **Choice D → Sodium** is not involved in spermatogenesis anything
 - **Choice E → Zinc deficiency** would cause physical examination findings. **Dermatitis, Diarrhea, Alopecia, and Infertility.** Physical examination findings here are unremarkable. So unlikely to be zinc deficiency.
 - **Best Answer here is A (Fructose)**
-

Q36

A 17-year-old boy is evaluated for constitutional delay in growth and puberty. Serum gonadotropin concentrations are in the low-normal range. X-ray of the skull shows suprasellar calcifications. Which of the following is the most likely explanation for his condition?

- A. Craniopharyngioma
- B. Histiocytosis X
- C. Idiopathic
- D. Optic glioma
- E. Prolactinoma

▼ Explanation

• Answer is A (Craniopharyngioma)

◦ IMP Clues:

- Constitutional delay in growth & puberty
- Serum gonadotropin concentrations are in the low-normal range (pituitary is affected)
- X-ray of the skull shows suprasellar calcifications (this here is buzzy af for craniopharyngioma)

• Dx → Craniopharyngioma

- Most common supratentorial tumor in children & teens
- Remnants of **Rathke's pouch (Ectoderm)**

Calcification is Common & histology reveals Cholesterol Crystals in "motor-oil" like fluid

- Most HY Complications are **bitemporal hemianopia** & **pituitary compression**, causing affection of hormone release.
 - In this Q here, **the GH secretion was affected** → **Poor Growth**
 - Other possible presentations are **DI (decreased ADH)** and **Delayed Puberty (decreased FSH & LH)**



Pituitary Gland Embryology Rapid Review:

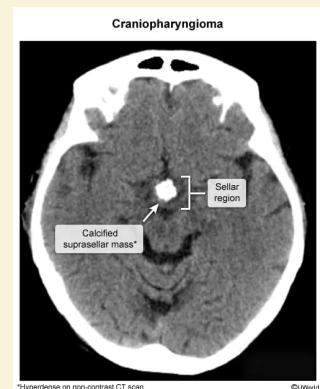
Pituitary Gland is made up of **2 parts** → The **anterior (adenohypophysis)** & **posterior (neurohypophysis)**

- **Adenohypophysis** is formed by the **Rathke's pouch** (an **ectodermal** diverticulum from the primitive **oral cavity**) growing **UPWARDS**
- **Neurohypophysis** is formed from a **DOWNWARD** extension of the **diencephalon (neuroectoderm)**

Both parts meet in the **Sella turcica** → The Pituitary Gland.



USMLE can give you the following CT in a child with signs of increased ICP/bitemporal hemianopia/Poor Growth and ask for diagnosis.



▼ Other Choices

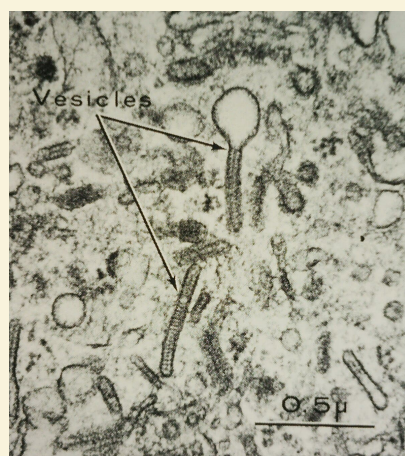
- **Choice B** → **Langerhans Cells Histiocytosis** causes *osteolytic lesions*. No calcification or hormonal affection



What structure seen on EM is characteristic of LCH?

▼ Answer

Birbeck granules - unique *tennis-racket* or *rod-shaped* organelles associated with LCH



- **Choice C** → Idiopathic & has suprasellar calcification? No. For it to be idiopathic, every disease has to be ruled out.
- **Choice D** → **Optic glioma** doesn't cause suprasellar calcification. **It is associated with NF1** & is actually a very common Q asked by the USMLE.
- **Choice E** → **Prolactinoma** presents as infertility & amenorrhea in females, and as gynecomastia & impotence in males. It doesn't cause suprasellar calcification. It can however cause bitemporal hemianopia.



Prolactinoma Arrows Q Hack!

Choose **down** arrow for everything.

EXCEPT prolactin & aldosterone → choose **up** arrow

Q37

A 47-year-old man has jaundice. Laboratory findings include an increased serum bilirubin concentration and a positive urine bilirubin test. Which of the following is most likely associated with the positive urine bilirubin test?

- A. Bleeding ulcer
- B. Folic acid deficiency
- C. Hemolysis
- D. Hemophilia
- E. Obstruction of the bile duct
- F. Pernicious anemia

▼ **Explanation**

- **Answer is E (Obstruction of the bile duct)**
 - **IMP Clues:**
 - Jaundice (hyperbilirubinemia)
 - Increased serum bilirubin (confirmed)
 - Positive urine bilirubin test (bilirubin in urine means that bilirubin is water soluble, so underwent conjugation at liver)
 - **Dx → Direct Hyperbilirubinemia**
 - Patient has **jaundice + hyperbilirubinemia** so it might be **either direct or indirect**.
 - The vignette differentiates between them via the **positive urine bilirubin**.
 - For something to be excreted in urine, it has to be **water soluble**.
 - **Indirect bilirubin must get conjugated in the liver to be water soluble. It is then sent to the kidney to be excreted.**

▼ **Other Choices**

- **Choice A → A** bleeding ulcer will cause melena in **STOOL. Not urine**. Irrelevant here.
- **Choice B → Folic acid deficiency** causes **hypersegmented neutrophils** and **megaloblastic anemia + NTD in pregnant women**. Nothing urine related.
- **Choice C → Hemolysis** causes **indirect hyperbilirubinemia** which will yes cause **jaundice** but **NOT bilirubin in urine**.
 - Unconjugated bilirubin is carried in the blood by albumin.
 - Albumin doesn't pass the renal filters.
- **Choice D → Hemophilia** is a bleeding disorder. **Hemophilia A is factor VIII deficiency**, while **Hemophilia B is factor IX deficiency**. Both cause **prolonged PTT**.
- **Choice F → Pernicious anemia** causes **vitamin B12 deficiency** which, similarly to b9 deficiency, cause **hypersegmented neutrophils** and **megaloblastic anemia**. It also causes **subacute combined degeneration**.

Q38

A 36-year-old man with AIDS elects to participate in a clinical study designed to test the effects of CCR5-receptor inhibitors on viral replication in patients with AIDS. Which of the following molecules is the natural ligand for this HIV coreceptor?

- A. Chemokine
- B. Complement protein
- C. Immunoglobulin
- D. Low-density lipoprotein
- E. Protease

▼ **Explanation**

- **Answer is A (Chemokine)**
 - **CCR5** stands for **Cysteine-Cysteine Chemokine Receptor type 5**. Straight forwards question.



What are the HIV Entry Inhibitor Drugs?

▼ Answer

1. Maraviroc

- Binds to **CCR5 Receptor** on the **CD4 cell**
- This prevents the binding of **Gp120** of HIV to the CD4 cell → Inhibits HIV **docking** & entry

2. Enfuvirtide

- Binds to **Gp41** on **HIV virion**
- This prevents binding of **Gp41** of HIV to the CD4 cell → Inhibits HIV **fusion** & entry

Q39

A healthy 25-year-old man is participating in a study of blood glucose. During the study, he is found to have a serum glucose concentration of 100 mg/dL after 20 hours of fasting. Which of the following precursors would contribute to the normal glycemia in this man at this time?

- A. Acetoacetate
- B. Alanine
- C. β -Hydroxybutyrate
- D. Stearic acid
- E. Valine

▼ Explanation

• Answer is B (Alanine)

◦ IMP Clues:

- Serum glucose concentration of 100mg/dl (okay, so decent glucose despite fasting from gluconeogenesis)
- After 20 hours of fasting (this is how I know it is gluconeogenesis, after 16-18hr, the glycogen is depleted so gluconeogenesis happens)

- Q asks which precursor contributes to the **normal blood glucose** levels at this time.

- Okay, let's keep this simple.
- > 16-18 hours of fasting is **gluconeogenesis**.

- Where do we get the substrates from?

1. Muscle breakdown (mainly alanine & glutamine)

- a. **Alanine** → **Pyruvate (Cahill's cycle)** → **Oxaloacetate** → **PEP** → gluconeogenesis

2. Lactate

- a. **Lactate** → **Pyruvate (Cori's cycle)** → **Oxaloacetate** → **PEP** → gluconeogenesis

3. Glycerol (from TAGs)

- a. **Glycerol** → **glycerol-3-phosphate** → **DHAP** → gluconeogenesis

▼ Other Choices

- **Choices A & C** → These are ketone bodies. They do have a very important role in starvation; however, they don't get transformed into glucose. So they don't maintain the body's glycemia.
- **Choice D** → Long chain FA cannot be transformed into glucose.
 - Odd-chain FA on the other hand can be used in gluconeogenesis.
 - **Odd-Chain FA** → **Propionyl-CoA** → **Succinyl-CoA** → gluconeogenesis.
- **Choice E** → Valine actually is a gluconeogenic amino acid. It can be transformed into glucose via gluconeogenesis. However, it is not the main driving amino acid for gluconeogenesis. Alanine & Glutamine are.

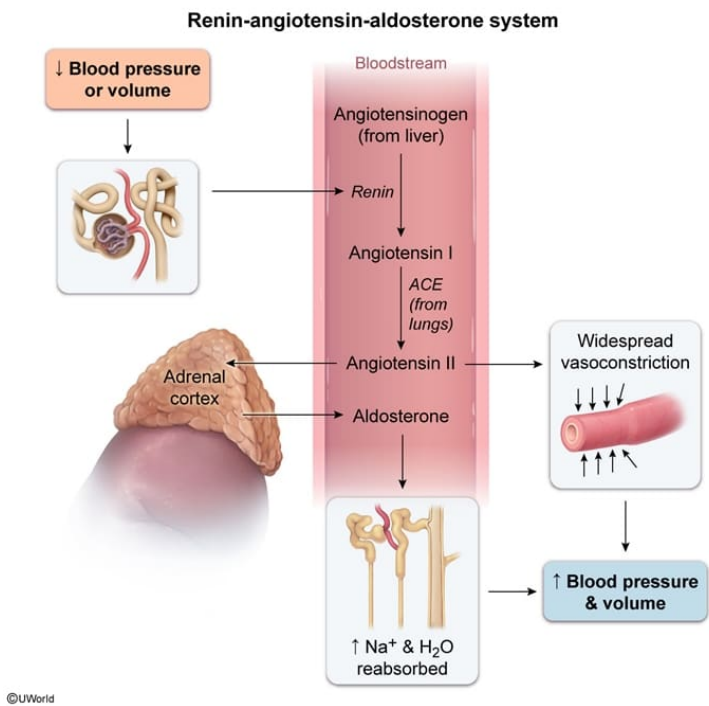
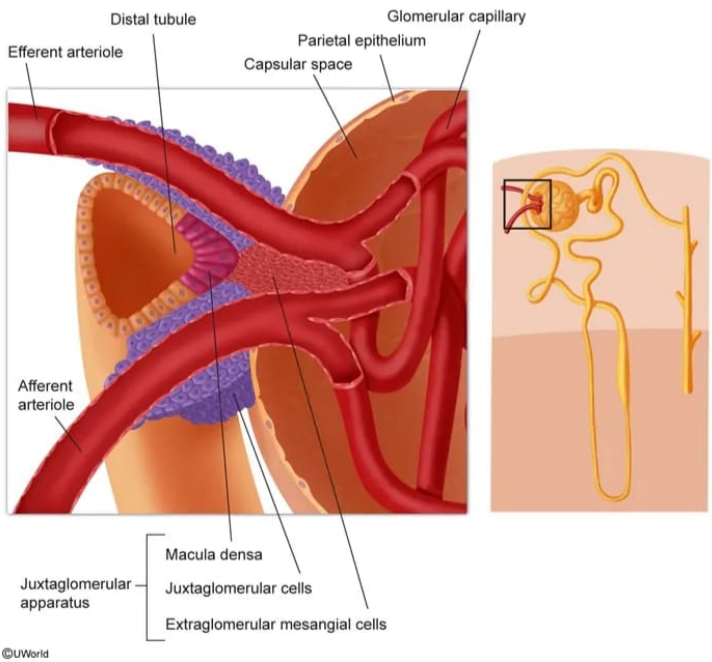
Q40

A 55-year-old man is diagnosed with renal artery stenosis. The stenosis results in a 50% reduction in arcuate artery pressure. Which of the following regions of the kidney is most likely to have the highest concentration of renin in response to the reduction in arcuate artery pressure?

- A. Cortex
- B. Inner medulla
- C. Outer medulla
- D. Papilla
- E. Renal pelvis

▼ Explanation

- **Answer is A (Cortex)**
 - **IMP Clues:**
 - Renal artery stenosis + 50% reduction in arcuate artery pressure (decreased blood supply to kidney)
 - Q asks which is most likely to have **highest concentration of renin**.
 - Renin is **produced by Juxtaglomerular cells** found in the **cortex**.
 - Renin is secreted in response to **low volume / perfusion**.
 - It makes sense that **the site that secretes renin is the site that would have THE MOST renin**.
 - What are the effects of renin?



▼ Other Choices

- JG Cells are found in cortex, so as you get away from the cortex, the level of renin decreases. This makes all other answer choices have **less renin in comparison to the cortex**.

Q41

A 40-year-old man with interstitial pulmonary fibrosis has a greater maximal expiratory flow rate than predicted. Which of the following best explains this finding?

- A. Hypercapnic bronchodilation
- B. Hyperinflation of the lungs
- C. Hypoxic bronchodilation
- D. Increased radial traction on airways
- E. Increased surfactant secretion

▼ Explanation

- **Answer is D (Increased radial traction on airways)**

- Okay so patient has IPF + increased in maximal expiratory flow. Let's find out why.
- **First, what is Maximal Expiratory Flow?**
 - It is the maximum speed at which air can be *forcefully expelled from the lungs* during a forced exhalation.
- **What influences Maximal Expiratory Flow?**
 - **Airway resistance** - the *less* the airway resistance, the *faster* the air will be expelled out of the lungs
 - **Elastic Recoil (compliance)** - the *more* the recoil (the *less* the compliance), the *faster* the air will be expelled out of the lungs.
 - So, having **wide airways + high "pushing" strength (high recoil) = More air expelled out.**
- **So, in IPF we have fibrosis.**
 - Fibrosis causes **less compliance & more recoil.**
 - Fibrosis also **pulls on surround structures (airways)**, so if the lung is fibrotic, the airways will be pulled on and will be wider. **Wider airways = less resistance**
 - **Okay, so more recoil / less compliance + wider airways / less airway resistance = Higher maximal expiratory flow.** Boom this Qbank is fucking awesome.
- **"Increased Radial Traction on airways" (Choice D)** is just rephrasing **"fibrosis pulls on airways and makes them wider."**

▼ Other Choices

- **Choice A** → Hypercapnia *can* cause some bronchodilation; however, this is not the primary underlying cause.
- **Choice B** → Hyperinflation of the lungs is a feature of COPD not lung fibrosis (Restrictive lung disease)
- **Choice C** → Hypoxia can also cause some bronchodilation, but like hypercapnia, this is not the cause.
- **Choice E** → Lung fibrosis damages pneumocytes. Surfactant actually **increases** compliance & **decreases** elasticity, so this **decreases** expiratory flow. Not increase.



What type of pneumocytes produce surfactant?

▼ Answer

Type 2 pneumocytes - They have lamellar bodies which produce surfactant. They also are responsible for lung regeneration

Q42

An investigator is conducting a study of antiretroviral agents. The plan is to identify which agents inhibit entry of the HIV virus into the CD4+ T lymphocytes. Which of the following antiretroviral agents is most likely to be identified in this study?

- A. Didanosine (ddI)
- B. Enfuvirtide
- C. Lamivudine (3TC)
- D. Nevirapine
- E. Tenofovir

▼ Explanation

- **Answer is B (Enfuvirtide)**
 - Would you look at that. I asked that a few Qs back. See, I told you we'd master the NBMEs together.
 - Q asks which drug inhibits entry of HIV virus into the CD4 cells. **Enfuvirtide.**
 - **MOA: Binds to Gp41 on HIV virion so that it can't bind to CD4 cells.**

▼ Other Choices

- **Choice A** → NRTI that is known to cause **pancreatitis**
- **Choice C** → NRTI. No unique side effects.
- **Choice D** → NNRTI. NNRTIs **cause rash & hepatotoxicity**

- **Choice E** → NRTI. What's unique is that it is a **nucleoTide analogue**. Also used for **HBV**.

Q43

A 19-year-old college student says he "hears voices." He was treated in the hospital 2 years ago for a similar problem. Which of the following drugs is most appropriate for treatment of this patient?

- A. Benztropine
- B. Diazepam
- C. Lithium carbonate
- D. Methylphenidate
- E. Nortriptyline
- F. Risperidone

▼ **Explanation**

- **Answer is F (Risperidone)**
 - **IMP Clues:**
 - "Hears voices" (auditory hallucinations)
 - Treated in the hospital 2 years ago (recurrent episodes)
 - Q asks what drug to give her. Well, she's probably **psychotic**, so makes sense to give her an anti-psychotic → **Risperidone (Choice F)**

? What type of anti-psychotic is Risperidone?

▼ **Answer**
Atypical Anti-psychotic -

These are all the **atypical anti-psychotics**:
Olanzapine, Clozapine, Quetiapine, Risperidone, Aripiprazole, Ziprasidone
Olanzapine & Clozapine cause metabolic syndrome (weight gain & obesity), so if the patient is obese → use **Aripiprazole or Ziprasidone**

HY Side Effect of **Clozapine** → **Agranulocytosis (Neutropenia)**

▼ **Other Choices**

- **Choice A** → **Anti-cholinergic that is used mainly for anti-psychotics side-effects**
 - USMLE will give you a patient who *recently* started anti-psychotics + now has **crooked neck, muscle stiffness, oculogyric crisis, or shuffling gait** & will ask you what to give him??
 - Answer is **Benztropine (Anti-Cholinergic)**
- **Choice B** → **Diazepam is a benzodiazepine.**



Benzodiazepines vs Barbiturates MOA:

📄 Ben likes it more frequent

📄 Barb likes it longer

- **Benzodiazepines** → Binds to an **allosteric site** on GABA A receptors → increase frequency of **Chloride channel** opening → **Agonizes GABA**
- **Barbiturates** → Binds to an **allosteric site** on GABA A receptors → increase duration of **Chloride channel** opening → **Agonizes GABA**

- **Choice C** → **Lithium** is used in bipolar disorder.
- **Choice D** → **methylphenidate** is used in ADHD
- **Choice E** → **Nortriptyline** is a TCA that is used in elderly because it has less anticholinergic side effects in comparison to other TCAs

Q44

A 47-year-old man is treated with colchicine for acute gouty arthritis. The drug acts by inhibiting which of the following in this patient's leukocytes?

- A. Cyclooxygenase activity
- B. Lipoxygenase activity

- C. Tubulin polymerization
- D. Urokinase activity
- E. Xanthine oxidase activity

▼ **Explanation**

- **Answer is C (Tubulin Polymerization)**
 - You have to be a pro at this now. On this one exam, this concept has been repeated like what? 4 times now?
 - Q asks for **Colchicine MOA**. Choices appear a little funky; however, this is what the USMLE does.
 - We know **colchicine is a microtubule inhibitor**, but this is too easy so sometimes they rephrase the sentence: **inhibits tubulin polymerization**.

▼ **Other Choices**

- **Choice A** → **COX** activity is inhibited by **NSAIDs**
- **Choice B** → **LOX** activity is inhibited by **LOX inhibitors (zileuton)** or **LTs Receptor antagonists (montelukast and zafirlukast)**
- **Choice D** → **Urokinase** is used as a **thrombolytic therapy**
- **Choice E** → **XO inhibitors** are **Allopurinol & Febuxostat**

Q45

A 28-year-old woman with chronic renal failure (creatinine clearance less than 20 mL/min) requires treatment for volume overload and pulmonary edema. Which of the following is the most appropriate pharmacotherapy?

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

▼ **Explanation**

- **Answer is C (Furosemide)**
 - **IMP Clues:**
 - Chronic renal failure + volume overload & pulmonary edema (evidently in need of a diuretic)
 - **Loop diuretics are the MOST EFFECTIVE diuretics**, so they are 1st line in most cases of fluid overload.
 - Also, patient has CKD, so electrolytes will be messed up.
 - Most importantly is potassium → **Kidney is diseased & cannot excrete potassium** → **Hyperkalemia**.
 - Loops are also known to cause the most potassium diuresis.



Diuretics Recap!

1. Loop Diuretics

- Site of action → **Ascending Loop of Henle** (hence the name loop diuretics)
- MOA → Blocks **Na/K/2Cl channels**

2. Thiazide Diuretics

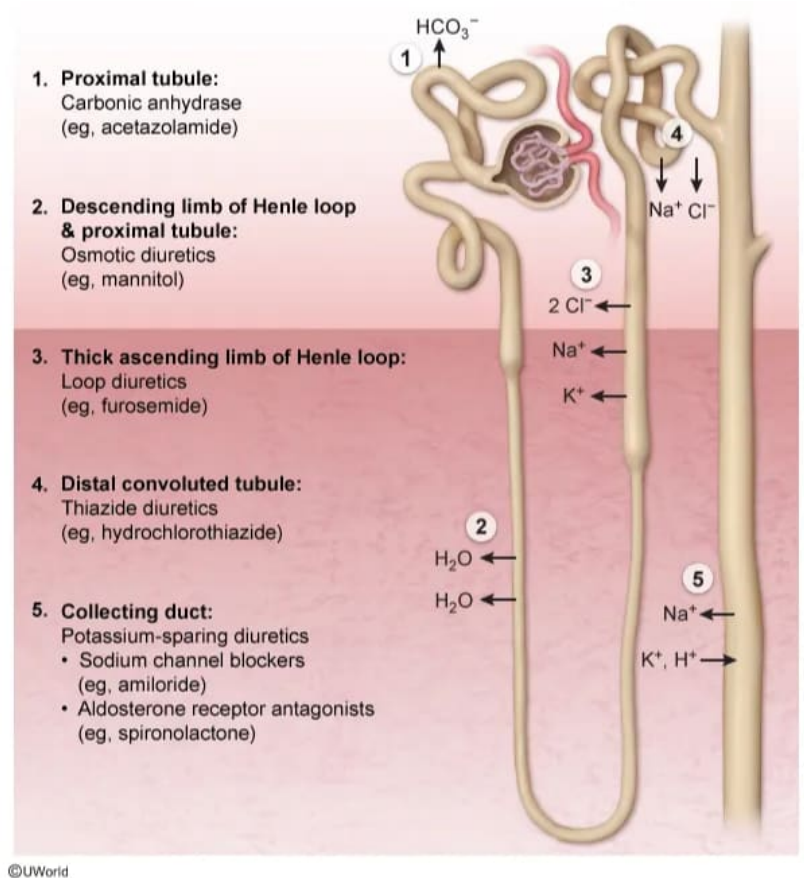
- Site of action → **DCT**
- MOA → **Blocks Na/Cl channels**

3. Potassium-Sparing Diuretics

- Site of action → **CD**
- MOA → **Aldosterone antagonists & ENaC inhibitors**

4. Acetazolamide

- Site of action → **PCT**
- MOA → **Carbonic Anhydrase inhibitor**



▼ Other Choices

- Choice A → CA inhibitor
- Choice B → Potassium sparing ENaC inhibitor
- Choice D → Thiazide diuretics
- Choice E → Potassium sparing Aldosterone Antagonist

Q46

A 47-year-old woman with aplastic anemia is being treated for disseminated aspergillosis with an antifungal drug that binds to specific sterols in the plasma membrane. This patient is most likely taking which of the following drugs?

- A. Amphotericin B
- B. Caspofungin
- C. Fluconazole
- D. Terbinafine
- E. Tolnaftate

▼ Explanation

- Answer is A (Amphotericin B)
 - What's up with all these pharm questions? Anyways, patient has disseminated aspergillosis (fungal infection) + is being treated with an antifungal that binds to "specific sterols in the plasma membrane" (they're referring to Ergosterol)
- Amphotericin B
 - MOA → **Ionophore**; meaning it binds to **ergosterol in plasma membrane** & form **holes** in it, essentially killing the fungus.
 - Side Effects → **Hypersensitivity-like reaction** (fever, chills, headache), **Hypokalemia**, and **Hypomagnesemia**



What other drugs share the same MOA of Amphotericin B?

▼ Answer

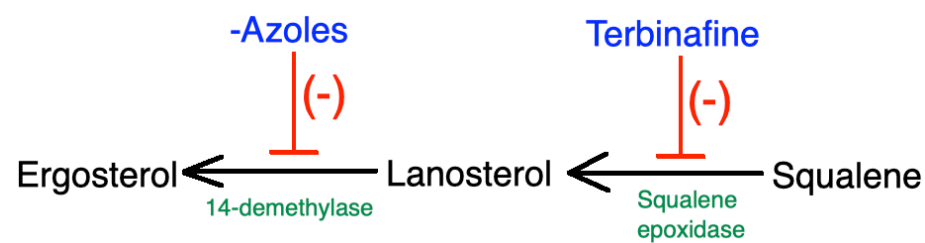
Nystatin - used as a mouth wash for *oral candidiasis* & locally for *vaginal candidiasis*

Natamycin - used as eyedrops for *fungal eye infections*

▼ Other Choices

- Choice B → Echinocandins *inhibit synthesis of 1,3-B-D-glucan* that forms the **cell wall** of fungi. **CELL WALLS NOT CELL MEMBRANES.**

- **Choice C** → **-azoles** family that **inhibit synthesis of ergosterol** by inhibiting *14-demethylase*
- **Choice D** → **Terbinafine** also inhibits the synthesis of ergosterol by **inhibiting the synthesis of Lanosterol** (which forms ergosterol) by *inhibiting Squalene epoxidase*
- **Choice E** → Garbage & you will not get assessed on it. It is a topical squalene epoxidase inhibitor.



Q47

A 17-year-old boy returns to the locker room after football practice on an especially warm day. His uniform is soaked with sweat. The characteristic odor associated with his sweat is most likely the result of secretion by which of the following glands?

- A. Apocrine
- B. Ceruminous
- C. Eccrine
- D. Sebaceous
- E. Tarsal

▼ Explanation

- **Answer is A (Apocrine)**
 - 17-year-old boy (post-puberty sweating)
- Q here asks what glands secretes the **sweat with the bad odor**
 - **Apocrine sweat glands** are post-puberty glands found in **hairy parts like the axilla, groin, and scalp**.
 - They **mature post-puberty**. This is why kids don't smell as adults.

▼ Other Choices

- **Choice B** → **Ceruminous glands** produce ear wax & are found in the ear canal
- **Choice C** → **Eccrine glands** produce watery sweat for thermoregulation. They are found in non-hairy areas like palms & soles
- **Choice D** → **Sebaceous glands** are found on face, back, and chest. They are associated with hair follicles & produce sebum to lubricate the hair.
 - Their occlusion & inflammation is the underlying pathophysiology of acne.
- **Choice E** → **Tarsal glands** are found in eyelids & they are what produce the protective oily layer on top of your eyes to prevent tears evaporating

Q48

A 4-year-old boy falls and lacerates his lower leg to the subdermal connective tissue. Which of the following is the first step in the tissue repair process?

- A. Angiogenesis
- B. Formation of fibrin clot
- C. Formation of granulation tissue
- D. Influx of macrophages
- E. Proliferation of fibroblasts

▼ Explanation

- **Answer is B (Formation of fibrin clot)**
 - This Q tests Wound Repair pathophysiology, so let's go through it.

Time Frame:

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

▼ **Other Choices**

- **Choice A** → Proliferation phase
- **Choice C** → Proliferation phase
- **Choice D** → Inflammation phase
- **Choice E** → Proliferation phase

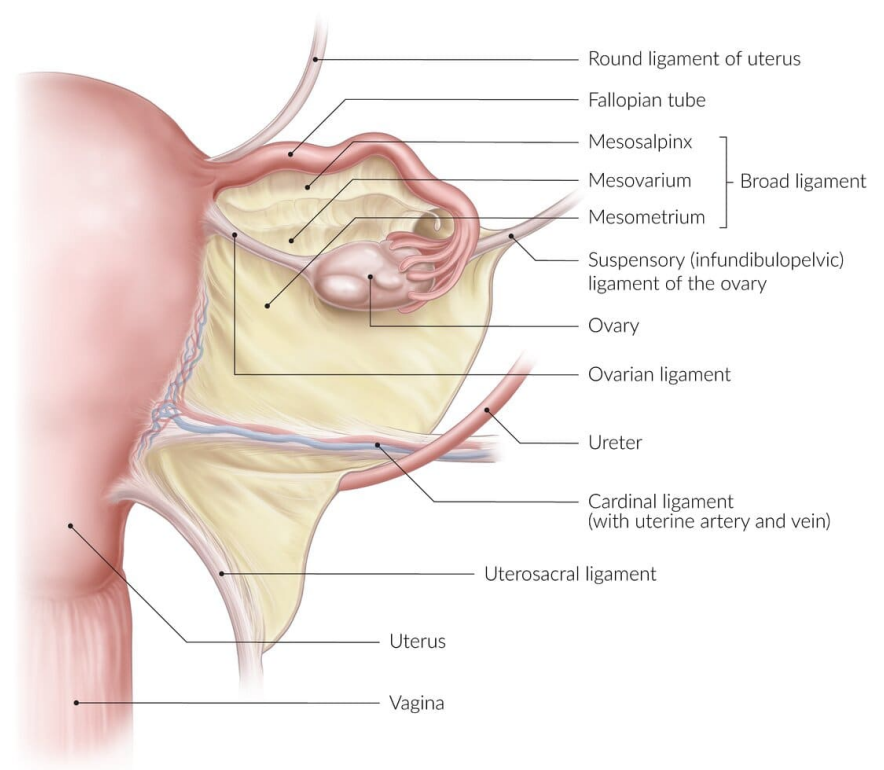
Q49

A 50-year-old woman has azotemia. Renal ultrasonography shows bilateral hydroureters and hydronephrosis. The most likely cause of these findings is primary carcinoma of which of the following?

- A. Colon
- B. Kidney
- C. Ovary
- D. Ureter
- E. Uterine cervix

▼ **Explanation**

- **Answer is E (Uterine Cervix)**
 - **IMP Clues:**
 - 50-year-old women + asking about cancer (so we know it maybe a women's cancer)
 - Azotemia (okay so renal failure, so urea cannot be excreted = azotemia)
 - U/S shows bilateral hydroureters & Hydronephrosis (both the ureters & kidneys are dilated bilaterally)
 - **Dx → Cervical Carcinoma**
 - Cervical Carcinoma is one of the most common cancers in women
 - One of the common complications is **ureteric obstruction**.
 - As both ureters are **closely related to the cervix**, it makes sense that cervical carcinoma compresses both ureters. This causes the ureters **above the level** of obstructions to dilate, which in turn causes both kidneys to dilate.





Sites of Ureter injury in Gynecology:

1. Cervical Carcinoma

- Infiltration of Ureters bilaterally.

2. Hysterectomy

- During ligation of **uterine vessels** in the **cardinal ligament**

3. Oophorectomy

- During ligation of **ovarian vessels** in the **suspensory ligament**



What is greatest risk factor for developing cervical cancer?

▼ Answer

HPV infection - Human Papilloma Virus is the most important risk factor on the USMLE.

- E6 protein

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

- E7 protein

- **Increased phosphorylation** of Rb
 - → Rb separates from EF-2 → EF-2 then causes mitosis

▼ Other Choices

- **Choice A** → **Colon carcinoma** can cause **Intestinal Obstruction**. Not ureteric.
- **Choice B** → **Renal Carcinoma** would cause **azotemia**. However, for something to dilate, the obstruction must be distal to it.
- **Choice C** → Very rare cause.
 - On the USMLE **ovarian tumors present as hormone-secreting tumors**.
 1. **Estrogen-secreting Granulosa cell tumors** → present either as precocious puberty in a kid or as endometrial hyperplasia (possibly carcinoma) in an adult.
 2. **Androgen-secreting Sertoli/Leydig-cell tumor** → presents as a girl / woman with virilization
- **Choice D** → **Ureter carcinoma** will cause unilateral hydroureter & hydronephrosis. Very very rare for someone to have bilateral ureter carcinoma.

Q50

Acetaminophen and nonsteroidal antiinflammatory agents reduce fever by decreasing the synthesis of which of the following factors in the hypothalamus?

- Interleukin-1 (IL-1)
- IL-6
- Leukotriene C₄
- Prostaglandin E₂
- Tumor necrosis factor-α

▼ Explanation

- **Answer is D (Prostaglandin E2)**
 - If you didn't know, **PG E2 is what controls our body temperature**. It is synthesized via the **COX pathway** then goes to the **hypothalamus** & increases the temperature set-point.
 - So, antipyretics work by **inhibiting the COX pathway**.
 - Another way you could've solved this Q is by seeing that the Q said, "Acetaminophen & NSAIDs reduce fever by". We know that both **inhibit the COX pathway** which produces **PGs**.
 - **PG E2** is the only PG in the answer choices.

▼ Other Choices

- **Choice A** → **IL-1** is also known as osteoclast activating factor & is involved in the pathophysiology of Osteoporosis, Rheumatoid Arthritis, and Osteoarthritis.
- **Choice B** → **IL-6** is an acute phase protein.
- **Choice C** → **LT-C4** is formed via the LTs pathway (LOX) & is involved in bronchoconstriction & vasoconstriction

- **Choice E** → **TNF-alpha** on the USMLE is the cytokine that causes hypotension & cachexia



Patient was diagnosed with pancreatic cancer. In the last 6 months he lost 20kg. What cytokine is involved in the weight loss?

▼ **Answer**

TNF-alpha



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