



NBME EXPLANATIONS

NBME 23 Block 2

from CrackNBME

23-Block 2

Q1

A 40-year-old man comes to the physician for a routine health maintenance examination. He has an active lifestyle that includes swimming and cycling. Physical examination shows no abnormalities. He is concerned that his male-pattern baldness is affecting both his professional image and his ability to attract sexual partners. Which of the following treatments is the most appropriate recommendation for this patient?

- A. Danazol
- B. Finasteride
- C. Methyltestosterone
- D. Oxandrolone
- E. Stanozolol

▼ Explanation

- Answer is B (Finasteride)
 - IMP Clues
 - He is concerned that his male pattern baldness is affecting his image...
 - Q asks what ttt is recommended for this patient
- Dx → Male Pattern Baldness
 - Also known as “**Androgenic (or androgenetic) Alopecia**”
 - Caused by **DHT** (Dihydrotestosterone)
 - **DHT causes hair follicles to shrink, which overtime causes the hair to thin & fall.**
 - This is referred to as “**miniaturization**” of hair follicles.
 - So, the treatment would be targeted to decrease DHT:
 - **Testosterone is converted to DHT via 5-alpha reductase enzyme**
 - **Finasteride** is a **5-alpha reductase inhibitor** that is used for androgenic alopecia (Male-Pattern Baldness)

? What is another drug widely used for baldness?

▼ Answer
Minoxidil

- MOA: **Topical K channel opener** → **hyperpolarization** of scalp blood vessels → **vasodilation** → **increased blood flow to hair follicles** → **hair growth**
- Side Effect: **Hypotension**

? What are the other HY use of finasteride on the USMLE?

▼ Answer
BPH - prostate *glandular tissue* also grows in response to DHT

- **Finasteride** (5-alpha reductase inhibitor) is used for **BOTH** BPH & Androgenic Alopecia

📌 Female vs Male Androgenic Alopecia presentation

- Males → **Frontal & Vertex** scalp recession with occipital sparing
 - This is due to **high androgen receptor concentration** in frontal & vertex scalp.
- Females → **Diffuse thinning** of hair over the **crown** with preservation of frontal hairline

Q2

A 33-year-old woman comes to the physician for a routine follow-up examination. She has celiac sprue and fat malabsorption. Physical examination shows asthenia. Laboratory studies show a serum calcium concentration of 7.8 mg/dL. Which of the following additional sets of serum findings is most likely in this patient?

Choices	Inorganic Phosphorus	Parathyroid Hormone	Calcitriol
A	Increased	increased	increased
B	Increased	decreased	increased
C	Increased	decreased	decreased
D	Decreased	increased	increased
E	Decreased	increased	decreased
F	Decreased	decreased	decreased

▼ Explanation

- Answer is E
 - IMP Clues
 - She has celiac sprue and fat malabsorption (Fat-soluble vitamins “KEDA” will be affected, what we care about here is Vitamin D “calcitriol”)
 - Serum calcium concentration of 7.8 mg/dL (Vitamin D deficiency → Less Calcium absorption from intestines & less calcium reabsorption from DCT of kidney → Hypocalcemia)
 - Q asks for most likely additional serum findings in this patient.

- Let's go over the basics.
 - Active Vitamin D /1,25-OH-Cholecalciferol/ Calcitriol actions:**
 - Increases Intestinal absorption of calcium & phosphate**
 - Increases renal reabsorption of calcium (from DCT) & phosphate (from PCT)**
 - Balances bone resorption & mineralization**
 - Negative feedback on PTH (decreases PTH secretion)**

? What type of 2nd messenger does Vitamin D use?

▼ Answer

Intracellular Receptors - USMLE can refer to this as "**Binds to receptors in cytoplasm with translocation into the nucleus**"

- In diseases where **fat malabsorption is present** → **Vitamin D deficiency** → **decreases Calcium & Phosphorus intestinal absorption & renal reabsorption**
 - This causes **less negative feedback inhibition of parathyroid gland** → **increase in PTH levels**, which causes an increase calcium levels (or tries to at least) & **further decrease phosphate levels**.
 - So, answer would be → **decreased Inorganic phosphorus, increased PTH, decreased Calcitriol**.

Q3

A 40-year-old man comes to the physician because of a 3-month history of episodes of an abnormal tingling or pins-and-needles sensation that starts in his left hand and then spreads to his left arm and face. The episodes last approximately 1 minute. Physical and neurologic examinations show no abnormalities. The most likely cause of these symptoms is a lesion in which of the following gyri of the cerebral cortex?

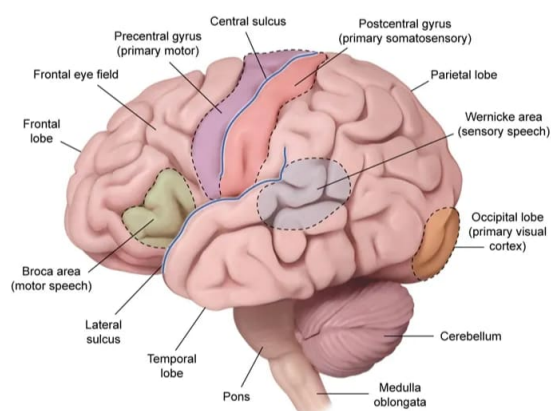
- A. Cingulate
- B. Occipitotemporal
- C. Postcentral
- D. Precentral
- E. Superior temporal

▼ Explanation

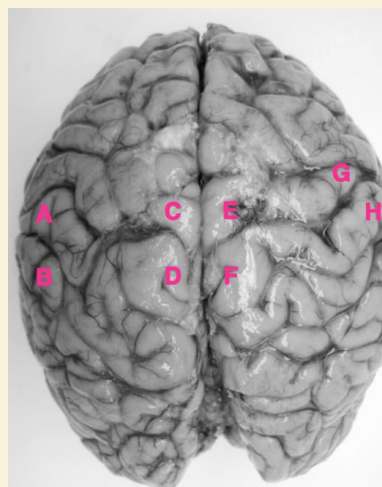
- Answer is C (Postcentral)**
 - IMP Clues**
 - Abnormal tingling or pins-and-needles sensation that starts in his left hand and then spreads to his left arm & face (pure sensory affection, so we know that it is the Primary sensory cortex of the brain)

• Q asks for site of lesion

- Postcentral gyrus ⇒ Primary Sensory Cortex**
(what we have here)
- Precentral gyrus ⇒ Primary Motor Cortex**



? What would a lesion in each of the following sites cause?



▼ Answer

A → **Weakness/Paralysis of RIGHT arm & face**

B → **Numbness/Pain of RIGHT arm & face**

C → **Weakness/Paralysis of RIGHT leg**

D → **Numbness/Pain of RIGHT leg**

E → **Weakness/Paralysis of LEFT leg**

F → **Numbness/Pain of LEFT leg**

G → **Weakness/Paralysis of LEFT arm & face**

H → **Numbness/Pain of LEFT arm & face**

Q4

An 18-month-old girl is brought to the physician because of failure to thrive and frequent wet diapers. She is at the 3rd percentile for length and weight. Physical examination shows dehydration, decreased muscle tone, and bowing of the legs. Slit lamp examination shows crystals in the corneas. Serum studies show hypophosphatemia, hypokalemia, and a nonanion gap metabolic acidosis. Urine studies show a pH of 5, glucosuria, phosphaturia, and generalized aminoaciduria. Which of the following is the most likely cause of the metabolic acidosis in this patient?

- A. Decreased carbonic anhydrase activity in the distal tubule
- B. Decreased carbonic anhydrase activity in the proximal tubule
- C. Decreased hydrogen ion secretion in the distal tubule
- D. Decreased hydrogen ion secretion in the proximal tubule
- E. Decreased sodium bicarbonate reabsorption in the distal tubule

F. Decreased sodium bicarbonate reabsorption in the proximal tubule

▼ Explanation

- Answer is F (Decreased sodium bicarbonate reabsorption in the proximal tubule)
 - IMP Clues
 - Bowing of the Legs (usually hints to ricket)
 - Slit lamp examination shows crystals in the corneas ("crystals in the corneas" are super buzzy & distinctive of cystinosis on the USMLE)
 - Serum studies show hypophosphatemia, hypokalemia, nonanion gap metabolic acidosis
 - Urine pH of 5, glucosuria, phoshphaturia, and aminoaciduria
- Dx → Cystinosis
 - **"Underrated diagnosis on the USMLE in my opinion."**
 - AR disease; characterized by a defect in **Cystinosin** (a lysosomal cystine transporter)
 - Clinical Features are basically **"Crystals in the Cornea" + Fanconi Syndrome**
 - **Fanconi Syndrome is the inability of the PCT to reabsorb what it normally reabsorbs → decreased reabsorption of amino acids, glucose, phosphate, and bicarbonate.**
 - So, the answer to our Q is basically **"decreased sodium bicarbonate reabsorption in the proximal tubule" (Choice F)**
 - Another way USMLE can assess this is by asking for the Renal Tubular Acidosis Type expected in this patient?
 - **Type 2 RTA**; expected other findings they may ask about are:
 - **Hypokalemia**
 - **Metabolic Acidosis**
 - **Urine pH (starts alkaline >5.5 but then as HCO₃ gets depleted → acidic urine <5.5)**

? What is another HY cause of Fanconi Syndrome?
▼ Answer
Ingestion of expired Tetracyclines



Renal Tubular Acidosis Rapid Review:

Type 1 RTA → decreased H secretion from alpha-intercalated cells in CD

- **Metabolic Acidosis**
- decreased acidity of urine (urine is **alkaline** pH >5.5)
- **Hypokalemia** (as less H is secreted in exchange for K)
- Alkaline urine causes deposition of **calcium phosphate stones**
- HY causes → **Amphotericin B toxicity - autoimmune diseases - Kidney Stones**

Type 2 RTA → decreased Bicarb reabsorption from PCT

- **Metabolic Acidosis**
- Urine pH **starts alkaline** then as HCO₃ gets depleted → **acidic urine**
- **Hypokalemia** (loss of K from PCT)
- HY causes → **Fanconi Syndrome - CA inhibitors**
- If caused by **Fanconi Syndrome**, associated with **hypophosphatemic rickets**

Type 4 RTA → Hypoaldosteronism or Aldosterone Resistance

- **Metabolic Acidosis**
- increased acidity of urine (urine is **acidic** pH <5.5)
- **Hyperkalemia** (low aldosterone/resistance → decreased K secretion)
- **decreased ammonium secretion**
- HY causes → **decreased aldosterone production (ACEi/ARBs, NSAIDs, Adrenal insufficiency) or Aldosterone Resistance (Spironolactone)**

Q5

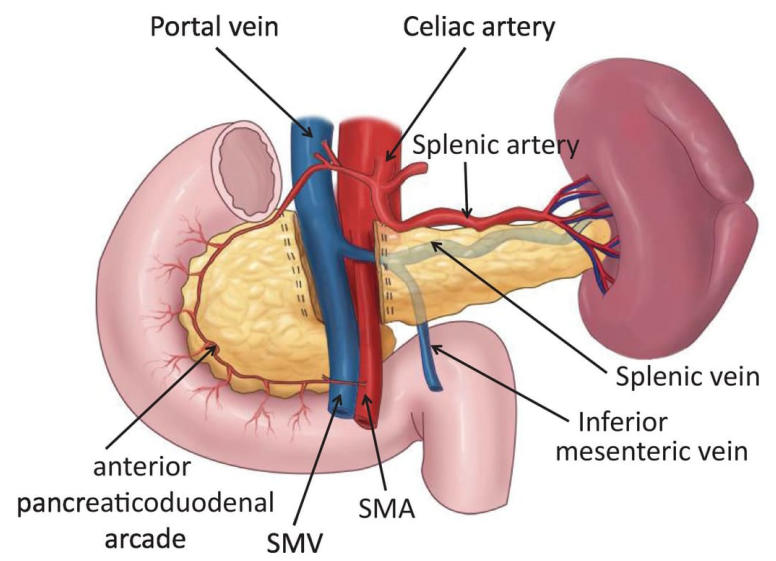
A 16-year-old girl is brought to the emergency department 30 minutes after being injured in a motor vehicle collision. Her blood pressure is 70/40 mm Hg. Physical examination shows cold, clammy skin. A chest x-ray shows fracture of the 9th rib on the left. An exploratory operation shows a rupture of the spleen. Ligation of the blood supply to the spleen is most likely to damage which of the following additional structures?

- A. Descending colon
- B. Horizontal duodenum
- C. Left kidney
- D. Pyloric portion of the stomach
- E. Tail of the pancreas

▼ Explanation

- Answer is E (Tail of the pancreas)
 - IMP Clues
 - Ligation of the blood supply of the spleen is most likely to damage which of the following structures

- Blood Supply of the Spleen**
 - Splenic Artery** is a branch from the **Celiac Trunk**, which is one of the anterior/single branches of the **abdominal Aorta**
 - Long & Tortuous** (so that it can accommodate for splenic enlargement) and passes on the **superior** border of the **Pancreas** → **splenorenal (lienorenal) ligament** to reach the **spleen**.
 - Splenic Vein** courses **posterior** to the pancreas & joins with the **SMV** to form the **Portal Vein**
 - Splenic Vein Thrombosis** causes **increased** pressure in veins it drains (**Short Gastric Veins**) → **Fundal Gastric Varices** [asked on NBMEs]
 - The **site of the spleen** (close proximity to ribs) and **its vascularity** count for it **being the most common injured abdominal organ in trauma**
 - To control the bleeding, the **splenic hilum** (in the **splenorenal/lienorenal ligament**) gets **clamped/ligated**.
 - This causes the nearby **tail of pancreas** to be at risk of injury (**Choice E**)



? At what level does the celiac trunk arise from the abdominal aorta?

▼ Answer

T12

? Due to the close proximity of the tail of pancreas to the splenic vascular supply, what is a HY complication of pancreatitis?

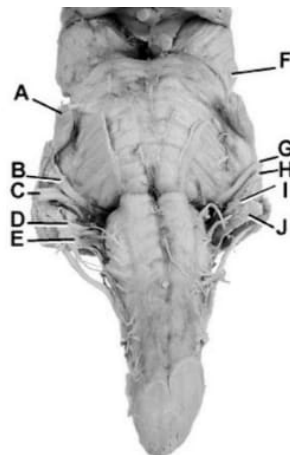
▼ Answer

Splenic Vein Thrombosis

Inflammation of the pancreas (**Pancreatitis**) → Local injury to the nearby **splenic vein endothelium** → **Thrombosis Formation** → Patient develops **Fundal Gastric Varices & Hematemesis**.

Q6

A 48-year-old man has complete loss of hearing in his right ear. Which of the following labeled cranial nerves on the photograph of the ventral surface of the brain stem is most likely to be damaged?



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

▼ Explanation

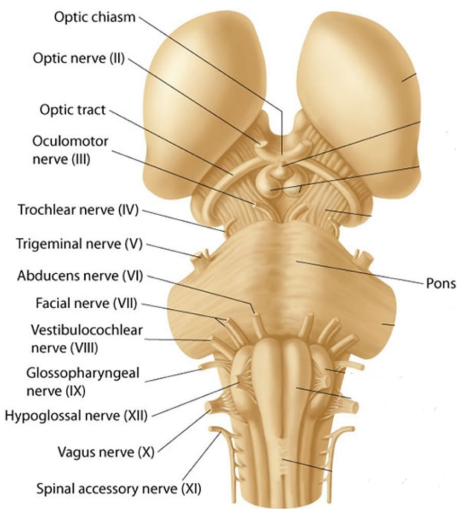
• Answer is C

◦ IMP Clues

- Complete loss of hearing in his right ear + Pic of brainstem is given (so it is evident that this is a vestibulocochlear nerve injury)

• Brainstem Neuroanatomy:

• First Learn:



Some Tips to Make It Easier:

1. Know how the **pons** looks like

- 4 Cranial Nerves **in the Pons**:
 - **CN 5, 6, 7, 8**

- 4 Cranial Nerves **below the Pons** (In the Medulla):
 - **CN 9, 10, 11, 12**

2. **Midline Cranial Nerves** are **1, 3, 6, 12**



Vestibulocochlear Nerve:

- **Pure sensory nerve** with 2 components

1. **Cochlear Nerve** ⇒ Hearing

- If damaged → Sensory-Neural Hearing Loss [ADD WEBER]

2. **Vestibular Nerve** ⇒ Balance & Spatial Orientation

- If damaged → Vertigo, Imbalance, and Nystagmus

- HY Conditions where vestibulocochlear nerve is affected:

- **Unilateral/Sporadic Acoustic Neuroma (Vestibular Schwannoma)**

- USMLE loves to give you an *elderly person* + unilateral SNHL; This is **sporadic**.

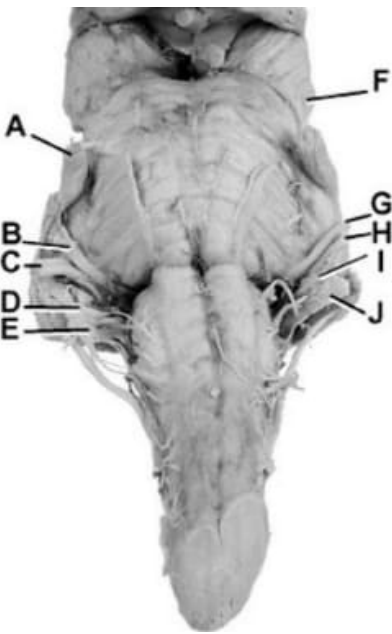
- **Bilateral Acoustic Neuroma (Vestibular Schwannoma)**

- USMLE loves to give you a *younger person* + Unilateral/Bilateral SNHL; This is **NF2**.

- **Ototoxic Drugs** (damage organ of Corti hairs cells → Bilateral SNHL)

- Most HY drugs are **Aminoglycosides** (gentamycin is a USMLE favorite), **Loop diuretics**, and **Cisplatin**.

Then Test Yourself:



▼ Answers

- Choice A → Right Trochlear Nerve
- Choice B → Right Facial Nerve
- Choice C → Right Vestibulocochlear Nerve
- Choice D → Right Glossopharyngeal Nerve
- Choice E → Right Vagus Nerve
- Choice F → Left Trigeminal Nerve
- Choice G → Left Facial Nerve
- Choice H → Left Vestibulocochlear Nerve
- Choice I → Left Glossopharyngeal Nerve
- Choice J → Left Vagus Nerve



Marker of Schwannoma is?

▼ Answer

S-100



Don't forget that Neurofibromatosis Type 2 is an **AD** disease caused by a mutation in **NF2 gene** on **chromosome 22**, which is characterized by **Bilateral Schwannoma**, **Cataracts**, and **Meningioma**.

Q7

A 42-year-old woman comes to the office because of a 1-year history of an enlarging, painless mass on her right wrist. Examination of the right wrist shows the findings in the photograph. The mass is firm and nontender and transilluminates with the application of a pen light. Without treatment, which of the following is most likely to occur in this patient?



- A. Malignant degeneration
- B. Paresthesias
- C. Radial nerve palsy
- D. Spontaneous regression
- E. Synovitis

▼ **Explanation**

- **Answer is D (Spontaneous regression)**

- **IMP Clues**

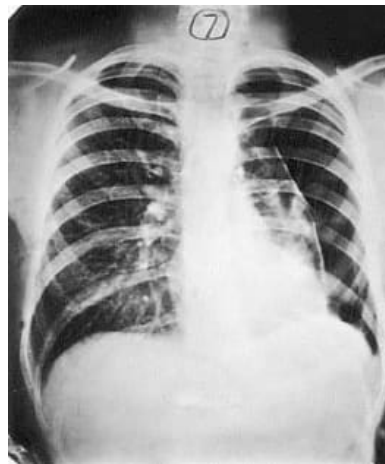
- Enlarging painless mass on her wrist + Image is given
- Mass is firm and nontender and transilluminates
- Q asks what would happen without ttt?

- **Dx → Ganglion Cyst**

- A **benign mass** filled with **gelatinous, mucinous fluid**, which is from the **degenerated connective tissue** + the **synovial fluid** that herniated from the **nearby joint capsule/tendon sheath**
- Most common site → **dorsal aspect of wrist** at the **scapholunate joint** (seen in the pic above)
- **Caused by overuse & worsened by repetitive movements**
- The mass is described as "**well circumscribed**", "**firm**", "**nontender**" that **transilluminates** (most IMP, as it differentiates it from other masses)
- Dx is **clinical** & management is **observation** (**regresses spontaneously**)
 - Can be **aspirated if symptomatic** (causing pain or limited wrist ROM) but can recur.
 - If recurs → **Surgical Excision**

Q8

An otherwise healthy 26-year-old scuba diver has difficulty breathing immediately after ascending from a 30-minute dive to a depth of 15 m. Which of the following physical signs is most consistent with the x-ray of the chest shown?



- A. Bronchial breath sounds over the middle lobe
- B. Cardiac impulse displaced to the left
- C. Hyperresonance over most of the left side of the chest
- D. Increased parasternal dullness due to a mediastinal shift to the left
- E. Increased tactile fremitus over the left lower lobe

▼ **Explanation**

- **Answer is C (Hyperresonance over most of the left side of the chest)**
 - This CXR shows pneumothorax. Left Lobe of the lung is "**jet black**" with **no "pulmonary markings"** and you can see the **outer border of the pleura**.

- Findings of pneumothorax are super HY
 - **Breath Sounds** → **Decreased**
 - **Percussion** → **Hyperreasant**
 - **TVF** → **Decreased**

? Arrow points to the collapsed lung's outer edge. Which layer is pointed to?

▼ **Answer**
Visceral Pleura

🚫 One of the major PEEP complications is **pneumothorax** (Barotrauma)!



Pneumothorax Classifications:

1. Spontaneous Pneumothorax

a. **Primary**

- **Tall, thin young male** +/- smoker
 - What is the **major risk factor** in this patient ⇒ **Habitus** [asked on NBME]
- Collapsed lung → **ipsilateral** mediastinal shift

b. **Secondary**

- Patient with **Diseased Lung** (COPD - Marfan - Infection)
- **Barotrauma** (High pressure mechanical ventilation)
- Collapsed lung → **ipsilateral** mediastinal shift

2. Traumatic Pneumothorax

- Caused by **Trauma** (Blunt - Iatrogenic - Penetrating)
- Collapsed lung → **ipsilateral** mediastinal shift

3. Tension Pneumothorax

- Any cause, but characterized by **CONTRALATERAL MEDIASTINAL SHIFT**
- Air gets in & can't get out due to "valve mechanics"
 - Mediastinum is pushed to **opposite side**
 - Trachea **deviates** & Vena Cava **kinks**
 - Decreased VR → Decreased CO → **Obstructive Shock**
 - **Hypotension & JVD**

Q9

In a study of the use of ultrasonography for the early detection of prostate cancer, 35 of 50 men with prostate cancer have abnormal test results, and 20 of 100 men without prostate cancer have abnormal test results. Which of the following best represents the specificity of this test?

- A. 20%
- B. 30%
- C. 50%
- D. 70%
- E. 80%

▼ **Explanation**

- **Answer is E (80%)**
 - 35 of 50 men with prostate cancer have abnormal test results:
 - **TP = 35**
 - **FN = 15**
 - 20 of 100 men without prostate cancer have abnormal test results:
 - **FP = 20**
 - **TN = 80**
 - Q wants **specificity**, which is $TN / (FP + TN) = 80 / (20+80) = 80/100 = 80\%$ (Choice E)

? What is the sensitivity of this test.

▼ **Answer**
Sensitivity = TP / (TP + FN)

- $35 / (35 + 15) = 35/50 = 0.7 = 70\%$

		Disease/Reality	
		+	-
Test/Study	+	TP	FP
	-	FN	TN

made by: @_ahmadraef

Q10

A man accidentally touches the surface of a hot stove; 20 minutes later, a blister develops at the site. Biochemical analysis of the blister fluid at this time is most likely to show the presence of which of the following?

- A. Histamine
- B. IgE
- C. γ -Interferon
- D. Interleukin-1 (IL-1)
- E. Interleukin-2 (IL-2)

▼ Explanation

- **Answer is A (Histamine)**
 - **IMP Clues**
 - Touches a hot stove
 - 20 mins later, a blister develops
- Q asks analysis of blister fluid is most likely to show presence of what?
 - Heat causes **local tissue injury** → **direct-mast cell degranulation** → release of **histamine**, bradykinin, PGs, substance P, cytokines...
 - **Histamine** then acts on **Histamine Receptors**, causing **vasodilation** → **erythema, warmth, and swelling (the "blister")**, **pruritis, and urticaria**



USMLE can refer to the answer to similar Qs as "**Vasodilation**" OR "**Widening of endothelial spaces**" OR "**Increased vascular permeability**" OR "**Separation of endothelial junctions**"



What are other causes of direct-mast cell degranulation on the USMLE?

▼ Answer

- **Morphine Injection**
- **Contrast Injection**
- **Vancomycin ("Red Man Syndrome")**
- **Physical stimuli (Cold, Heat, Friction)**

Q11

A 3-day-old female newborn delivered at term is brought to the emergency department by her mother because of a 4-hour history of yellowing of the eyes. Pregnancy and delivery were uncomplicated. The newborn has been breast-fed. Physical examination shows jaundice. Serum studies show a total bilirubin concentration of 14.5 mg/dL (N<12). The newborn is placed in an incubator equipped for phototherapy. Which of the following best describes the mechanism of the underlying phototherapy?

- A. Decreased conjugation of bilirubin to amino acids
- B. Decreased conversion of biliverdin to bilirubin
- C. Decreased rate of hemolysis
- D. Increased conjugation of bilirubin to glucuronide
- E. Increased conversion of bilirubin to water-soluble isomers
- F. Increased synthesis of UDP glucuronosyltransferase

▼ Explanation

- **Answer is E (Increased conversion of bilirubin to water-soluble isomers)**
 - **IMP Clues**
 - 4-hour history of yellowing of the eyes + physical examination shows jaundice
 - Serum Studies show a total bilirubin concentration of 14.5 mg/dL
 - Newborn was placed in an incubator equipped for phototherapy
- **Phototherapy**
 - Phototherapy is used in **neonates with unconjugated hyperbilirubinemia**
 - **why unconjugated?**
 - Unconjugated/Indirect bilirubin is **lipid-soluble** so can't be excreted in urine
 - **"Our Head of Peds basically bullied us into memorizing the wavelength for some fucking reason."**
 - **Phototherapy** (basically **blue light** with wavelength 460-490nm) **isomerizes** bilirubin deposited in the skin **into a water-soluble isomer** [\[For Nerds: called lumirubin\]](#)
 - As this isomer is **water-soluble**, it can be excreted in urine, bypassing hepatic conjugation.
 - Can be used in neonates with **BOTH physiological jaundice AND pathological jaundice** (G6PD deficiency - Hemolytic Diseases - Crigler-Najjar Syndrome)



7M + came to the ED with his parents because they think he is yellow. Upon taking with the family, you learn that they are vegan. On examination, patient is anicteric with yellow skin. What would be expected bilirubin levels of this patient?

▼ Answer

Normal.

This me being an asshole like the NBMEs. This child doesn't have jaundice. He has **hypercarotenemia, basically bro ate so many carrots, he turned orange. Not a joke.**

- Jaundice appears in the **eyes, soft palate, then the skin**. So, if a patient has **yellow skin with NORMAL sclera** (anicteric), this excludes jaundice.

? What would happen if phototherapy were used in a newborn with conjugated hyperbilirubinemia?

▼ Answer

Bronze Baby Syndrome - basically conjugated bilirubin gets oxidized & gets deposited in the skin, causing the "bronze baby."

? Why do newborns get jaundiced physiologically?

▼ Answer

Newborns have **immature liver enzymes** still, most commonly **UDP-GT**, which **picks up** indirect bilirubin into the liver to get conjugated.

- If **UDP-GT is functioning immaturely**, then **inadequate indirect bilirubin uptake** → **Indirect Hyperbilirubinemia**.
- After a few days, the baby's organs/enzymes mature → **spontaneous resolution**.

Q12

A female neonate is delivered at 38 weeks' gestation by cesarean section. Physical examination shows macrocephaly and shortening of the proximal segments of all limbs. A diagnosis of achondroplasia is made. DNA sequencing shows a G → A mutation in the fibroblast growth factor 3 receptor gene on chromosome 4. The biosynthesis of this protein requires a functional signal recognition particle receptor. This receptor is most likely found in which of the following cellular locations?

- A. cis-Golgi complex
- B. mRNA
- C. Ribosome
- D. Rough endoplasmic reticulum
- E. Secretory granule
- F. Smooth endoplasmic reticulum
- G. trans-Golgi complex

▼ Explanation

- Answer is D (Rough endoplasmic reticulum)

◦ Basically, we have a **mutation in FGF3R gene**, which requires a **functional signal recognition particle receptor**. The Q asks where is that receptor?

- **SRP receptor is found on the Rough Endoplasmic Reticulum outer membrane** (Choice D)

◦ Essentially, what happens is **DNA → RNA (via transcription) → Protein Synthesis (via translation)**

- Protein Synthesis passes by many stages, depending on end-goal, however, generally speaking for proteins that would be used outside the cell, the order is as follows:
 - **Ribosomes → RER → Golgi → Many options depending on protein.**
 - Proteins exiting the Ribosomes **find the RER via SRP receptors** (our answer)
 - From RER, Proteins are sent to the Golgi via **COP2 [asked on NBME]**

! The **N-terminus** of the peptide contains the "signal sequence", which is **recognized by the SRP** in the cytosol. Together, they form a complex, which is then **carried to the SRP Receptor on the RER membrane**.

? What is the protein responsible for delivery of vesicle from Golgi to RER?

▼ Answer

COP1

? What mediates transport between Golgi & Endosomes?

▼ Answer

Clathrin-coated vesicles

Q13

A 28-year-old man has hypertriglyceridemia that has not responded to gemfibrozil. Nicotinic acid therapy is started, and the dose is gradually increased to 3 g/day. Which of the following drugs should be administered concurrently to prevent the most common adverse effect of this therapy?

- A. Acetaminophen
- B. Aspirin
- C. Glyburide
- D. Hydrochlorothiazide
- E. Ranitidine

▼ Explanation

- Answer is B (Aspirin)

◦ **IMP Clues**

- Nicotinic acid therapy is started

- Q asks which of the following drugs should be administered concurrently to prevent the most common adverse effect of this therapy

• **Nicotinic Acid**

- More commonly referred to as **“Niacin”** or **“Vitamin B3”**
- Niacin (Vitamin B3) is used in the treatment of hypertriglyceridemia, for its following mechanisms:
 1. **Decreased VLDL synthesis & export from the liver**
 2. **Inhibits hormone-sensitive lipase (HSL)**
- HY Side Effects:
 - **MOST COMMON: Flushing** due to *PGs release* (so, ttt is via **NSAIDs “Aspirin”, not antihistamines**)
 - **Hyperuricemia**
 - **Type 2 DM & Insulin Resistance**



USMLE wants you to know that Niacin **increases HDL** more than any other agent



What does niacin deficiency cause?

▼ Answer

Pellagra

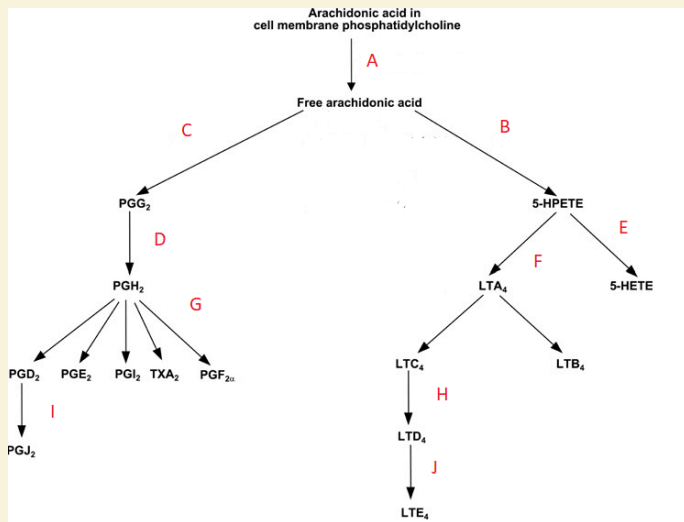
- **“4Ds”**: **D**iarrhea, **D**ementia, **D**ermatitis (Sun-hypersensitivity → hyperpigmented rash on sun-exposed areas), and **D**eath
- HY causes of niacin deficiency: Decreased Intake (duh), **Hartup disease**, **Carcinoid Syndrome**, **INH therapy**

These causes are if you want to be a USMLE gunner; Basically, niacin can be made endogenously from tryptophan, so disorders that decrease tryptophan predisposes Pellagra:

- **Hartup disease**: defective tryptophan absorption/reabsorption
- **Carcinoid Syndrome**: Increased serotonin synthesis causes depletion of tryptophan
- **INH therapy**: depletes vitamin B6 (HY), which impairs tryptophan → niacin



Choose the letter inhibited by Aspirin.



▼ Answer

Choice C (COX1/2) - Aspirin is an irreversible nonselective COX inhibitor

Q14

A 74-year-old woman comes to the physician because of a 3-month history of progressive shortness of breath with exertion; her symptoms are not exacerbated by lying down. She has smoked 1 pack of cigarettes daily for 56 years. She is seated with her hands placed on her knees, using accessory muscles of respiration. Her temperature is 37.2°C (99°F), pulse is 88/min, and respirations are 17/min. Physical examination shows no jugular venous distention. Chest examination shows an increased anteroposterior diameter. Breath sounds are decreased, and heart sounds are distant on auscultation of the chest. There is no peripheral edema. In addition to albuterol, which of the following is the most appropriate pharmacotherapy for this patient?

- A. Acetylcysteine
- B. Amantadine
- C. Cromolyn
- D. Ipratropium
- E. Montelukast

▼ Explanation

- **Answer is D (Ipratropium)**

◦ IMP Clues

- Progressive SOB with exertion; her symptoms are not exacerbated by lying down (this excludes cardiac causes of SOB; as they worsen by lying down “Orthopnea”)
- Smoked 1 pack of cigarettes daily for 56 years (Most important risk factor for COPD)
- She is seated with her hands placed on her knees + using accessory muscles of respiration + respirations are 17/min
- Chest examination shows an increased anteroposterior diameter (Barrel Chest which is buzzy for COPD) + breath sounds are decreased + heart sounds are distant (Increased air trapping, causes distant HS)
- NO JVD + No peripheral edema (all of these are clues excluding cardiac causes)

◦ Dx → COPD

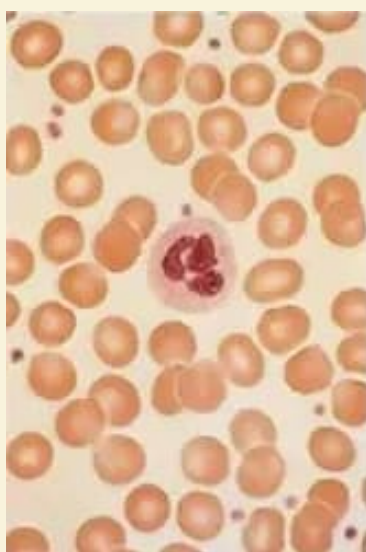
- Management of **COPD** in regard to **STEP 1** is → **B2 agonist (Albuterol) + Muscarinic Antagonist (Ipratropium) (Choice D)**
 - **B2 Agonists** → **stimulates B2 receptors** in the lungs → **bronchodilation**



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

- **Muscarinic Antagonists** → **Block M receptors** in the lungs → **inhibit** bronchoconstriction
- **Smoking is the biggest risk factor for COPD**
 - **why Smoking?**
 - **Smoking activates proteases** → **increased protease activity** → **elastic fibers breakdown** → **emphysema**
 - Emphysema (Break down of elastic fibers) causes **decreased alveolar recoil** → **increases lung compliance** [asked on NBME]
 - HY to know that **smoking** causes **Centrilobular/Centriacinar emphysema** (**Upper Lobes**)
- Another HY cause of COPD is **alpha-1 antitrypsin deficiency**
 - **alpha-1 antitrypsin inhibits proteases**, so its deficiency causes **increased protease activity** → **elastic fibers breakdown** → **emphysema**
 - Associated with **Liver Failure** (USMLE can give this as “parent died of a liver disease” or the patient himself is affected)
 - HY to know that **alpha-1 antitrypsin deficiency** causes **Panacinar emphysema** (**Lower Lobes**)

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



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

📌 **Ways the USMLE hint that this person has COPD:**

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



📌 **Chronic Bronchitis:**

- A type of **COPD** caused by **smoking & irritants**, which causes **hypertrophy & hyperplasia** of mucous-secreting glands → **productive cough with foul smelling sputum & airway obstruction**

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

- ▼ Answer
Tremors - B2 agonists cause tremors (USMLE likes **hand tremors**)

Q15

A 44-year-old woman comes to the physician because of steatorrhea, flatulence, and a 10-kg (22-lb) weight loss over the past 6 months. Findings on physical examination are unremarkable. Laboratory studies show:

Hemoglobin	9.6 g/dL
Mean corpuscular volume	74 μm^3
Serum	
Iron	40 $\mu\text{g/dL}$
Ferritin	10 ng/mL

Test of the stool for occult blood is negative; stool cultures and stool examination for parasites are negative. A lateral x-ray of the chest shows mild osteopenia. Which of the following is the most likely explanation for these findings?

- Atrophic gastritis
- Bacterial overgrowth
- Celiac sprue
- Intestinal pseudo-obstruction
- Irritable bowel syndrome

▼ **Explanation**

- Answer is **C (Celiac sprue)**
 - **IMP Clues**
 - Steatorrhea, flatulence, and weight loss + physical examination are unremarkable (Fat Malabsorption)
 - Hemoglobin 9.6g/dL + MCV 74 (Microcytic Anemia)
 - Serum Iron 40 + Ferritin 10 (Low serum Iron & Low Ferritin, the stored form of Iron)

◦ Dx → Celiac Disease

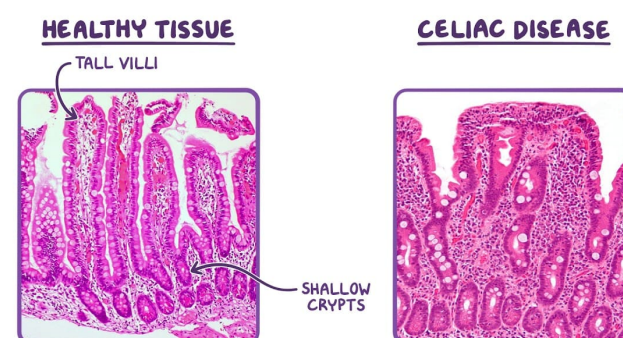
- On the USMLE there are 2 diseases that present similarly but can be differentiated via the presence/absence of Iron Deficiency Anemia: Celiac Disease & Lactose Intolerance.

- **Celiac Disease** → Flatulence, bloating, abdominal pain, diarrhea (they might give you “diarrhea”, not steatorrhea to make the Q harder) + **PRESENCE** of Iron Deficiency Anemia
- **Lactose Intolerance** → Flatulence, bloating, abdominal pain, diarrhea + **ABSENCE** of Iron Deficiency Anemia

- Let's discuss them in detail as I guarantee you that they will show up on your exam:

1. **Celiac Disease**

- Flatulence, bloating, abdominal pain, diarrhea (they might give you “diarrhea”, not steatorrhea to make the Q harder)
- **IRON DEFICIENCY ANEMIA IS PRESENT**
- Pathophysiology (HY AF): Gliadin (part of **gluten**, which is found in wheat, barley, rye) is **detected by APCs** in the intestines → **T-cell activation & infiltration of the intestinal walls** → **destruction**
- Biopsy shows → **Blunting/Atrophy of duodenal villi + Crypt hyperplasia + Intraepithelial lymphocytosis**
 - Due to **destruction of duodenal villi**, nutrients normally absorbed by the duodenum **WILL NOT BE ABSORBED**
 - what are they?
 - Iron → **Iron Deficiency Anemia**
 - Fats (including Fat-soluble vitamins) → **Steatorrhea, Vitamin K deficiency, Vitamin E deficiency, Vitamin D deficiency, Vitamin A deficiency**
 - They gave you “osteopenia” in the vignette, hinting to **Vitamin D deficiency**.
 - **Vitamin K** → is *rare tbh*, and I don't think I've ever seen it assessed in celiac.
 - **Vitamin A** → look for **abnormal skin keratinization & ocular affection (RP, night blindness)**
 - **Vitamin E** → *Ataxia, Peripheral neuropathy, Weakness*



- Dx → **Serology (anti-tissue transglutaminase IgA & anti-endomysial IgA antibodies) + Biopsy (definitive diagnosis)**

“HY AS FUCK to know that patients with **IgA deficiency + Celiac** give **NEGATIVE** serology test.”

📌 **IgA deficiency** presents as **triad of recurrent infections** (usually respiratory) + **Giardia Infection** + **Atopy**

- Associated with **anaphylaxis to blood products** (they lack IgA, donor plasma has IgA)

- Complications → **Dermatitis Herpetiformis (HY) & T-cell Lymphoma** (less-HY) & **Intestinal adenocarcinoma (LY)**
 - Dermatitis Herpetiformis is HY & is seen on NBMEs/Free120s/USMLE exams, so knowing the picture is IMP. **Biopsy shows** → **IgA deposits at dermal papillae [asked on NBME]**
 - **Chronic stimulation of T-cells by chronic antigen exposure** → increased T-cell proliferation “**polyclonal**” → more chance of mutations & “**monoclonal**” proliferation → **T-cell Lymphoma**

? 18M in tropical area + steatorrhea + abdominal pain + flatulence + Megaloblastic anemia. What is diagnosis?

▼ Answer

Tropical Sprue

- Malabsorptive disease of **Infectious etiology** that presents similarly to celiac disease.
 - **Same Biopsy findings**, however, **not** limited to the duodenum (*involves entire small bowel*)
 - As **terminal ileum is affected** → **Vitamin B9 & B12 deficiency (Megaloblastic anemia)**
- ttt → Tetracyclines

Dermatitis Herpetiformis:



*** USMLE has a similar picture on one of the OLD OLD NBMEs so knowing it is a plus.

⚠️ **Don't mix-up T-Cell Lymphoma of Celiac Disease with B-Cell Lymphoma of H.pylori**

- *H.pylori* → **B-cell stimulation**
- **Celiac** → **T-cell stimulation**

2. **Lactose Intolerance**

- a. Flatulence, bloating, abdominal pain, diarrhea
- b. **IRON DEFICIENCY ANEMIA IS ABSENT**
- c. Pathophysiology: **Loss of intestinal brush border lactase enzyme** → can't metabolize lactose → bacteria ferment it → **Osmotic Diarrhea + Gases & Fatty Acids**
- d. Biopsy shows → **Normal Intestines [asked on NBME]**
- e. Dx → **Positive Hydrogen Breath test & decreased stool pH [asked on NBME]**

📌 **Lactose Intolerance Different Presentations:**

1. **Primary**: As we grow, genetic expression of lactase decreases. (Most common type)
2. **Secondary**: **Damage to mucosa (MOST HY is viral GE) causes transient/chronic deficiency of lactase**
3. **Congenital**: Infant with no hx of infection (to differentiate it from secondary) + has no lactase.

Q16

An 85-year-old woman is brought to the physician by her daughter because of a 3-year history of progressive forgetfulness. Mental status examination shows moderate difficulty learning and recalling new verbal and nonverbal material. She also has mild difficulty with naming and calculations. Which of the following is the most appropriate pharmacotherapy to improve her symptoms?

- A. Coenzyme Q
- B. Donepezil
- C. Riluzole
- D. Selegiline
- E. Zinc

▼ Explanation

• Answer is B (Donepezil)

◦ IMP Clues

- 3-year hx of progressive forgetfulness (Could be normal aging or Alzheimer Disease/Dementia. We differentiate via MMSE)
- Mental State Exam (MMSE) shows moderate difficulty learning and recalling new verbal and nonverbal material + mild difficulty with naming and calculations (These are the items tested in the MMSE, here she's not really doing great → low MMSE score)
- Q asks for appropriate ttt to improve her symptoms

◦ Dx → Alzheimer Disease

- Gradual-onset **cognitive decline**, **progressive memory loss**, and **disorientation** with **low MMSE score (low 20s)**

• **NO** Sensory or Motor affection

- Pathophysiology: accumulation of **Beta-amyloid plaques** & **Neurofibrillary tangles** ⇒ **Neuronal loss** & **Cortical Atrophy**, which causes:

- **Widening of the sulci and narrowing of the gyri**
- **"apparent" ventriculomegaly 2ry to cortical atrophy ⇒ Hydrocephalus Ex Vacuo [asked on NBME]**
- **Atrophy of the hippocampus ⇒ Memory Loss**
- **Neuronal loss ⇒ decreased ACh** (this is why ttt is **AChE inhibitors** → **increases ACh**)
 - Neuronal loss/death causes **release of glutamate**, which **activates NMDA receptors**
 - NMDA causes excessive Calcium influx into neurons, causing **Excitotoxicity**
 - This is also why ttt is **NMDA antagonists**, to decrease excitotoxicity & slow disease progression

- Biopsy shows → **extracellular Beta-amyloid plaques** & **intracellular Neurofibrillary tangles** (hyperphosphorylated tau proteins)

⚠ **Frontotemporal dementia (Pick Disease)** also has **accumulation of hyperphosphorylated tau proteins** but in **round silver staining inclusion bodies**, named **Pick Bodies**.

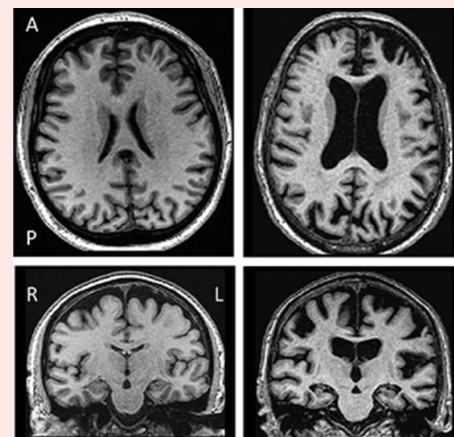
• Genetics:

- **Down Syndrome** is associated with Early onset Alzheimer due to the presence of **"Amyloid Precursor Protein"** gene on **chromosome 21**, they have 3 chromosomes 21s, so higher chance.
- **Presenilin Gene** mutations also cause Alzheimer.
 - **Presenilin-1/2** (on chromosomes 14/1, respectively) is a *protein that cleaves Amyloid* → if mutated → amyloid **accumulates**
- **ApoE ε4** ⇒ **Late-Onset Alzheimer Disease**; however, **ApoE ε2** ⇒ **Protective from Alzheimer Disease**.

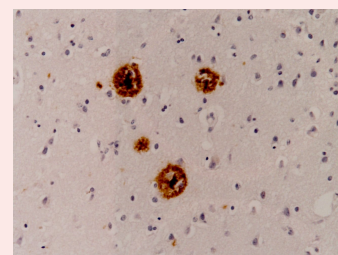
- Treatment: **AChE inhibitors** (Donepezil - Galantamine - Rivastigmine) or **Memantine** (NMDA glutamate antagonist)

⚠ Dementia + sensory/motor affection → **Vascular Dementia**

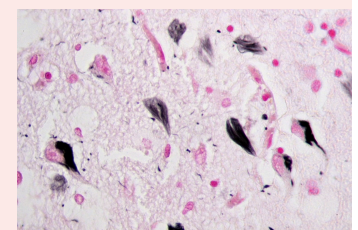
Normal vs AD patient Brain MRI:



Extracellular B-amyloid plaques:



Intracellular Neurofibrillary Tangles:





Underrated HY Alzheimer Disease Complications:

1. **Amyloid Angiopathy** in brain parenchyma → **ICH**
2. **Infections** (most notably **UTIs** on the USMLE) cause worsening of dementia → **Delirium**

Sundowning is worsening of dementia at night that can resemble delirium

- **ttt is decreasing ambient noise & distraction.**

Q17

Investigators conduct a prospective, community-based study to assess the effectiveness of an intervention to promote early language acquisition among children during the first 3 years of life. Delivered over 6 months across five day-care centers, the intervention consisted of providing monthly classes to a cohort of mothers, beginning when each child was 2 years of age. Each child's language skills were assessed independently at the ages of 2 and 3 years; scores were normalized for age. The results are summarized as follows:

Number of Class Sessions Attended by Mother	Mean Change in Child Language Score (Standard Deviation) At the Age of 3 Years
1	5.2 (3.1)
2	8.3 (3.2)
3	12.1 (2.8)
4	17.9 (3.4)
5	18.2 (2.7)
6	22.6 (2.6)

Which of the following sets of characteristics of this study best supports a causal relationship between the intervention and child language scores?

- A. Dose-response gradient, specificity, biologic plausibility
- B. Dose-response gradient, specificity, sensitivity
- C. Dose-response gradient, temporal relationship, sensitivity
- D. Strength of association, dose-response gradient, consistency of other studies
- E. Strength of association, specificity, sensitivity
- F. Strength of association, temporal relationship, dose-response gradient

▼ **Explanation**

- **Answer is F (Strength of association, temporal relationship, dose-response gradient)**
 - 2 way you can solve this question:
 1. **You know the STEP 3 fucking Bradford Hill Criteria (discussed in Mehlman ethics btw), which is the criteria of causality.**
 - a. **Empirical Association (Strength of Association)** ⇒ A change in an independent variable is associated with a change in dependent variable
 - **The change in number of class sessions → change in mean change in child language score**
 - b. **Time Order (Temporal Relationship)** ⇒ Independent variable change should precede dependent variable change
 - **Class sessions "the change" should happen before "the effect" the change in child language score**
 - c. **Nonsupuriousness (Dose-response gradient)** ⇒ Change is caused by direct relationship between the 2 variables, not a third variable
 - **Increase in Number of class sessions → increase in Child Language score mean**
 2. **You don't know the Bradford Hill Criteria, so you exclude to find the answer:**
 - **Choices A, B, C, E → Specificity & Sensitivity are for diagnostic/screening tests.** There is no test here. No TP or TN; You can't figure out or calculate them.
 - **Choice D → Consistency of other studies doesn't apply here, because there are **no other studies mentioned**.**
 - **Choice F → Correct Answer.**

Q18

A 36-year-old nulligravid woman and her 40-year-old husband come to the physician for genetic counseling prior to conception. They have no family history of genetic syndromes. They have been reading on the internet about certain inherited diseases and ask about their risk for being carriers of an autosomal recessive neurodegenerative disorder that occurs in 1 in 10,000 individuals. Which of the following best represents the carrier frequency of this condition?

- A. 1 of 25
- B. 1 of 50
- C. 1 of 75
- D. 1 of 100
- E. 1 of 150

▼ Explanation

• Answer is B (1 of 50)

◦ This is **Hardy-Weinberg** formula.

$$p^2 + 2pq + q^2$$

- p^2 = healthy
- q^2 = affected
- $2pq$ = carrier

◦ They have no family hx, so all we need is the population prevalence, which is **1 in 10,000**

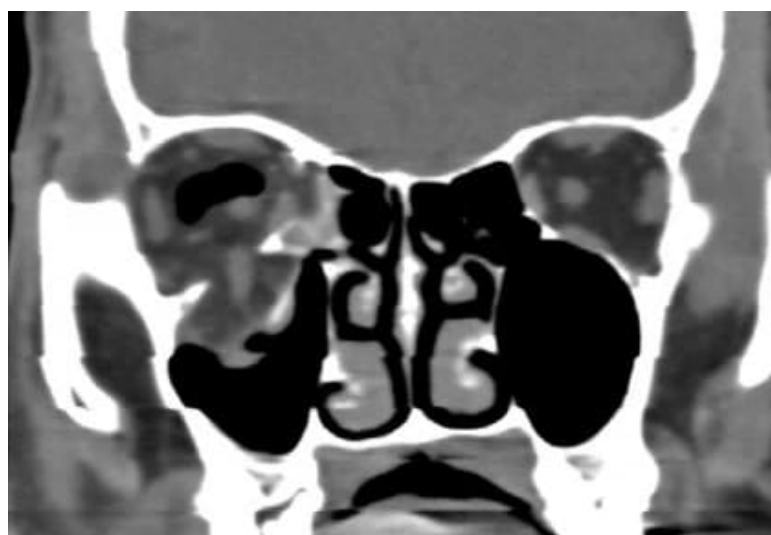
◦ So, $q^2 = 1/10,000$; making **$q = 1/100$**

◦ For p, always calculates it as 1, trust me. You know by now.

- $2 \times 1 \times (1/100) = 1/50$ (Choice B)

Q19

A 44-year-old man is brought to the emergency department by police 45 minutes after he sustained injuries in a bar fight. There are multiple facial fractures and contusions, including a severely swollen right eye. Complete physical examination cannot be done because of facial edema. He refuses to try to open his eyes because when he does, he has double vision. A CT scan of the head is done, and a coronal image through the midface is shown. Which of the following is the most likely explanation for this patient's visual complaints?



- A. Avulsion of the optic nerve
- B. Dislocated optic lens
- C. Entrapment of the inferior rectus muscle
- D. Free blood within the anterior chamber
- E. Globe pierced by bone fragment
- F. Injury to the optic tract posterior to the chiasm

▼ Explanation

• Answer is C (Entrapment of the inferior rectus muscle)

◦ IMP Clues

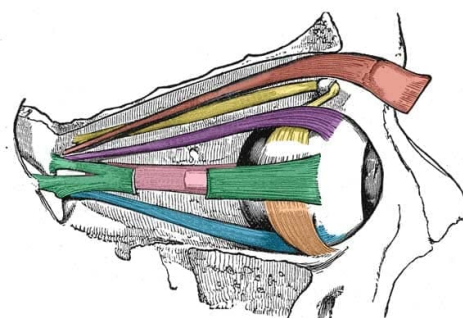
- Severely swollen right eye
- He has double vision (Double vision post-trauma is usually due to abnormal eye movement coordination due to affected muscles)
- CT scan is shown (shows fracture of right eye orbital floor)

• Dx → Orbital Floor Fracture Entrapment

◦ What we have here is **Blow-out Fractures** (could refer to *Orbital Floor Fracture* or *Medial wall Fracture* due to **blunt eye trauma**, specifically **Orbital Floor Fracture** (the most common, btw)

▪ What are the structures of the orbital floor?

- **Inferior rectus muscle**
- **Inferior oblique muscle**
- **Infraorbital nerve** (Qs might mention that sensation over right zygoma area is decreased. This is the reason.)



Levator palpebrae superioris
Superior oblique
Inferior oblique
Superior rectus
Medial rectus
Lateral rectus
Inferior rectus

© teachmeanatomy
The #1 Applied Human Anatomy Site on the Web

- So, injury of orbital floor would cause **entrapment of eye downwards, injury to rectus & inferior oblique muscles, and Infraorbital nerve.**

- Findings would be **double vision on upward gaze & loss of sensation over zygoma and upper lip.**

? What nerve supplies the inferior rectus muscle?

▼ Answer

Oculomotor nerve (CN III)

- CN IV (Trochlear Nerve) ⇒ Superior Oblique muscle
- CN VI (Abducens Nerve) ⇒ Lateral Rectus muscle
- CN III (Oculomotor Nerve) ⇒ Others
 - Medial Rectus, Superior Rectus, Inferior Rectus, Inferior Oblique, and Levator palpebrae superioris

Q20

A 45-year-old woman is scheduled to undergo a lymph node biopsy under local anesthesia. A surgical resident asks a third-year medical student to get signed consent from the patient before the procedure is performed. Which of the following actions by the student is most appropriate?

- A. Accompany the resident while the resident obtains signed consent
- B. Get signed consent from the patient
- C. Get signed consent from the patient with another medical student acting as a witness
- D. Refuse to obtain signed consent

▼ Explanation

- Answer is A (Accompany the resident while the resident obtains signed consent)

◦ This type of Q is all over the NBME/USMLE, so mastering the concept is a must. Let's discuss consent:

- Consent is made up of 2 parts: **The Doctor & The Patient:**

- For a doctor to have the consent of a patient, **the doctor is required to inform the patient of:**

1. The **doctor** who is doing the procedure/intervention
2. The **nature of the procedure/intervention** (reason - techniques)
3. The **risks & benefits of the procedure/intervention**
4. **Any alternative treatment options**
5. The **risks & benefits of the treatment options**

- For a patient to give consent, **the patient must:**

- **Show Capacity** (Understands his condition/risks/options, can reason & reach a decision, and can communicate a choice)
- **Accept Voluntarily** (with no manipulation or coercion)



USMLE can test this concept by giving you a Q & ask you **what else should the doctor tell the patient to acquire proper "informed consent"** OR give you a **MED student** (like here) OR a **RESIDENT who knows nothing about the procedure** (or doesn't know enough).

Q21

A 17-year-old girl with type 1 diabetes mellitus comes to the physician for a follow-up examination. She has had multiple admissions to the hospital during the past 5 months for diabetic ketoacidosis. She appears well. Physical examination shows no abnormalities. Laboratory studies show a hemoglobin A1c of 11.5%. She tells the physician that she does not take her insulin regularly because she either forgets to or is too busy. Which of the following is the most appropriate initial step by the physician?

- A. Acknowledge the patient's reasons for missing insulin injections
- B. Discuss the patient's noncompliance with her parents
- C. Educate the patient about the long-term complications of untreated diabetes
- D. Tell the patient's parents to ensure that their daughter is compliant
- E. Refer the patient to a psychologist

▼ Explanation

- Answer is A (Acknowledge the patient's reasons for missing insulin injections)

◦ **The First Step in approaching medical nonadherence on the USMLE is Exploring the reasons for nonadherence and assessing the barriers.**

- Remember that you'd have to do this in a way that is **non-judgmental** and most importantly **empathetic**, by acknowledging the patient's barriers.
- **Choice A** is exactly what we need **"Acknowledge the patient's reasons for missing insulin injections"**

▼ Other Choices

- **Choices B & D** → Involving the parents usually creates more tension between the family and the child. Also, this may worsen the patient-physician relationship.
- **Choice C** → What she needs is guidance, not you listing the complications of untreated DM.
- **Choice E** → Why?

Q22

A 60-year-old woman with type 2 diabetes mellitus comes to the office because of a 6-week history of right shoulder pain. The pain occurs when she attempts to raise her arm and when lying on her right side. She has not had weakness, tingling, or numbness. Physical examination shows tenderness to palpation in the region of the right deltoid muscle just lateral to the acromioclavicular joint. While sitting upright, she is able to abduct her arm to nearly 90 degrees, but additional abduction is prevented by pain. Muscle strength is 5/5, the right upper extremity sensation is intact, and there is no impingement sign. Which of the following is the most likely diagnosis?

- A. Adhesive capsulitis
- B. Bicipital tendinitis
- C. Pancoast tumor
- D. Rotator cuff tear
- E. Rotator cuff tendinitis
- F. Subacromial bursitis

▼ Explanation

• Answer is F (Subacromial bursitis)

◦ IMP Clues

- Type 2 diabetes mellitus (DM is a HY risk factor found in most Shoulder Joint pathologies)
- Right shoulder pain that occurs when she attempts to raise her arms & when lying on her right side (Okay something is affection abduction + something is inflamed as pressure from lying causes pain)
- She has not had weakness, tingling, or numbness (This excludes Pancoast tumors as they compress the brachial plexus, causing these symptoms)
- Tenderness to palpation in the region of the right deltoid muscle just lateral to acromioclavicular joint (The literal site of acromion)
- She is able to abduct her arm to nearly 90 degrees, but additional abduction is prevented by pain (Abduction is only affected, so either the muscle or tendon or bursa involved in abduction. Adhesive capsulitis causes loss of ROM in ALL directions)
- Muscle strength is 5/5 (Excludes the “muscle” weakness, which is rotator cuff tear)
- There is no impingement sign (Excludes the “tendon”, which is rotator cuff tendinitis)

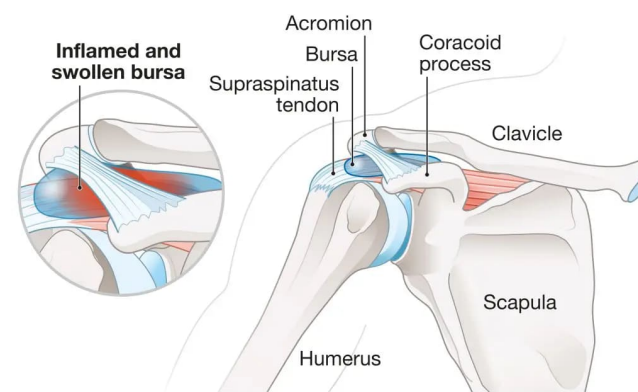
◦ Dx → Subacromial Bursitis

- Inflammation of the **subacromial bursa**, which is found between the acromion and the supraspinatus tendon.
 - This is why when the patient *tries to abduct her arm*, the **inflamed bursa frictions** with the humerus/supraspinatus tendon & acromion ⇒ **Pain with abduction**
 - Also, due to its lateral site, *when the patient lies on that side*, the **pressure compressed the inflamed bursa** ⇒ **Pain when lying on her side + Lateral Shoulder Tenderness**

USMLE can show you the X-Ray below & ask for the diagnosis; answer is Subacromial Bursitis.



Subacromial Bursitis



? What is the test used to assess supraspinatus muscle injury?

▼ Answer

Empty Can Test

Q23

A 2-week-old female newborn of Mexican descent is brought to the physician by her mother for a well-child examination. The mother reports that the baby has been doing well, except that she often cries inconsolably for about an hour after feeding with formula. The mother says, "I am sure that she has got the evil eye". The mother has been passing an egg over the baby's body, then cracking the egg into a glass of water and placing the glass underneath the baby's bed. However, there has been no change in the baby's behavior. The newborn is at the 50th percentile for length and 35th percentile for head circumference. Her vital signs are within normal limits. Physical and abdominal examinations show no abnormalities. Which of the following is the most appropriate statement by the physician?

- A. "Have you considered talking to a faith healer to see if there might be other measures you should try?"
- B. "I think your baby has gas, not the evil eye. Why don't we try giving her medication?"
- C. "I'm not very knowledgeable about your folk beliefs. Would you like me to refer you to a doctor who is?"
- D. "There's not a lot of evidence in modern medicine to support what you are doing, but it isn't harming the baby."
- E. "Why don't you continue with what you're doing, and let's try changing her to a different formula."

▼ Explanation

- Answer is E ("Why don't you continue with what you're doing, and let's try changing her to a different formula.")
 - USMLE exam writers are obsessed with testing *how you would react to different cultural beliefs*. Here for example, the child is **healthy**; however, she just cries after feeding with formula.
 - This is probably due to **ingestion/gas**. The mother, however, thinks this is **evil eye**, so she's passing an egg over the baby's body, then cracking the egg into a glass of water and placing the glass underneath the baby's bed.
 - So basically, the baby is **healthy**, and the mother is **not harming the baby** (The egg is under the bed, not on the baby) → **Let her do what she's doing & change the formula.**
 - In approaching these types of Qs, the first thing you need to do is RESPECT THE CULTURE/BELIEFS, then Reassure the mother, then Educate.
 - Let's go through the choices:
 - Choice A → You're basically advising superstitions, which is unethical. What you need to do is RESEPECT what they are doing, not tell them to try more superstitions.
 - Choice B → You're dismissing her culture/beliefs.
 - Choice C → "Your folk beliefs" sounds racist doesn't it. Giving off White Supremacy vibes.
 - Choice D → You're also dismissing her culture/beliefs
 - Choice E → This is the **best answer**. It is not perfect tbh as it sounds a little judgmental. **However, you acknowledged her beliefs and tried to treat the baby's formula.**

Q24

A 65-year-old man comes to the physician because of a 1-year history of erectile dysfunction. He has a 20-year history of type 2 diabetes mellitus and is currently taking insulin. Physical examination and laboratory studies show no abnormalities. It is most appropriate for the physician to prescribe a drug that increases the actions of cGMP in which of the following cell types in the penis?

- A. Endothelial cells of the deep dorsal artery
- B. Endothelial cells of the dorsal artery
- C. Endothelial cells of the dorsal vein
- D. Smooth muscle cells of the deep artery
- E. Smooth muscle cells of the deep dorsal vein

▼ Explanation

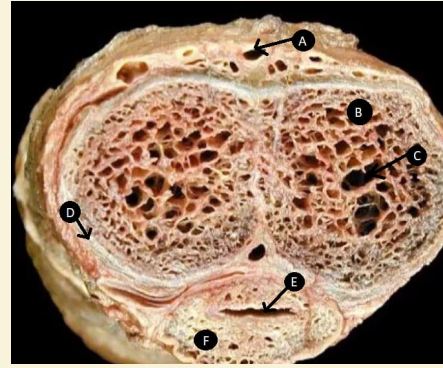
- Answer is D (Smooth muscle cells of the deep artery)
 - IMP Clues
 - 1-year hx of erectile dysfunction
 - Q wants a drug that increases the action of cGMP

- Sildenafil (more commonly known as Viagra)
 - PDE-5 inhibitor that causes **vasodilation of the Deep Penile Artery** that supplies the **corpus cavernosum** *[asked on NBME]*
 - Uses: Erectile Dysfunction & Pulmonary HTN.
 - HY Side Effects:
 - **Hypotension** (especially if taken with other drugs that cause hypotension, like nitrates)
 - **Bluish tint in color vision.**

? How does PDE-5 Inhibitors work?

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

? Label the following.



- ▼ Answer
A → **Dorsal Vein**
B → **Corpus Cavernosum** *[asked on NBME]*
C → **Deep Artery**
D → **Tunica Albuginea**
E → **Urethra**
F → **Corpus Spongiosum**

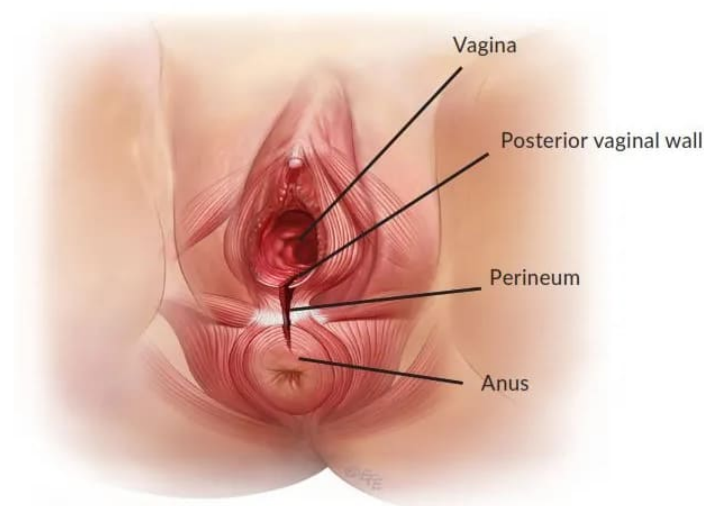
Q25

A 35-year-old woman, gravida 2, para 1, undergoes vaginal delivery at term. Physical examination shows crowning of the newborn's head and perineal blanching. A median episiotomy is done to hasten delivery. During this procedure, an incision is made posteriorly from the posterior vaginal commissure. Which of the following muscles is at greatest risk for damage if this incision is torn further during delivery?

- A. Bulbospongiosus
- B. External anal sphincter
- C. Ischiocavernosus
- D. Obturator internus
- E. Sphincter urethrae

▼ Explanation

- Answer is B (External anal sphincter)
 - **Posterior Episiotomy** is usually **NOT** preferred due to risk of causing **anal sphincter damage**, which causes **fecal incontinence in a female since giving birth** *[asked on NBME]*



[For Nerds/STEP2] Degrees of Perineal Tears:

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

Q26

A 65-year-old man develops a progressive ataxia with gait unsteadiness. There is an intention tremor on the right side. The most likely cause is damage to which of the following areas of the brain?

- A. Left cerebellar hemisphere
- B. Left frontal lobe
- C. Left pyramidal tract
- D. Left ventrolateral nucleus of the thalamus
- E. Right cerebellar hemisphere
- F. Right pyramidal tract

▼ Explanation

• Answer is E (Right cerebellar hemisphere)

◦ IMP Clues

- Ataxia with gait unsteadiness (ataxia on the USMLE is either cerebellum lesion or Dorsal Column Lesion/Peripheral Neuropathy)
- Intentional Tremors (Cerebellar lesion) on the right side (Right Lobe, as cerebellum supplies ipsilateral side)
- Q asks for which are is damaged in the brain?

• Cerebellum

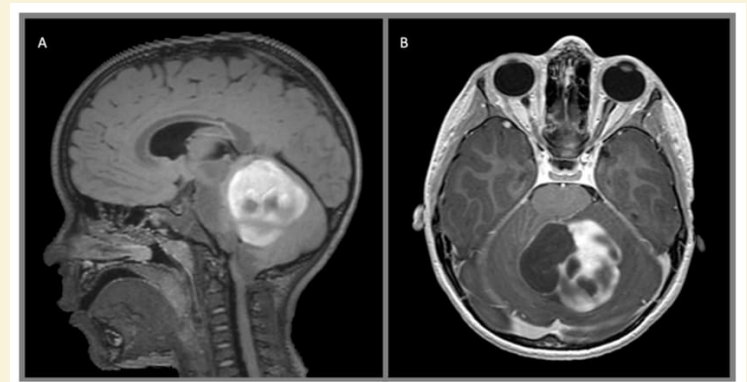
- This is pass-level and very evidently a cerebellar hemisphere lesion.
- **The Cerebellum hemispheres control the *ipsilateral* side of the body, so right hemisphere → Right Limb; while, left hemisphere → Left Limb**
 - **Vermis**, however, controls the **trunk**.
 - *USMLE tests this by giving you **intentional tremors** in a patient in right vs left limbs vs trunk & asks for site of lesion*
- **Cerebellar lesion symptoms are very distinctive on the USMLE → Ataxia, Tremors, Dysmetria, Dysdiadochokinesia**
 - How to differentiate ataxia of Dorsal Column lesions/Peripheral Neuropathy from Cerebellar lesions?
 - Dorsal Column/Tabes Dorsalis/Peripheral Neuropathy ⇒ **POSITIVE ROMBERG SIGN** (patient leans to one side/falls when closing his eyes)
 - Cerebellar lesions ⇒ **NEGATIVE ROMBERG SIGN**
 - How to differentiate different tremors from cerebellar tremors?
 - Cerebellar (Intention) tremors → **absent at rest, appears with voluntary movement**, and **increases as target is approached**
 - Parkinson (Resting) tremors → **present** at rest, **decreases** with voluntary movement, and has **“pill-rolling”** characteristic movement pattern
 - Essential (Familial) tremors → **increases** with stress & fatigue, **decreases with alcohol** & beta-blockers, and **positive** family hx
 - Drug-Induced tremors → **B2 Agonists** & **Lithium** are the most HY drugs that cause tremors on the USMLE.

? 4F with projectile vomiting at mornings, headaches, difficulty in preforming repetitive hand movements. What is most likely seen on histological biopsy?

▼ Answer

Rosenthal Fibers (Eosinophilic Corkscrew Filaments)

- **Pilocytic Astrocytoma** is the most common pediatric brain tumor
- Made up of Solid (White) & Cystic (Black) Components
- Brain Tumor ⇒ high ICP ⇒ **headaches & vomiting**
 - Cerebellar Tumor ⇒ **Dysdiadochokinesia** (difficulty in preforming repetitive hand movements)



! **Medulloblastoma** (another pediatric brain tumor) causes **truncal ataxia** as it usually involves the **vermis**

Q27

A 76-year-old woman is brought to the physician by her son who is concerned that she has become more forgetful during the past few months; he thinks she should be placed in a long-term care facility. She says she feels well, thinks that her son is overly concerned, and clearly does not want to leave her apartment. She has no medical problems and appears cheerful. Which of the following findings is most crucial in determining her decision-making capacity?

- A. She can write a sentence
- B. She correctly identifies political leaders
- C. She expresses clear and consistent values
- D. She follows simple written commands
- E. She has memory of childhood events

▼ Explanation

• Answer is C (She expresses clear and consistent values)

- Remember when we talked about informed consent? **We said for a patient to have a say in her medical ttt (*autonomy*), she must be deemed to have capacity.**
 - **Remember what capacity referred to?**
 - **Show Capacity → Understands** his condition/risks/options, **can reason** & reach a decision, and can **communicate** a choice.
 - It is all about checking for **mental presence**, where you are sure that the patient is **100% mentally capable of taking her decision**.
 - **Choice C shows exactly that → She expresses clear and consistent values.**
 - **“Expresses Clear” = Can communicate.**
 - **“Clear and Consistent Values” = Her values are not altered, which means her ability to reason is intact = Mentally capable.**

Q28

A 61-year-old woman comes to the physician for a health maintenance examination. She says that she has been feeling well. A split S₁ is heard over the left sternal border. Which of the following best explains the first component of this sound?

- A. Closure of the aortic valve
- B. Closure of the mitral valve
- C. Closure of the pulmonic valve
- D. Closure of the tricuspid valve
- E. Opening of the aortic valve
- F. Opening of the mitral valve
- G. Opening of the pulmonic valve
- H. Opening of the tricuspid valve

▼ Explanation

- Answer is B (Closure of the mitral valve)

- Easy Free Q.

- Heart Sounds:

- **S1 ⇒ Closure of Mitral & Tricuspid valve**

- 1st Component is **Mitral**
- 2nd Component is **Tricuspid**

- **S2 ⇒ Closure of Aortic & Pulmonary valve**

- 1st Component is **Aortic (A2)**
- 2nd Component is **Pulmonary (P2)**



Splitting of S2 is super HY:

1. **Physiological Splitting** ⇒ **Normal Finding** (inspiration causes increased VR, so more blood passes by pulmonary valve so delayed closure sound of P2)
2. **Wide Splitting** ⇒ Delayed **RV emptying** (HY causes are **RBBB, RVH, Pulmonary Stenosis**)
3. **Paradoxical Splitting** ⇒ Delayed **LV emptying** (HY causes are **LBBB, LVH, Aortic Stenosis**)
4. **Fixed Splitting** ⇒ **ASD** [asked on NBME]

Q29

A 7-year-old boy is brought to the physician by his mother because of a 2-day history of an itchy red rash on his right arm and trunk after a hike in the woods. His mother says that the rash began on his arm 1 day after the trip, but it has now spread to his trunk. Physical examination shows 2-cm patches of raised, red, elongated blisters that ooze clear fluid on the upper extremities and trunk. The blisters are in a linear distribution with patches of erythema. Which of the following best describes the mechanism of this patient's reaction?

- A. Activation of mast cells by IgE
- B. Deposition of antigen-antibody complexes
- C. Late phase reaction of a type I hypersensitivity
- D. Release of interferon gamma by Th1 cells
- E. Synthesis of high-affinity IgG by B lymphocytes

▼ Explanation

- Answer is D (Release of interferon gamma by Th1 cells)

- **IMP Clues**

- 2-day history of an itchy rash on his right arm & trunk after a hike in the woods (Hike in the woods on the USMLE is either an insect/tick/mosquito bite or poison ivy/oak rash)
- Rash began on his arm 1 day after the trip, but it has now spread to his trunk (This description fits both poison ivy/oak rash & Rickettsia rickettsii rash, which is however transmitted via Dermacentor tick)
- 2cm patches of raised, red, elongated blisters that ooze clear fluid + blisters are in a linear distribution with patches of erythema (This here locks in the dx as poison ivy/oak rash, as blisters + linear distribution is consistent with poison ivy. R.rickettsii is macular/petechial rash)

- **Dx → Poison Ivy-induced Allergic Contact Dermatitis**

- **Poison Ivy/Oak/Sumac** all contain **urushiol**, which is the antigen that triggers the immune system:

- **Antigen is presented by APCs to MHC1/2 → CD8/CD4 T-cells activation (Choice D)**
- Process takes **1-3 days**, hence known as **Delayed Type 4 Hypersensitivity Reaction**



Langerhans cells are the macrophages/APCs of the skin.

- **Activated Lymphocytes (CD4/8) release cytokines, which increase vascular permeability causing leakage into the epidermis.**
 - This leakage causes the **keratinocytes to separate** from each other (+ fluid accumulated under) → **Blister Formation** “This is referred to as **spongiosis**”
 - So, the final histological appearance seen is “**Spongiosis and Lymphocytic Infiltration, with vesicle/blister formation**”
 - Clinical Features:
 - **Pruritis, Erythema, Vesicles/Blisters, and Linear Streaked Lesions on “contacted” skin.**
 - why are there streaks linear?
 - Basically, when plants come in contact with your skin, **they usually brush your skin in that pattern.**

Poison Ivy Contact Dermatitis:



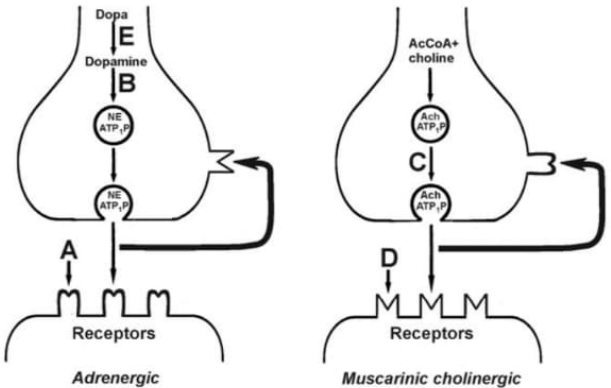
? What are some HY causes of T4 HS reaction on the USMLE?

▼ Answer

1. Contact Dermatitis
 - **Poison Ivy/Oak/Sumac**
 - **Nickle** (Necklace, Bracelet, Belts)
 - **Latex**
2. Skin Tests
 - **PPD**
 - **Candida Skin Test**
3. Granuloma Formation
 - **TB** (caseating)
 - **Sarcoidosis** (noncaseating)
 - **Crohn’s disease** (noncaseating)
4. Transplant Rejection
 - **Graft-versus-Host (GVHD)**
 - **Acute/Chronic Rejection**

Q30

A 44-year-old man who is a farmer and has been spraying his orchards with insecticides is brought to the emergency department by his wife because of vomiting, diarrhea, wheezing, and sweating for the past 12 hours. He has excess salivation and generalized muscle weakness. He is confused and his pupils are small. A drug acting at which of the following labeled sites is most appropriate after stabilization of this patient's airway?



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

▼ Explanation

- **Answer is D**
 - **IMP Clues**
 - Farmer + spraying his orchards with insecticides
 - Vomiting, diarrhea, wheezing, and sweating + excess salivation and generalized muscle weakness
 - Confused and his pupils are small
 - Q asks a drug acting on which site is appropriate for that patient after stabilization of airway?

- Dx → Organophosphate Compounds (OPC) Poisoning
 - Almost always a **farmer** on the USMLE, sometimes can be **a child who is messing around in a kitchen cabinet**.
 - **OPC are irreversible AChE inhibitors, causing excessive ACh effects on both nicotinic and muscarinic receptors.**
 1. Overstimulation of **Muscarinic Receptors** causes “Cholinergic Toxidrome”

Mnemonic: “**DUMBBELSS**”

- **D**iarrhea
- **U**rination
- **M**iosis
- **B**radycardia
- **B**ronchospasm
- **E**mesis
- **L**acrimation
- **S**alivation
- **S**weating

2. Overstimulation of **Nicotinic Receptors** cause **Skeletal Muscle Weakness, Fasciculation, and Paralysis.**

- Treatment:
 - **FIRST** ⇒ **ATROPINE, Muscarinic Antagonist**, that **reverses** the **muscarinic** overstimulation “Cholinergic Toxidromes”
 - **THEN** ⇒ **Pralidoxime, regenerates AChE**, that **reverses BOTH muscarinic and nicotinic** overstimulation

 **Organophosphorus Compounds:**

Knowing their names are important and asked on NBME/Free120, so know them:

- **Parathion/Malathion (Insecticides)**
- Sarin
- Soman
- Tabun

 **What are the differences between Nicotinic & Muscarinic Receptors?**

▼ Answer

- Nicotinic** → Ligand-gated ion channels
 - **Neuromuscular Junctions**, Autonomic Ganglia, and Adrenal Medulla
- Muscarinic** → G-protein-coupled receptors
 - **CNS, Heart, GI, Smooth muscles, Glands.** (Basically, everything else)

 **USMLE asks about this differentiation when assessing Myasthenia Gravis. They are antibodies against post-synaptic ACh Nicotinic Receptor (NMJ affection, hence the weakness)**

Q31

A study was conducted to investigate the mean age at onset in one type of muscular dystrophy. Based on a mental evaluation, patients were divided into two groups: normal intelligence and subnormal intelligence. The results are given in the table.

Intelligence Level	Age at Onset in Years (n)	Mean	Standard Deviation
Normal	36	3.8	1.8
Subnormal	16	3.5	1.5

If age at onset has a normal (gaussian) distribution, the percentage of children with normal intelligence who will have onset of the disease at less than 9 years of age is closest to which of the following?

- A. 99%
- B. 95%
- C. 90%
- D. 68%
- E. 50%

▼ Explanation

- Answer is A (99%)
 - The Q asks for the % of children with normal intelligence who will have onset of disease at less than 9 years of age.
 - Normal Intelligence level → **Mean is 3.8 + 1.8 SD.**
 - **+1 SD** → 5.6
 - **+2 SD** → 7.4
 - **+3 SD** → 9.2
 - So, **people with Mean age at onset ≥ 9.2 is +3SD, which is <1%.**
 - **Q wants mean age at onset LESS THAN (≤ 9), which is 99% (Choice A)**

Q32

A 15-year-old boy is brought to the physician for a well-child examination. During the interview, he asks the physician if he will develop severe acne like his 18-year-old brother did at this age. He says, "It was awful. My parents took him to the doctor, but nothing helped. Then one day it seemed to go away on its own." Physical examination shows mild, scattered open and closed comedones. If this patient develops severe acne vulgaris that resolves spontaneously over the next 3 years, a rapid increase in the secretion of which of the following substances will have been the most likely cause of the acne?

- A. Androstenediol
- B. Estradiol
- C. Gonadotropin-releasing hormone
- D. Luteinizing hormone
- E. Testosterone

▼ Explanation

- **Answer is E (Testosterone)**

- **IMP Clues**

- Physical examination shows mild, scattered open and closed comedones (Comedones are the primary lesions of acne)
- Q asks a rapid increase in the secretion of which of the following is the most likely cause of acne?

- **Dx → Acne Vulgaris**

- Acne is chronic inflammatory **pilosebaceous unit** [asked on NBME] disorder.
 - Steps of acne development is as follows:
 1. **Follicular Hyperkeratinization** → blocks the follicles [Forms the “**keratin plug**”]
 2. **Increased Sebum Production** (caused by **androgen** stimulation) → mediates an infection-ideal environment [These here are the **Comedones**]
 3. **Colonization with Propionibacterium acnes** (referred to lately on USMLEs as “**Cutibacterium acnes**”) → Causes inflammation [This is where the papules, pustules, nodules, and cysts form]
 - In **teenagers & girl with PCOS**, the **increased androgen** (Choice E) drives **more sebum production** → Ideal environment for **Propionibacterium acnes infection** ⇒ **Acne**

⚠ Another HY cause of acne is “**occlusive clothing**.” USMLE will give you a girl that started running/gym a few weeks ago and throw in “**wears headband while exercising**.” The examination will then show **acne on the forehead ONLY** (the site of the headband); They then ask for cause of acne; answer → **occlusive clothing**.

- Treatment:

- **Topical Retinoids** → Benzoyl Peroxide → **Topical Clindamycin** → **Oral Tetracycline** → **Oral Isotretinoin**

? What is the most HY piece of info regarding Acne ttt?

▼ Answer

Isotretinoin (Oral) is teratogenic, so women of child-bearing age **MUST** be on contraceptives (COCs) while using the drug.

- Why is it teratogenic?

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

⚠ USMLE can be sneaky, and give you a patient on “**acne treatment**” that develops **burns** after **going to the beach/playing in the sun** and ask you for the drug; answer is **Tetracyclines** (**photosensitivity** is HY side effect)

Q33

An investigator is conducting a study to determine the cause of an outbreak of illness at a skilled nursing care facility. A total of 13 residents developed fever, an erythematous rash, and varying degrees of renal impairment during a 2-week period. A previously unidentified virus is recovered from urine specimens collected from seven of these patients. Physical characterization of the virus shows that viral infectivity is essentially destroyed by heating to 60°C for 30 minutes. Based on this finding, this virus most likely has which of the following characteristics?

- A. Enveloped
- B. Genome consisting of DNA
- C. Genome consisting of RNA
- D. Icosahedral capsid symmetry
- E. Nonenveloped

▼ Explanation

- **Answer is A (Enveloped)**

- **IMP Clues**

- Viral infectivity is essentially destroyed by heating to 60C for 30 mins (this means this virus is heat-labile)

- Q asks based on these findings, this virus most likely has which of the following characteristics?

- If you found this Q hard, then most likely you don't know what “**Enveloped**” really means?
 - Viruses that are “**enveloped**” **get their “envelope” from the host's cell membrane**, so it would make sense for that envelope to have the same structure as the cell's membrane.
 - Envelope is **Lipid Bilayer**, and as we know (hopefully, you do) ⇒ **Lipid Layers are easily disrupted by Heat, Acidity, and Detergents**

- So, when a virus is exposed to **heat** (Heat-Labile), **Acid** (Acid-Labile), and **detergents** → **They *lose* their envelope.**
 - **So why is their infectivity destroyed?**
 - Enveloped Viruses use their envelope **to attach to host cells.**
 - **NO envelope = NO attachment = NON-INFECTIVE**

Q34

A 24-year-old man has a grade 3/6 systolic murmur. Cardiac catheterization shows:

	Pressure (mm Hg)	O ₂ Saturation (%)
Right atrium	6	75
Right ventricle	30/5	75
Pulmonary artery	30/20	75
Left atrium	10	98
Left ventricle	180/10	98
Aorta	110/70	98

Which of the following is the most likely diagnosis?

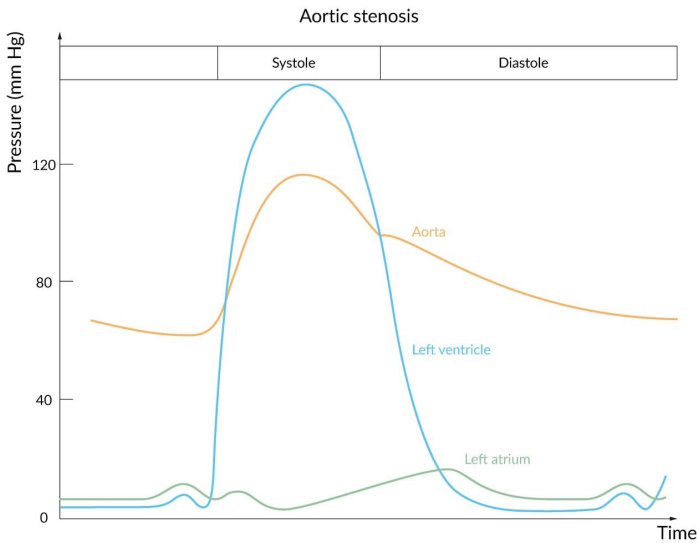
- A. Aortic stenosis
- B. Atrial septal defect
- C. Mitral regurgitation
- D. Pulmonic stenosis
- E. Tricuspid regurgitation
- F. Ventricular septal defect

▼ Explanation

- **Answer is A (Aortic stenosis)**
 - When getting these types of cardiac catheterization Qs on the USMLE, you need to look for 2 things:
 1. Abnormal **O2 Sat pattern**, which may reveal ASD, VSD, or PDA.
 2. Abnormal **Pressure pattern**, which may reveal valvular stenosis or regurgitation.
 - It is always helpful to draw the graph on the right, especially when they **DON'T** give you the catheterization results in order.
 1. **O2 Sat pattern looks normal.**
 - a. Deoxygenated Blood from RA → RV → PA → Oxygenated at the Lungs → Oxygenated Blood to LA → LV → Aorta
 2. **Pressure Pattern looks abnormal.**
 - They are *all slightly increased*, except LV & Aorta:
 - **LV → GREATLY Increased**
 - **Aorta → Normal/Slightly Decreased**
 - This means that there is a **valvular at the Aortic Valve**
 - Given that the Q says **"Systolic Murmur"** ⇒ **THIS IS AORTIC STENOSIS**

RA	LA
5	10
RV	LV
25/5	120/10
PA	Ao
25/10	120/80

The below cardiac curve is important & maybe seen on your exam:



- Aortic Stenosis is characterized by a **LV pressure >>> Aortic**

Q35

A 32-year-old man has a diastolic blood pressure that consistently ranges between 100 and 110 mm Hg. He is otherwise healthy and is not taking any medications. Serum concentrations of potassium, glucose, creatinine, and uric acid are within the reference range. Urine contains only trace amounts of protein and no albumin. He is unlikely to develop peripheral tissue edema because of regulatory adjustments in which of the following?

- A. Capillary membrane permeability
- B. Lymphatic flow
- C. Plasma oncotic pressure
- D. Postcapillary resistance
- E. Precapillary resistance
- F. Systemic venous pressure

▼ Explanation

- **Answer is E (Precapillary resistance)**

- Patient has **diastolic HTN (≥ 90)** and the Q asks, he is unlikely to develop peripheral tissue edema due to regulatory adjustment in which of the following?

- To understand this, you'd have to understand the structure of our capillary system, which is made up of 3 parts:

1. **Precapillary Arterioles**

- **Major Regulator of diastolic pressure**, which if constricts:

- **Increases systemic vascular resistance**
- **Decreases hydrostatic capillary pressure**

2. **Capillaries**

- **Site of exchange**

- Changes in *pre-capillary arterioles* can affect the capillary exchange:

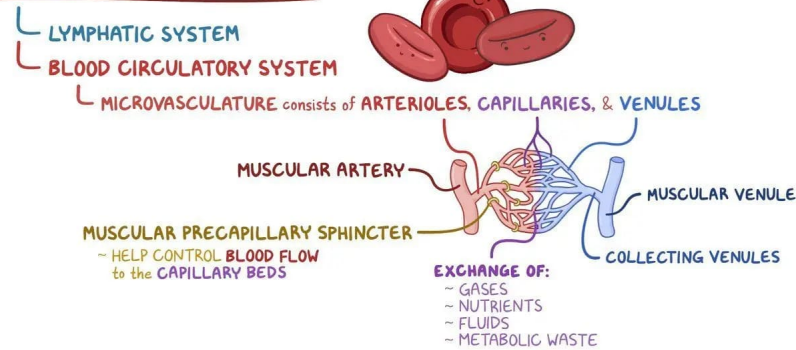
- **Precapillary arterioles constrict $\rightarrow$ decreased hydrostatic pressure $\rightarrow$ decreased filtration $\rightarrow$ decreased tissue edema**
- The question here asks "due to regulatory adjustments in which??" The answer is **arterioles** as they **control flow** to the capillaries (**Choice E**)
- If the Q were to ask about the **SITE** of peripheral edema, then capillaries would be the correct answer.

3. **Postcapillary Venules**

- **Major Site of Inflammation**

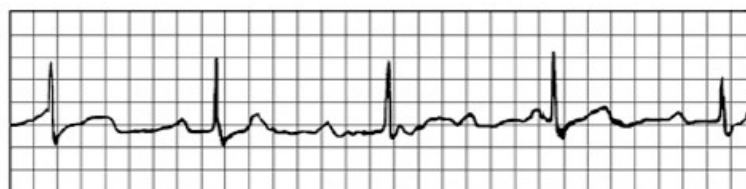
- When tissue is inflamed, **inflammatory mediators cause dilation of post-capillary venules $\rightarrow$ extravasation of fluid & inflammatory cells.**

THE CIRCULATORY SYSTEM



Q36

Electrophysiology of the heart is studied in an anesthetized experimental animal. Initially, an ECG shows no abnormalities. Which of the following procedures is most likely to produce the ECG abnormality shown?



- Ablation of the atrioventricular node
- Ablation of bundle-branch fibers
- Ablation of the sinoatrial node
- Destruction of part of the left ventricle
- Destruction of part of the right atrium

▼ Explanation

- **Answer is A (Ablation of the atrioventricular node)**

- ECG shown is for **Third-degree Heart Block/AV Block**

- Due to **ablation of AV Node**, which transmits electrical impulse from atria to ventricles.

- **If AV Node is completely ablated, the atria & ventricles contract independently of each other, which causes:**

- **p-waves > QRS complexes** (as atria contraction rate is faster than ventricular rate) $\Rightarrow$ **AV-Dissociation**
- **p-waves are at regular intervals**
- **QRS complexes are at regular intervals**

- Picture below shows a classic Third-Degree Heart Block:



? What infection is a HY cause of third-degree heart block on the USMLE?

▼ Answer
Lyme Disease

Cardiac Tissue Conduction Velocities:

| Fastest $\rightarrow$ Slowest

1. Purkinje Fibers
2. Bundle of His
3. Atrial muscle
4. Ventricular muscle
5. AV Node

| You're going to be like, "wait, this looks nothing like the above ECG given in the Q!"

- Yes, the ECG I showed you is the **CLASSIC Third Degree HB/AV block**.
 - **QRS Complexes** should be **wide**, as ventricular cell depolarization & movement of impulse to all other ventricular cells are slow.
 - **Slow Depolarization → Wide QRS.**
- Then why the fuck is the ECG in the Q different?
 - This is **Third-Degree HB/AV Block WITH AN ESCAPE JUNCTIONAL RHYTHM**.
 - What this means is that **instead of the ventricular cells becoming the pacemaker of the ventricles, the Bundle of His does**.
 - This causes the QRS (Ventricular) depolarization to happen at a **faster rate** than it classically would, causing a **narrow QRS complex**.

| Weird as fuck to have this as a STEP 1 Q, but game is game.



AV node conduction is the **slowest** to allow completion of atrial contraction before ventricles & to prevent excessive impulse conduction to ventricles to prevent ventricular tachycardia & arrhythmia (lethal).



- Differences between different types of AV Blocks:
- **First Degree** → PR interval **> 200 ms**
 - **Mobitz I** → PR interval **progressively increases until QRS drops**.
 - **Mobitz II** → PR interval is **constant**, but there are **sudden QRS drops**.
 - **Third Degree** → PR interval **varies widely due to p-QRS dissociation**.

Q37

A 16-year-old girl with bulimia nervosa is brought to the physician by her mother because of a 4-month history of nonbloody diarrhea. Her mother is concerned that she is abusing laxatives to maintain a low body weight. The patient is 165 cm (5 ft 5 in) tall and weighs 52 kg (115 lb); BMI is 19 kg/m². Her temperature is 37.5°C (99.5°F), pulse is 120/min, respirations are 30/min, and blood pressure is 89/61 mm Hg. Which of the following sets of serum electrolyte concentrations is most likely in this patient?

Choices	Potassium	Chloride	Bicarbonate
A	Increased	increased	normal
B	Increased	decreased	decreased
C	Unchanged	increased	decreased
D	Decreased	increased	decreased
E	Decreased	normal	increased

▼ Explanation

- Answer is D
 - IMP Clues
 - Bulimia Nervosa (by definition normal BMI + compensatory action post-binge eating; If BMI is low then this would be anorexia nervosa)
 - She is abusing laxatives
 - Blood pressure is 89/61 mmHg (she is dehydrated due to decreased fluid loss in stools)
 - Q asks for expected electrolyte concentrations
- Dx → Laxatives Abuse
 - When a person abuses laxatives, they're essentially having **diarrhea**.
 - So, the expected electrolyte derangement would be the same as someone with diarrhea.
 - **Diarrhea causes Hypokalemic Metabolic Acidosis (Choice D)**



- USMLE loves the distinction between **laxatives abuse vs diuretics abuse vs vomiting** (bulimia/anorexia nervosa emetic types):
- **Laxatives abuse/Diarrhea** ⇒ Hypokalemic Metabolic **Acidosis**
 - **Diuretics abuse** ⇒ Hypokalemic **Hyperchloremic Metabolic Alkalosis** + high Creatinine
 - **Vomiting** ⇒ Hypokalemic **Hypochloremic Metabolic Alkalosis**

Q38

A 43-year-old woman comes to the physician because she has fainted on three separate occasions during the past 5 months. After the most recent episode 2 weeks ago, she noticed weakness of her face and right arm, which resolved over the next 2 days. Her vital signs are within normal limits. Cardiac examination shows a mild grade 2/6 diastolic murmur over the apex that becomes more pronounced when the patient rises from a prone position. Which of the following is the most likely cause of this patient's syncope?

- A. Atrial septal defect
- B. Bicuspid aortic valve
- C. Fibrinous pericardial effusion
- D. Left atrial myxoma
- E. Right ventricular outflow tract obstruction

▼ Explanation

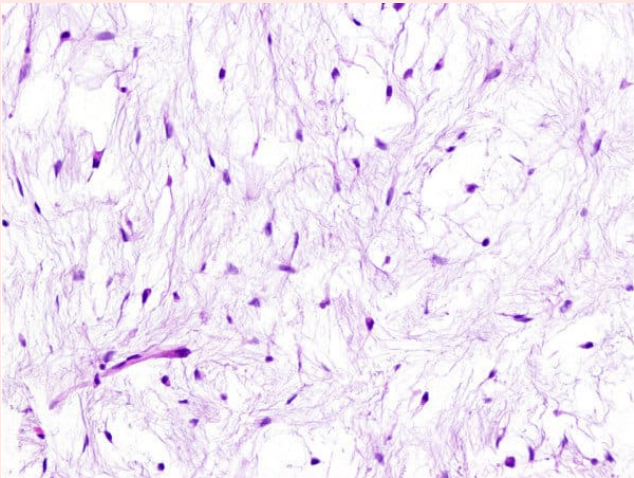
- **Answer is D (Left atrial myxoma)**
 - **IMP Clues**
 - Fainted on three separate occasions (Cardio + fainted is either outflow obstruction or arrhythmias)
 - Weakness of her face and right arm, which resolved (embolic manifestations)
 - Diastolic murmur over the apex that become more pronounced when the patient rises from a prone position (Diastolic murmur that changes with position is buzzy for cardiac myxoma)
 - **Dx → Cardiac Myxoma**
 - **Most common primary cardiac tumor (benign) that arises most commonly in the *Left Atrium* [asked on NBME]**
 - **Connected to the interatrial septum by a pedunculated stalk ⇒ moves freely & gives it its classic shape ⇒ *Polypoid Ball-in-valve mass* that obstructs LA**
 - Histology: ***Spindle cells in myxoid stroma* [asked on NBME]**
 - The Histology pic is HY and is on the NBMEs
 - **Clinical Features**
 1. **LA Outflow Obstruction ⇒ Fainting**
 2. **Pedunculated Mass ⇒ Diastolic murmur changes with position change**
 3. **Embolic Manifestations (Fragments break) ⇒ Stroke, Ischemia, Infarctions**



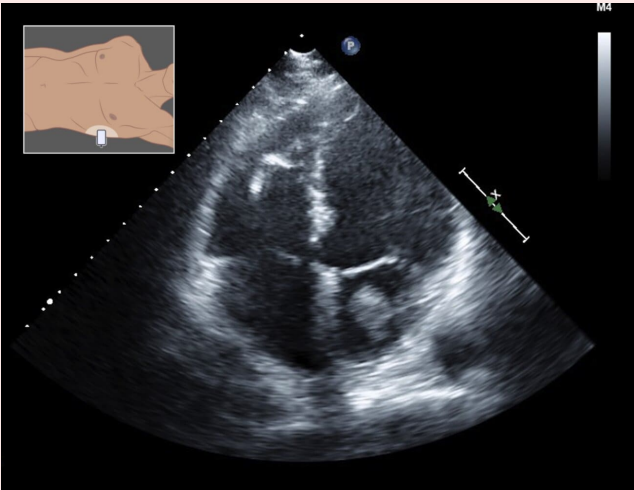
Myxoma presents in kids in ONLY ONE SYNDROME: *Carney Complex*

- **Child with *Hyperpigmentation*** (usually peri-oral melanosis similar to Peutz-Jeghers Syndrome but will not mention the hamartomatous colonic polyps but ask about the cardiac lesion)
- ***Atrial Myxoma*** (the cardiac lesion)
- ***Endocrine Hypersecretion*** (usually Cushing's)

Cardiac Myxoma Histology:



Left Atrial Myxoma ECHO:



Q39

A 2-year-old boy is brought to the emergency department because of severe, generalized abdominal pain and vomiting for 3 hours. He also has had episodes of abdominal pain during the past year. Physical examination shows yellowish white papules on the back, generalized abdominal tenderness, and hepatosplenomegaly. Serum studies show an increased amylase activity and increased concentrations of total cholesterol, triglycerides, and chylomicrons. This patient most likely has a deficiency in which of the following proteins?

- A. LDL-cholesterol receptor
- B. Lipoprotein lipase
- C. Lysosomal acid lipase
- D. Pancreatic lipase
- E. Phospholipase C

▼ Explanation

- **Answer is B (Lipoprotein Lipase)**
 - **IMP Clues**
 - Recurrent severe, generalized abdominal pain and vomiting + tenderness + Increased amylase activity (Screaming pancreatitis, recurrent. Pancreatitis in hyperlipidemia Q is either type 1 or type 4)
 - Yellowish white papules on the back (Xanthomas) + Hepatosplenomegaly (lipid accumulation)
 - Increased concentrations of total cholesterol, triglycerides, and chylomicrons (Chylomicrons is the keyword needed. This is Type 1, Hyperchylomicronemia)

- Dx → Type 1 Hyperchylomicronemia
 - Deficiency of **LPL or ApoC-2**
 - Labs: **high** chylomicrons, **high** TAGs, and **high** cholesterol
 - Turbid creamy plasma, **pancreatitis**, and xanthomas
 - On the USMLE, the moment we're talking about dyslipidemia, and "**creamy/turbid/milky plasma**" is mentioned ⇒ Choose **Type 1 Hyperchylomicronemia**

⚠ When serum **TAGs > 1000 mg/dL**, the patient is usually at risk of **hypertriglyceridemia-induced pancreatitis**

⚠ **Xanthomas** are skin **cholesterol** deposits.

? How does Insulin affect LPL?

▼ Answer

Insulin increases the activity of LPL

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

If you want to be **SUPER-SPECIFIC**

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

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

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



Familial Dyslipidemias Rapid Review

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

1. Type 1 (Hyperchylomicronemia)

📖 "**1LP**"

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

2. Type 2 (Hypercholesterolemia)

a. 📖 "**2 LD**" (**Type 2A**)

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

b. 📖 "**B adds V**" (**Type 2B**)

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

3. Type 3 (Dysbetalipoproteinemia)

📖 "**3 is E**"

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

4. Type 4 (Hypertriglyceridemia)

📖 "**4 gets More**"

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

Q40

A 2-week-old male newborn is brought to the physician by his parents because of yellow skin for 7 days. The mother is extremely obese. At birth, the newborn was severely lethargic and hypoglycemic and was fed both intravenously as well as orally with a soybean formula until the age of 4 days. He has been breast-fed since then, but he has been vomiting most of his feedings. Physical examination shows jaundice. There is no glucosuria, but reducing substances are detected in the urine. His serum direct bilirubin concentration is increased. An assay for which of the following would have most likely established the diagnosis in this patient at the age of 3 days?

- Fructokinase
- Fructose
- Galactose-1-phosphate uridylyltransferase
- Glucose-6-phosphatase
- Glucuronyl transferase
- Lactase

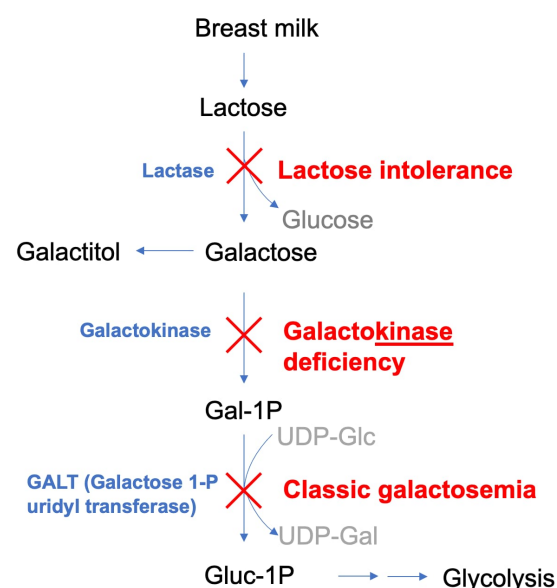
▼ Explanation

- Answer is C (Galactose-1-phosphate uridylyltransferase)
 - IMP Clues
 - Yellow skin + Jaundice + His serum bilirubin concentration is increased
 - The newborn was severely lethargic and hypoglycemic and was fed both intravenously as well as orally with a soybean formula until the age of 4 days
 - He has been breast-fed since then, but has been vomiting most of his feedings
 - No glucosuria, but reducing substances are detected in the urine

- **Dx → Classic Galactosemia**

- Deficiency of **GALT (Galactose-1-phosphate uridylyltransferase)**
- GALT is an enzyme in the **galactose metabolism**, which functions to transform *galactose into glycose/glycogen*.
- What happened here was that when the child was breastfed → Lactose → broken down **by lactase into glucose + galactose**.
 - Galactose → Galactose-1-phosphate (**via Galactokinase**)
 - Galactose-1-phosphate + UDP-glucose → UDP-galactose + Glucose-1-phosphate (**via GALT**)
 - Glucose-1-phosphate → Glucose-6-phosphate → glycolysis or glycogenesis
- **If GALT is deficient:**
 1. Galactose-1-phosphate **accumulates** in the liver (toxic) → **Hyperbilirubinemia & Jaundice +/- Liver Failure**
 2. Galactose builds up in the blood → converted via *aldose reductase* to **galactitol**, which accumulates in eye lens → **Cataract**
 3. Galactose build up into blood, so gets **secreted in urine** → **Reducing Substances in Urine**
 4. **Lethargy & Hypoglycemia** due to inability to form glucose from galactose.

⚠ The child was fine for the first few days as **soy-based formula** has **NO** lactose (and galactose).



Q41

A 65-year-old man is brought to the emergency department because of intermittent substernal chest discomfort over the past 24 hours. Which of the following eicosanoids is most likely contributing to his symptoms?

- Leukotriene B₄
- Leukotriene D₄
- Leukotriene F₄
- Prostaglandin E₂
- Prostaglandin F_{2a}
- Thromboxane A₂

▼ **Explanation**

- **Answer is F (Thromboxane A₂)**
- The functions of all of these are HY, so let's go through them:
 - **Leukotriene B₄ ⇒ Chemotactic Molecule** (induces migration of inflammatory cells into site of infection/inflammation)

⚠ **Chemotactic Molecules on the USMLE are LTB₄, IL-8, C5a, PAF, and Kallikrein.**

- **Leukotriene D₄ ⇒ Bronchoconstrictor**
- **Leukotriene F₄ ⇒ Doesn't Exist.**

⚠ **LTC₄, LTD₄, and LTE₄ main function is bronchoconstriction in asthma & anaphylaxis.**

- HY Related Drugs used as Asthma ttt:
 - **5-LOX inhibitors ⇒ Zileuton**
 - **LT Receptor Antagonists ⇒ Montelukast & Zafirlukast**

- **Prostaglandin E₂ ⇒ Vasodilation & Pain & GI mucosal protection**
- **Prostaglandin F_{2a} ⇒ Uterine Contraction**
- **Thromboxane A₂ ⇒ Induced Vasoconstriction and Platelet Aggregation**



Aspirin/NSAIDs inhibit all of the above PGs/TXA2, while **Celecoxib selectively inhibits COX-2 PGs**, which are involved in inflammation & Fever.

Q42

A 35-year-old man who is a veterinarian in a rural area comes to the physician because of headache, cough, fatigue, and myalgias 2 weeks after assisting in delivery of a lamb. His temperature is 38.9°C (102°F). Leukocyte count is 12,000/mm³, and hepatic transaminase activity is mildly increased. An x-ray of the chest shows the presence of patchy infiltrates. Gram stain of sputum and cultures of blood and sputum are negative for pathogens. After 2 days of doxycycline therapy, his symptoms are alleviated. Which of the following is the most likely causal organism?

- A. *Bacillus anthracis*
- B. *Chlamydia psittaci*
- C. *Coxiella burnetii*
- D. *Francisella tularensis*
- E. *Rickettsia rickettsii*

▼ Explanation

• Answer is C (*Coxiella burnetii*)

◦ IMP Clues

- Veterinarian (Risk factor for zoonotic infections)
- Headache, cough, fatigue, and myalgia 2 weeks after assisting in delivery of a lamb (This makes it even more likely that it is a zoonotic infection)
- Temperature is 38.9 and Leukocyte count is 12,000 (Infection)
- Hepatic Transaminase activity is mildly increased (Hepatitis)
- CXR shows the presence of patchy infiltrates (atypical pneumonia)
- Gram stain of sputum and cultures of blood and sputum are negative

• Dx → Q-fever

◦ Caused by *Coxiella burnetii*

- Gram negative **OBLIGATE** intracellular bacteria (hence, why culture of blood and sputum / Gram stain are negative)
- Transmitted via **spores in aerosols** → inhalation → picked up by **macrophages**, however, they are **resistant to phagolysosomes**.

◦ HY Reservoirs are **Farm Animals**

- So, most affected people on the USMLE are **veterinarians** or **farmers** that are exposed to these animals **OR** especially those who **assist in delivery** (*Coxiella burnetii* **LOVES placental tissue**)

◦ HY Features:

- **Headache**
- **Fever**
- **Atypical pneumonia** (the patchy infiltrates)
- **Hepatitis** (hence the elevated transaminases)



Q-fever DOESN'T present with a rash. This distinction is quite HY on the USMLE.

Q43

A study is planned to assess differences in hypertension control between patients in the USA and those in Western Europe. The study population includes 21,053 patients with hypertension receiving care from 291 cardiologists and 1284 primary care physicians in five Western European countries and the USA. The main outcome measure is hypertension control defined as a most recent blood pressure reading less than 140/90 mm Hg. Which of the following best describes this study design?

- A. Case-control study
- B. Clinical trial
- C. Cross-sectional study
- D. Prospective cohort study

▼ Explanation

- **Answer is C (Cross-sectional study)**
 - **IMP Clues**
 - Assess difference in hypertension control between patients in the USA and those in 5 Western Europe (So, we're just assessing the differences in populations ALL affected with HTN. This excludes clinical trials and Case-Control)
 - The main outcome measure is hypertension control defined as a most recent blood pressure reading less than 140/90 mmHg (So, they didn't even follow the patients for a period of time, excluding Cohort. All they did is that they defined a term based on "most recent blood pressure reading")
- **Cross-sectional Study**
 - A type of **observational study**, in which we take a **"snapshot"** of a population **at a specific time**.
 - Used to find **Prevalence OR Risk Factor ALONE**
 - **NO Causality**.
 - Measurements used in cross-sectional studies are **incidence & prevalence**.

Q44

Transmission of a bacterial agent by person-to-person contact is most likely to occur in which of the following infectious diseases?

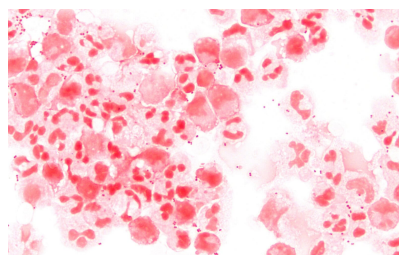
- A. Cholera
- B. Legionnaires disease
- C. Lyme disease
- D. Meningococcal meningitis
- E. Rocky Mountain spotted fever

▼ Explanation

- **Answer is D (Meningococcal meningitis)**
 - Easy Q.
 - **Choice A** → **Cholera** is transmitted via **feco-oral route**, usually via **contaminated water**.
 - **Choice B** → **Legionnaires disease** is also transmitted via **contaminated water**, especially ACs, Conference Rooms, Hotels.
 - **Choices C & E** → Both **Lyme disease & Rocky Mountain Spotted Fever** are transmitted via the **Dermacentor Tick**.
 - **Choice D** ⇒ **N.meningitides** is **highly contagious** and classically affects **college kids in dorms**.
 - HY to know that **ttt is Ceftriaxone**, while **close contacts take rifampin**.

• Let's Review N.meningitides

- **Gram negative facultative intracellular diplococci that grow on Thayer-Martin agar.**
- Both N.meningitides & N.gonorrhoeae ferment glucose, however, **only N.meningitides ferments Maltose (Differentiation Factor)**
- Virulence Factors:
 - **IgA Protease** ⇒ Cleaves mucosal IgA & allows bacteria to adhere/colonize mucous membranes [**Neisseria meningitides colonizes the nasopharynx**]
 - **Capsular Polysaccharide** ⇒ Vaccines are made against them; There is **no vaccine for Polysaccharide Capsule Serotype B [Serotype B is major cause of meningitis in USA]**
 - **Lipooligosaccharide (LOS)** ⇒ Cause of massive inflammatory Response, causing **widespread increased vascular permeability, hypovolemia, and shock**
- Diseases:
 - **Meningitis**
 - **Meningococcemia with petechial bleeding**
 - **Waterhouse-Friderichsen Syndrome**



Waterhouse-Friderichsen Syndrome

- Definition: **Acute Primary Adrenal Insufficiency caused by adrenal hemorrhage**
- Pathophysiology: Coagulopathy triggered by LOS endotoxin, which often leads to **hemorrhagic necrosis of the adrenal glands & acute failure**.
- Increased Risk in: **Asplenic Patients**
- Features:

- Treatment: **Ceftriaxone**
- Prophylaxis (For close contacts only): **Rifampin**

- Fever, Myalgia, Malaise
- **Severe Hypotension & Shock**
- **Widespread Non-blanching Petechial Rash (Mostly on trunk & limbs)**
- **DIC & Acute Adrenal Failure**

Q45

A 32-year-old man who lives at sea level travels to a mountainous region for a 2-month hiking vacation. On arrival at the mountainous area, he develops shortness of breath with exertion. At the end of his first 2 weeks of vacation, his exercise tolerance has increased. If this patient's bone marrow were examined at this time, it would most likely show increased numbers of which of the following cells?

- A. Adipocytes
- B. Megakaryocytes
- C. Metamyelocytes
- D. Normoblasts
- E. Siderophages

▼ Explanation

- **Answer is D (Normoblasts)**
 - **IMP Clues**
 - Lives at sea level travels to a mountainous region for a 2-month hiking vacation
 - On arrival, he develops SOB with exertion
 - At end of his 2 weeks of vacation, his exercise tolerance has increased
 - Q asks if his bone marrow were to be examined no, which cell will be increased?
- Patient was living at sea level and traveled to above-sea level, which causes hypoxia due to decreased FI_{O_2} .
 - Hypoxia causes **increased EPO secretion** from the kidney → EPO goes to **bone marrow** → binds to **EPO Receptors** on **erythroid progenitor cells** → **JAK-STAT2** pathway → **increases proliferation & differentiation** → **increases RBCs**
 - **Increased RBCs precursors (Erythroblasts, Normoblasts, and Reticulocytes) → Increased RBCs (Mature Erythrocytes)**
 - This is called **Reactive (Secondary) Polycythemia**.

? If this patient's blood were to be examined, what would be seen on the smear?

- ▼ Answer
Normal Blood Smear with increased RBCs.



Hypoxia causes increased RR → **Respiratory alkalosis**
This is why these patients on the USMLE are usually on **Acetazolamide (Carbonic Anhydrase Inhibitor)**

- **Acetazolamide causes decreased Bicarbonate reabsorption → Metabolic Acidosis.**
- The Kidneys does that automatically; however, it takes **24-28hr to adjust.**



USMLE can show you a picture of a nephron and ask you to pin-point the **site of action of acetazolamide**; choose **PCT**.

Q46

A 35-year-old man comes to the physician because of a 4-month history of persistent cough and intermittent nasal discharge. He feels well most of the day, but after going to sleep, he will often awaken with shortness of breath, wheezing, dry cough, and chest tightness. Vital signs are within normal limits. Physical examination shows no abnormalities. The most appropriate drug for this patient blocks the receptors for an endogenous substance that is a metabolite of which of the following?

- A. Arachidonic acid
- B. Histamine
- C. Prostacyclin (PGI_2)
- D. Tetrahydrofolic acid
- E. Tryptophan

▼ Explanation

- **Answer is A (Arachidonic acid)**
 - **IMP Clues**
 - Persistent Cough and Intermittent nasal discharge
 - He feels well most of the day, but after going to sleep, he will often awaken with SOB, wheezing, dry cough, and chest tightness (This is intermittent asthma, which worsens at night → wheezing, cough, chest tightness)

- Q asks the appropriate drug for this patient blocks the receptors for an endogenous product, which is a metabolite of which of the following?

- **Leukotriene Receptor Antagonists**

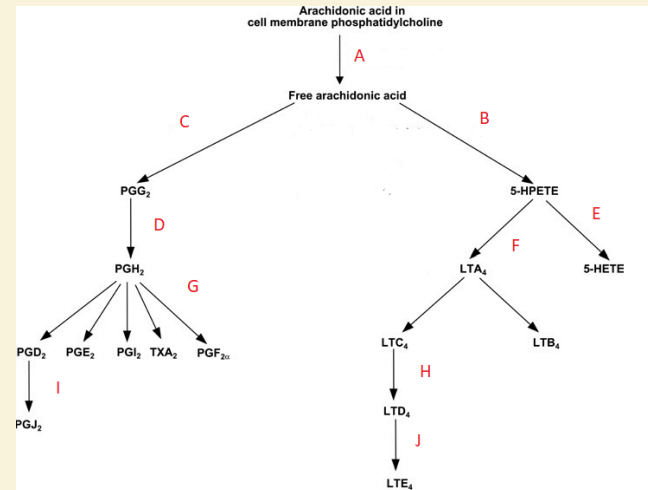
- **Montelukast & Zafirlukast** are **Leukotriene Receptor Antagonists** that block the effects of **LT-C₄, LT-D₄, and LT-E₄** on their receptors.
 - They cause **bronchoconstriction** ⇒ **Asthma**.
 - Leukotrienes are *metabolites of arachidonic acid*, which goes through the **Lipoxygenase pathway**.



Never forget that LT-B₄ is a chemotactic molecule (LT-B₄, C₅a, IL-8, PAF, Kallikrein)



Choose the site of action of Zileuton.



▼ **Answer**

Choices B & F (5-LOX) - Zileuton is a 5-Lipoxygenase inhibitor

Q47

A 12-year-old girl is admitted to the hospital for treatment following a generalized tonic-clonic seizure. She has mild mental retardation and scoliosis. She underwent surgical repair for partial dislocation of the lenses in both eyes 3 years ago. Her plasma cystathionine concentration is decreased. A CT scan of the head shows a small infarction in the right cerebral hemisphere. Which of the following serum amino acid concentrations is most likely increased in this patient?

- A. Glutamine
- B. Glycine
- C. Leucine
- D. Methionine
- E. Phenylalanine

▼ **Explanation**

- **Answer is D (Methionine)**

- **IMP Clues**

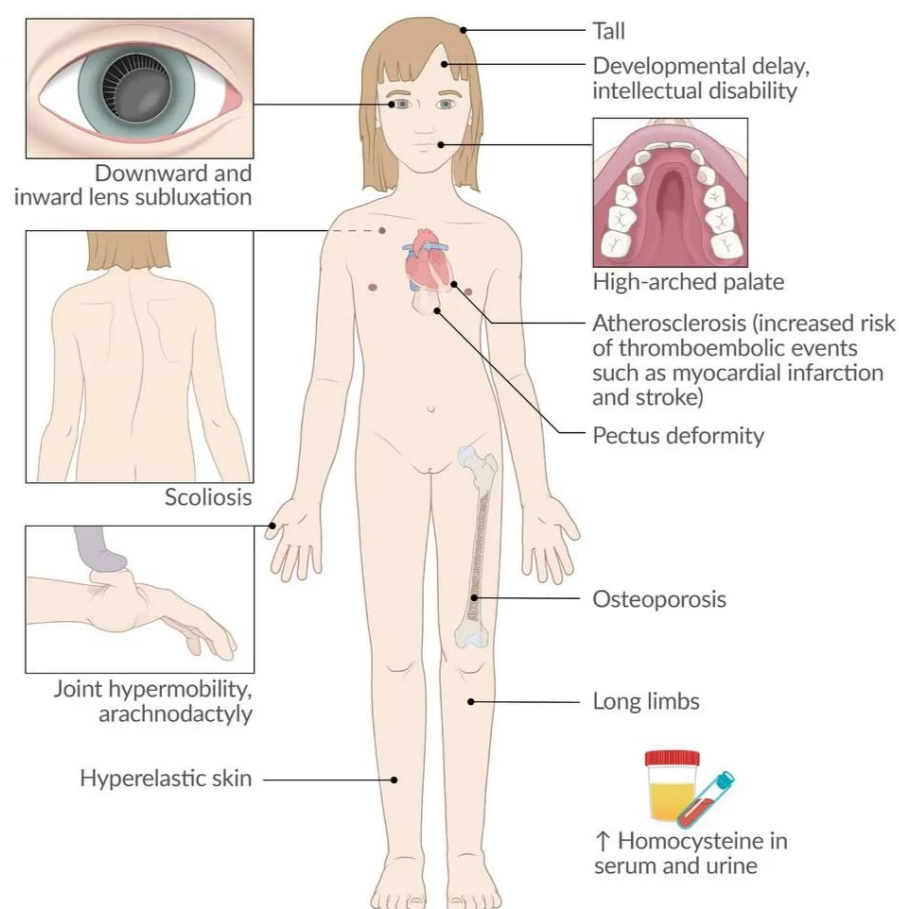
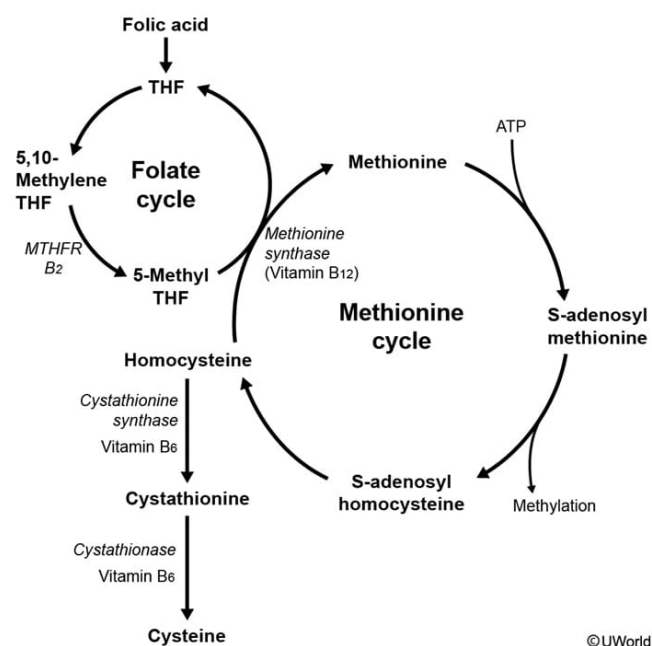
- Mild Mental Retardation & Scoliosis
- Partial dislocation of the lenses in both eyes
- Her plasma cystathionine concentration is decreased
- CT scan of the head shows a small infarction
- Q asks which amino acid is increased in this patient?

- **Dx → Homocystinuria**

- Dumbass Biochem, but bear with me.
- **Methionine → Homocysteine → Cystathionine → Cysteine**
 - **Homocysteine → Cystathionine** is carried out via **Cystathionine B-Synthase (CBS)**
 - **Homocysteine → Methionine** is carried out via **Methionine Synthase**
- If one of these 2 enzymes are deficient, we get homocystinuria.
 - **How to differentiate?**
 - **CBS deficiency** → **high methionine, high homocysteine, low cysteine** (what we have here)
 - **Methionine Synthase deficiency** → **low methionine, high homocysteine**

Homocysteine is toxic to **Connective Tissue** (Collagen & Elastin):

- **Connective Tissue in Lens** ⇒ **Lens Dislocation** [For Nerds → Infeonasal]
- **Connective Tissue in the Body** ⇒ **Marfanoid Habitus (Tall, Long Limbs, Arachnodactyly, Pectus Excavatum)**
- **Connective Tissue in Bone** ⇒ **Osteoporosis**
- **Connective Tissue in Vascular endothelium** ⇒ **Thrombosis, Stroke, MI in children & young adults**



Q48

A 40-year-old man with terminal small cell carcinoma of the lung becomes anorectic and lethargic. Fluid restriction is initiated because of a serum sodium concentration of 120 mEq/L, but there is no clinical improvement after 3 days. Which of the following is the next most appropriate therapy?

- A. Cyclophosphamide
- B. Demeclocycline
- C. Indomethacin
- D. Tricyclic antidepressant
- E. Vincristine

▼ Explanation

• Answer is B (Demeclocycline)

◦ IMP Clues

- Small cell carcinoma of the lung
- Serum sodium concentration of 120 mEq/L

• Dx → Syndrome of Inappropriate ADH (SIADH)

- **Small Cell Lung Cancer** is associated with multiple paraneoplastic syndromes, of which we have here **SIADH**.
 - **Ectopic ADH secretion** → **Binds to V2 Receptors on Principal cells of the Collecting Ducts** → **increases cAMP** → **activates Protein Kinase A, which results in:**
 - Insertion of **Aquaporin-2** channels → **increases water reabsorption**
 - What would this cause?
 - **Dilutional Hyponatremia** → Seizures, Lethargy, Weakness
 - **Decreased Serum Osmolality & Specific Gravity**
 - **Increased Urine Osmolality & Specific Gravity**
 - **Demeclocycline** is a **tetracycline** that causes **Nephrogenic DI** as a side effect; therefore, it is used in the treatment of **SIADH**.
 - **Nephrogenic DI** → **V2-Receptors Resistance to ADH**. Boom, no more SIADH.

? What are the other HY SCLC paraneoplastic syndromes

▼ Answer

- **SIADH** → **Ectopic ADH secretion**
- **Cushing's syndrome** → **Ectopic ACTH secretion**
- **Lambert-Eaton Syndrome** → antibodies against **presynaptic voltage-gated calcium channels**
- **Neurological Syndromes** → **anti-Hu/Yo**

📌 **Small Cell Lung Cancer Rapid Review:**

- **Neuroendocrine tumor** of the lung derived from **Kulchitsky cells**
- **Central mass** that most commonly affects **smokers**
- Causes **paraneoplastic syndromes** & **SVC Syndrome** (by compression of **mediastinum**)
- Biopsy → **"round cells with little cytoplasm that are twice the size of lymphocytes"** is a description used on NBME, **"small blue round cells"** can also be found

? What are other HY causes of SIADH on the USMLE?

▼ Answer

1. Central Causes: **Meningitis, Head Trauma, Brain Tumors, Idiopathic**
2. Peripheral Causes: **Small Cell Lung Cancer**
3. Drug-Induced: **Carbamazepine & SSRIs**

! ADH is **synthesized** by the **supraoptic & paraventricular nuclei of the hypothalamus** but stored in the **posterior pituitary**.

Q49

A 60-year-old man comes to the physician because of a 1-month history of headache and dizziness. His blood pressure is 160/85 mm Hg. Physical examination shows moderate splenomegaly. Laboratory studies show:

Hemoglobin	20.5 g/dL
Hematocrit	55%
Erythrocyte count	7 million/mm ³
Mean corpuscular volume	78 μm ³
Leukocyte count	18,000/mm ³
Segmented neutrophils	75%
Eosinophils	5%
Basophils	5%
Monocytes	5%
Lymphocytes	10%
Red cell distribution width	20% (N=13%–15%)
Arterial O ₂ saturation	normal

Which of the following analytes is most likely to be decreased in this patient?

- A. Erythropoietin
- B. Leukocyte alkaline phosphatase
- C. Platelet count
- D. Total red cell mass
- E. Uric acid

▼ Explanation

- Answer is A (Erythropoietin)
 - IMP Clues
 - Headache and dizziness
 - Blood pressure is 160/85 mmHg
 - Moderate Splenomegaly
 - Hemoglobin 20.5 + Erythrocyte count is 7 million + Leukocyte count is 18,000 + RDW is 20%
- Dx → Polycythemia Vera
 - On the USMLE, an **increase in Hemoglobin** is usually one of 2 things: **Polycythemia Vera OR Reactive (Secondary) Polycythemia**
 - How to differentiate?
 - Polycythemia Vera → **Increase** in RBCs + **at least another cell line** (WBCs, PLTs, or BOTH)
 - Reactive Polycythemia → **Isolated increase** in RBCs.
 - In this Q here, we have increase in RBCs (increased Hb, Hct, RBC count) + increase in WBCs
 - Pathophysiology: **JAK2 mutation**, which causes **activation and differentiation of hematopoietic progenitor cells [asked on NBME]**
 - This causes an **increase in RBCs** (increases count, Hb, Hct) + **at least another cell line** (WBCs, PLTs, or BOTH)
 - Due to this **increase** in RBCS → **EPO production decreases** (Choice A)
 - Clinical Features:
 - Plethora, **Headaches, Dizziness**, Blurred Vision (due to hyperviscosity)
 - **Splenomegaly** (due to extramedullary hematopoiesis)
 - **Pruritis** (especially **post-hot shower**, due to **mast cell degranulation**) **[Underrated & HY]**



Reactive (Secondary) Polycythemia has an **isolated** increase in RBCs.

- HY causes: **Hypoxia, COPD, Living at high altitudes, EPO-secreting tumors (RCC - HCC)**
- EPO is **INCREASED**

- Complications
 - **Thrombosis** → Strokes, Budd-Chiari Syndrome
 - **Gout** (due to increases cellular turn over)

? What is the MOA of EPO?

- ▼ Answer
- EPO goes to **bone marrow** → binds to **EPO Receptors** on **erythroid progenitor cells** → **JAK-STAT2** pathway → **increases proliferation & differentiation** → **increases RBCs**

 Chronic Myeloproliferative Disorders:

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

Q50

A 6-month-old infant is brought to the physician because of a 2-month history of failure to thrive and intractable diarrhea that is worse after he feeds. Physical examination shows eczematous dermatitis and mild lymphadenopathy. His heelstick blood glucose concentration is 260 mg/dL (N=60–100). Genetic testing shows a mutation in the gene encoding the transcriptional protein, FOXP3. The most likely cause of this patient's condition is a decrease in which of the following T-lymphocyte populations?

- A. CD8+ T lymphocytes
- B. Natural killer cells
- C. Regulatory T lymphocytes
- D. Th1 lymphocytes
- E. Th2 lymphocytes

▼ Explanation

- **Answer is C (Regulatory T lymphocytes)**
 - **IMP Clues**
 - Infant with failure to thrive and intractable diarrhea
 - Eczematous dermatitis and mild lymphadenopathy
 - His heel stick blood glucose concentration is 260 mg/dL
 - Genetic testing shows a mutation in the gene encoding the transcription protein, FOXP3
 - Q asks this patient's condition is caused by a decrease in which T-Lymphocyte populations?
 - **Regulatory T-Lymphocytes**
 - These are a subtype of lymphocytes that *regulate immunity* via *maintaining immune tolerance* and *preventing autoimmunity* via suppressing the activation of other lymphocytes & immune cells.
 - Surface Markers are **CD4, CD25, FOXP3** [asked on NBME]
 - If Regulatory T-Lymphocytes are deficient → **Autoimmune diseases**

"You don't need to know that syndrome, just knowing the above info is enough for STEP1"

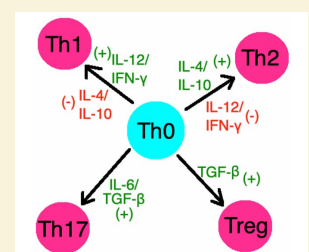
- **IPEX Syndrome (what we have here)**
 - **Immune dysregulation** (due to Regulatory T-cell mutation) ⇒ **Eczema & Dermatitis**
 - **Polyendocrinopathy** (Most common is **T1DM**, as seen here) ⇒ Blood glucose concentration is elevated
 - **Enteropathy** (autoimmune enteropathy) ⇒ **Chronic Watery Diarrhea & Malabsorption & Failure to thrive**
 - **X-Linked Disease**

[For Nerds] How do they suppress the immune system?

1. Secrete anti-inflammatory cytokines ⇒ **IL-10 & TGF-B**
2. CD25 expression consumes IL-2 ⇒ Decreased Signaling to T-cells
3. Direct Inhibition of APCs

? What main cytokine is responsible for differentiation of Th0 into Treg cells?

- ▼ Answer
- TGF-B**





Reading explanations isn't the hard part.

Knowing which mistakes are costing you points is.

That's what we do in our CrackNBME Mentorship Program™.

More free NBME explanations: cracknbme.com/nbme-explanations

Follow on X: @_ahmadraef