



NBME EXPLANATIONS

NBME 21 Block 2

from CrackNBME

21-Block 2

Q1

A 35-year-old woman comes to the physician because of a 2-day history of blistering lesions on the sun-exposed areas of her face, arms, and hands. She has had recurrent episodes of these skin lesions for several years. She has been taking a combined oral contraceptive for 15 years. Physical examination shows fluid-filled vesicles and bullae on the face and upper extremities. Laboratory studies show:

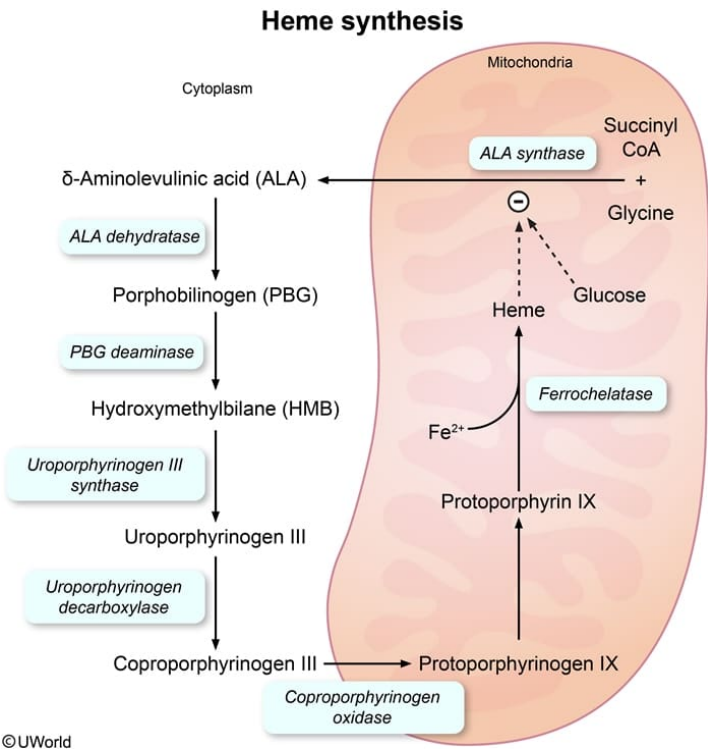
Serum	
AST	increased
ALT	increased
Total porphyrin	increased
Urine uroporphyrin III	increased

Deficiency of which of the following enzymes is the most likely cause of this patient's disorder?

- A. Porphobilinogen deaminase
- B. Protoporphyrinogen oxidase
- C. Uroporphyrinogen decarboxylase
- D. Uroporphyrinogen synthase

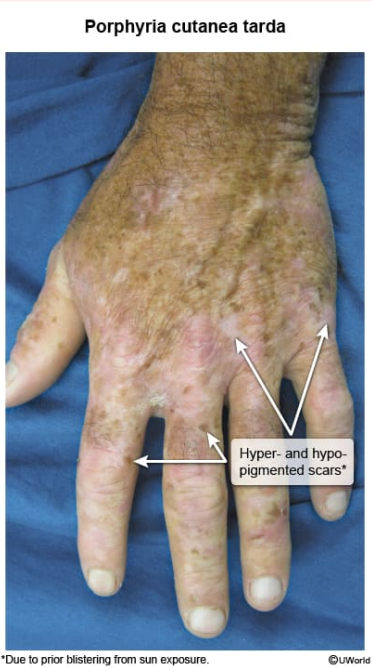
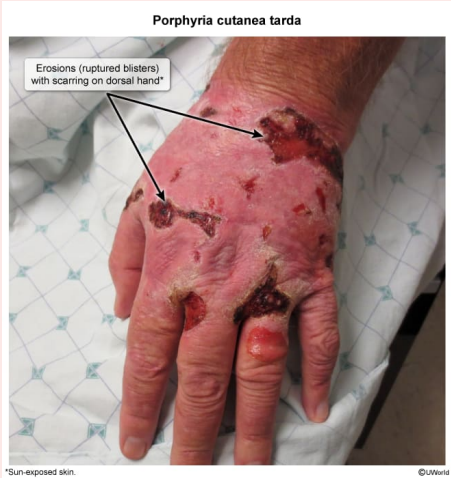
▼ Explanation

- Answer is C (Uroporphyrinogen decarboxylase)
 - IMP Clues:
 - blistering lesions on sun exposed areas (photosensitivity)
 - Fluid filled vesicles & bullae (blisters, again)
 - Labs show increased porphyrin & choices are heme synthesis pathway enzymes so we know it is a heme synthesis biochem Q (one of the HY Biochem pathways that you actually must know)
- Dx → Porphyria Cutanea Tarda
 - Enzyme deficiency → **Uroporphyrinogen Decarboxylase**
 - C/P → **Photosensitivity** that causes **blistering hyperpigmentation**
 - Exacerbating factors → **Ethanol & UV light**
 - Associated with → **HCV**



▼ Other Choices

This is the only HY heme synthesis pathway enzyme/disease that causes blistering hyperpigmentation:

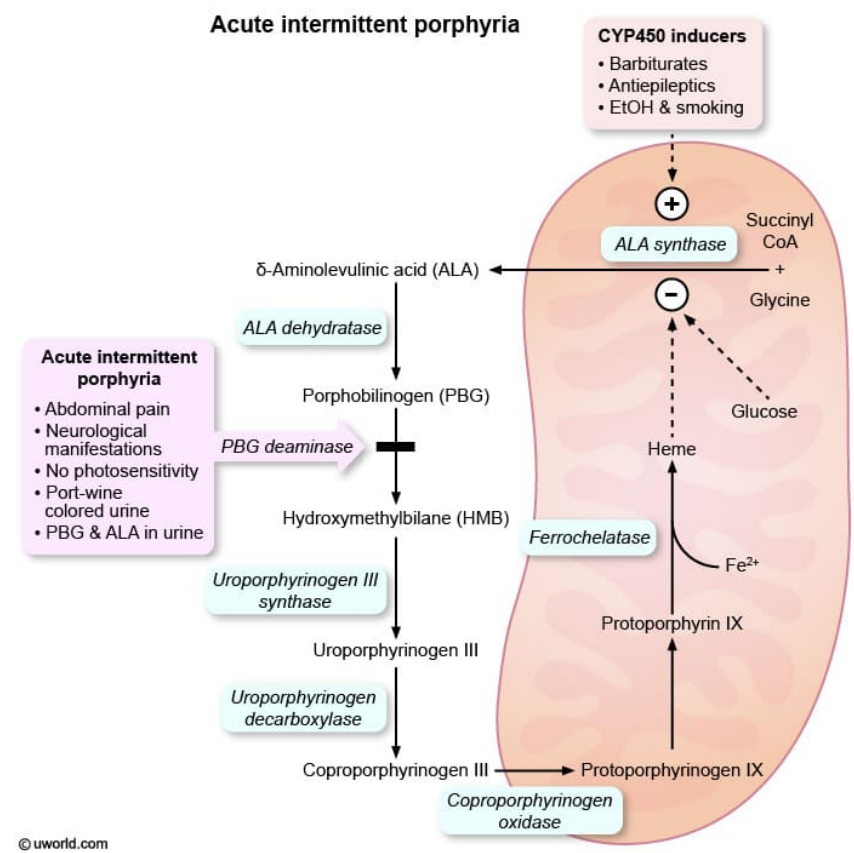


- **Choice A → Acute Intermittent Porphyria**

- Deficiency of **Porphobilinogen Deaminase**
- **Causes 5Ps:**
 1. Port-wine colored urine
 2. Polyneuropathy
 3. Psychiatric symptoms & signs
 4. Pain (abdominal)
 5. Precipitated by **P450 inducers** (Barbiturates are a HY example)

Dirty Medicine mnemonic → "AIPD"

- **Choices B & D →** Never saw the USMLE assess them.



▼ HY Related Disorders

- **Sideroblastic Anemia**

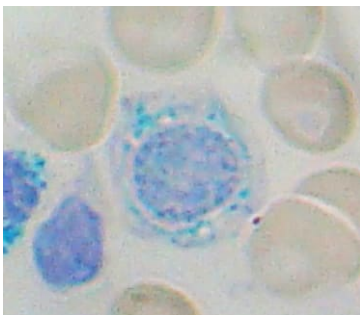
- Caused by **deficiency of ALA Synthase OR Vitamin B6 deficiency**

USMLE can be tricky and give you sideroblastic anemia in a patient using INH (causes vitamin B6 depletion)

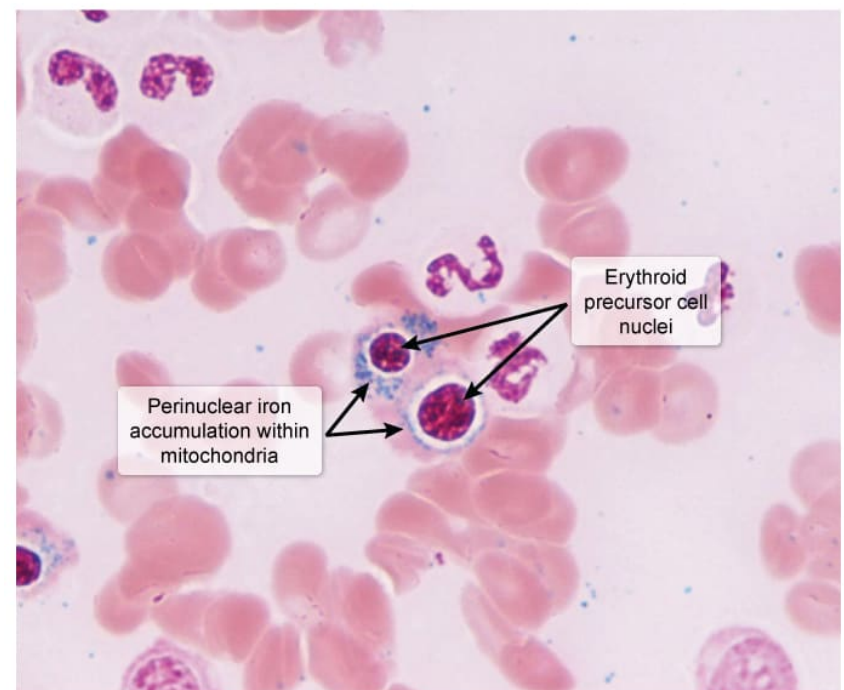
- **Labs:** **Increased Iron** - **Increased Ferritin** - **Decreased TIBC**

- Bone Marrow aspirate: **Ringed Sideroblasts**

- **Iron accumulated within mitochondria of erythroblasts seen with Prussian blue stain**
- Picture used on NBMEs:



Ring sideroblasts



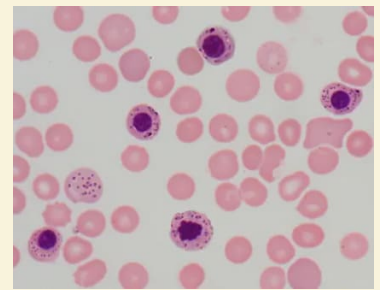
Bone marrow aspirate – Prussian blue stain

©UWorld

- Lead poisoning
 - Deficiency of OR Lead-induced inhibition of *ALA dehydratase or Ferrochelatase*
 - Features:
 - Microcytic Anemia (MCV < 80)
 - Abdominal Pain
 - Neuropathy (Foot/Hand drop)
 - Burton lines on Gums
 - Peripheral smear: **Basophilic stippling** (precipitated *ribosomes* in RBCs)
 - Bone X-Ray: **Lead-lines** (shown below)



Lead Poisoning:
Basophilic Stippling:



Burton Lines:



Q2

A 65-year-old woman comes to the emergency department because of a 4-hour history of vomiting bright red blood; she also has had dizziness and nausea during this period. Her pulse is 140/min, and blood pressure is 70/30 mm Hg. Physical examination shows pale, clammy skin, diaphoresis, and decreased capillary refill time. A diagnosis of hypovolemic shock is made. Placement of a catheter in the internal jugular vein for blood transfusions is planned. Improper insertion of the catheter is most likely to result in damage to which of the following sets of underlying structures?

- A. Common carotid artery and pulmonary artery
- B. Esophagus and common carotid artery
- C. Esophagus and pulmonary artery
- D. Lung and common carotid artery
- E. Lung and esophagus

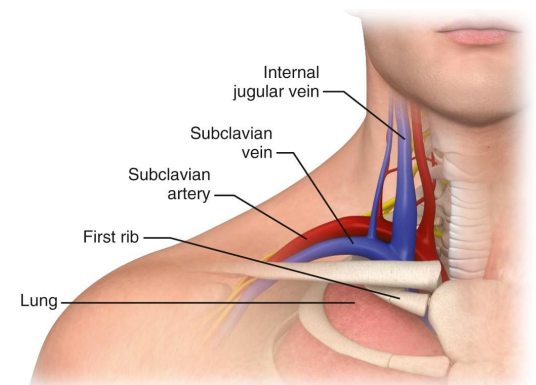
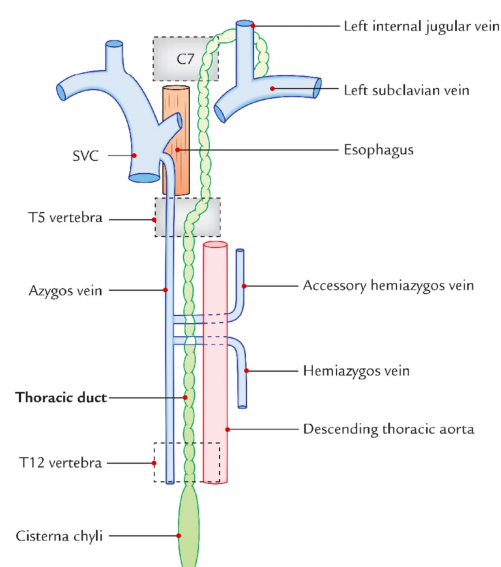
▼ Explanation

- Answer is D (Lung and common carotid artery)
- Complications of internal jugular vein catheterization:

- Damage to nearby structures:

- Common Carotid Artery
- Apex of lung
- Thoracic Duct

Below pictures shows close relations of IJV:



▼ Other Choices

- Pulmonary artery & esophagus are far away and are unlikely to be injured during this procedure

Q3

A 38-year-old woman comes to the physician because of a 10-week history of epigastric pain and frequent stools. She has had two episodes of renal calculi during the past 2 years. Physical examination shows multiple superficial lipomata and mild epigastric tenderness. Upper endoscopy shows two large, nonbleeding duodenal ulcers. Her gastric pH is 2.3, and serum gastrin concentration obtained immediately after the procedure is 2000 pg/mL (N<100). Proton pump inhibitor therapy is begun. Measurement of which of the following is the most appropriate next step in management?

- A. Serum calcium concentration
- B. Serum cortisol concentration
- C. Serum tissue transglutaminase activity
- D. Stool α 1-antitrypsin concentration
- E. Urine 5-hydroxyindoleacetic acid concentration

▼ Explanation

- Answer is A (Serum calcium concentration)

- IMP Clues:

- Epigastric pain & frequent stools (GI-related)
- 2 episodes of renal calculi
- Superficial lipomata
- 2 duodenal ulcers (MUST ring a bell in your ears: Zollinger Ellison Syndrome)
- Gastrin concentration 2000 (normal < 100) → Gastrin secreting tumor (aka ZE Syndrome)

- Dx → MEN 1 Syndrome

- Triad of:

1. Pituitary adenoma (not present here)
2. Pancreatic tumor (here we have a gastrin secreting tumor),
3. Parathyroid adenoma (causing hypercalcemia → increased renal calcium → renal calculi)

- Associated with:

- Meningioma
- Lipoma (present here)
- Collagenoma
- Angiofibroma

- Genetic Background:

- MEN1 is caused by a mutation in Menin (tumor suppressor gene) on chromosome 11

“Very HY to know that the USMLE will almost always NOT give you the triad, they may give you 2/3 or even 1/3 and you have to figure it out. So get used to it.”



Gastrinoma (Zollinger Ellison Syndrome):

Neuroendocrine pancreatic tumor that is characterized by **excess gastrin secretion**

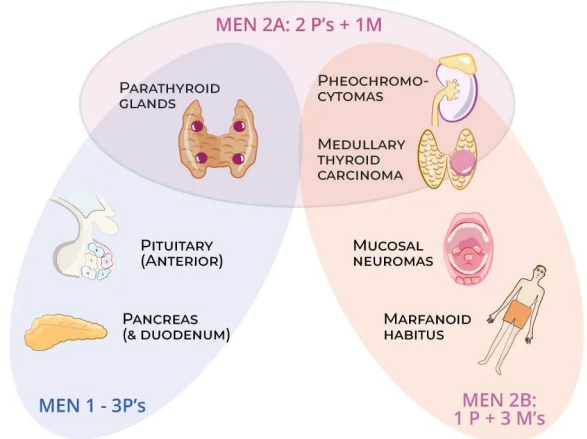
Most likely site of Gastrinoma: **HEAD of pancreas**

Symptoms include:

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

Diagnosis:

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





Compare between different MEN syndromes:

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

*Know which is a tumor suppressor gene VS proto-oncogene, as they might just ask you that instead of “Menin” or “RET”

Q4

A 32-year-old woman comes to the emergency department because of fever, intense headaches, and excruciating pains in the joints and muscles of the arms and legs that began 4 days ago when she returned from a Caribbean cruise. During the trip, she visited Cancun and the Yucatan region. Her temperature is 40°C (104°F), respirations are 32/min, and blood pressure is 130/80 mm Hg. Physical examination shows a mild macular rash over the trunk. The remainder of the examination shows no abnormalities. Which of the following is the most likely route of transmission of the causal organism?

- A. Arthropod vector
- B. Blood transfusion
- C. Contact with respiratory secretions
- D. Fecal-oral
- E. Maternal-fetal
- F. Sexual contact
- G. Small airborne droplets

▼ **Explanation**

• **Answer is A (Arthropod vector)**

◦ **IMP Clues:**

- Fever & Severe pain in muscles & joints
- Hx of travel
- Macular Rash

• **Dx → Dengue Fever**

- This is a very vague Q, but it just needs microbiology mastery
- Causative agent: **Dengue virus from Flavivirus family**
 - **Positive-sense non-segmented Enveloped RNA virus**
- Transmission: ***Aedes aegypti* mosquito (the arthropod vector)**
- Symptoms include:
 - **Break-bone fever** (Severe bone pain + fever)
 - **Rash**
 - **Thrombocytopenia & Hemorrhagic fever** (not present here)
 - **Renal Failure** (not present here)



Q5

A 59-year-old man comes to the physician because of a 3-month history of progressive difficulty swallowing; he has had a 6.8-kg (15-lb) weight loss during this period. He has smoked 1 pack of cigarettes daily for 40 years and consumes four to six beers daily. He is cachectic. Bilateral wheezes are heard on

auscultation of the chest. A chest x-ray shows enlargement of the paratracheal and hilar lymph nodes. Subsequent endoscopy shows a 6-cm mass in the mid esophagus. The mass is centrally ulcerated with an elevation of the surrounding mucosal rim. Examination of a biopsy specimen of the mass is most likely to show neoplastic cells with which of the following?

- A. Acinar formation
- B. Foci of keratinization
- C. Intracytoplasmic pigment
- D. Neuroendocrine granules
- E. Smooth muscle differentiation

▼ **Explanation**

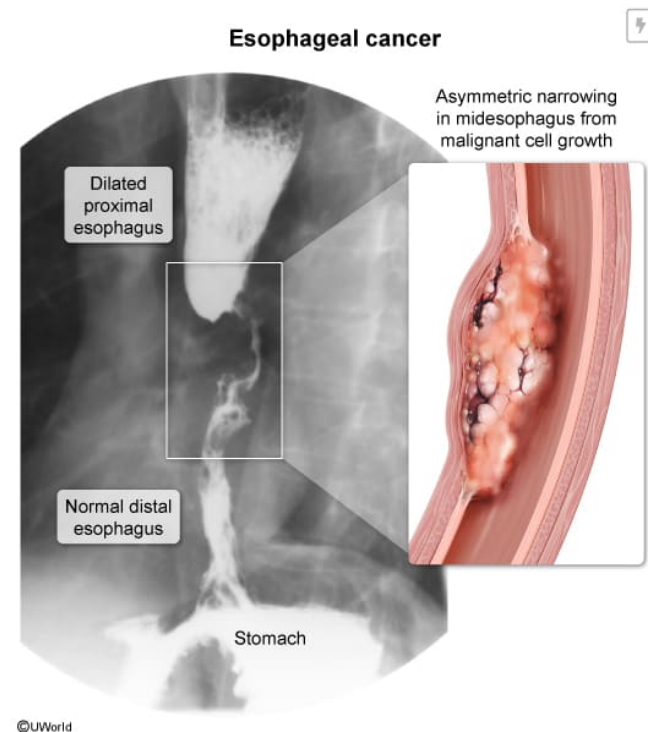
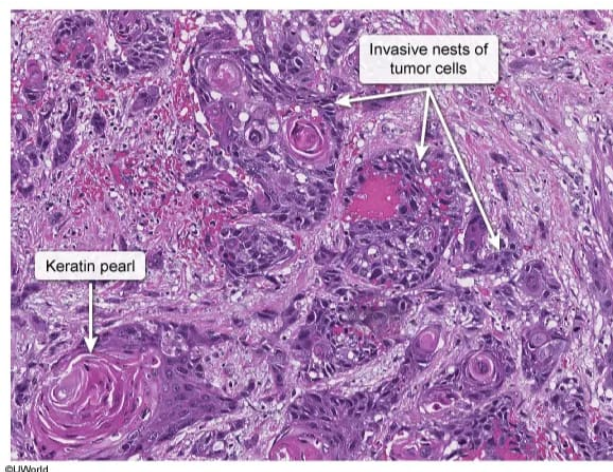
• **Answer is B (Foci of keratinization)**

◦ **IMP Clues:**

- 3-month thx of progressive difficult swallowing (Dysphagia)
- Weight loss & cachexia (Tumor)
- Smoker + Drinker (Risk Factors)
- Enlargement of paratracheal & hilar LNs (Lymphadenopathy)
- Malignant ulcer (elevated rims) in mid-esophagus (typical location of SCC; excludes adenocarcinoma which is in lower 1/3)

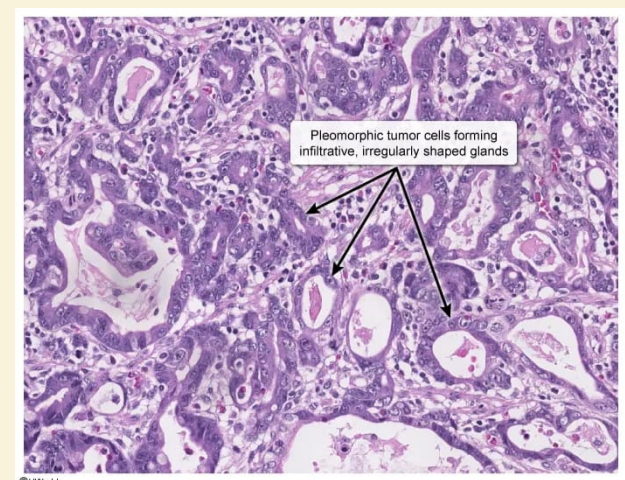
• **Dx → Squamous Cell Carcinoma of the Esophagus**

- Risk factors: **Smoking, alcohol, corrosives, achalasia, and immunosuppression**
- Site: **Middle 1/3** of esophagus (shown to the right)
- Gross: Fungating mass, Malignant ulcer, or Infiltrating mass (like any carcinoma)
- Microscopic picture: **Keratin pearls "keratin nests"** (shown below)



📌 **Adenocarcinoma of the Esophagus:**

- Risk Factors: **GERD, H.pylori, Barret's esophagus, and Hiatal hernia**
- Site: **Lower 1/3** of esophagus
- Gross: Fungating mass, Malignant ulcer, or Infiltrating mass (like any carcinoma)
- Microscopic picture: **Glandular tissue / Gland-like tissue / Intestine-like mucosa**



▼ **Other Choices**

- **Choice A** → refers to **Adenocarcinoma**
- **Choice C** → refers to **Melanoma** (the intracytoplasmic pigment is melanin)

- **Choice D** → refers to **Neuroendocrinal tumors**
- **Choice E** → refers to **Sarcoma** (leiomyosarcoma if malignant, or just a leiomyoma if benign)

Q6

A 55-year-old woman is brought to the emergency department by police 1 hour after she was found wandering around the city park at midnight, appearing confused. She told the police that she is a prominent physician and a member of the city council. She is unwashed, malodorous, and disheveled. She is 160 cm (5 ft 3 in) tall and weighs 55 kg (121 lb); BMI is 21 kg/m². Her pulse is 82/min, and blood pressure is 110/82 mm Hg. Physical examination shows a broad-based gait and nystagmus. She is not oriented to person, place, or time, but she is pleasant and cooperative. Results of alcohol and drug screening are negative. An MRI of the brain is most likely to show atrophy of which of the following?

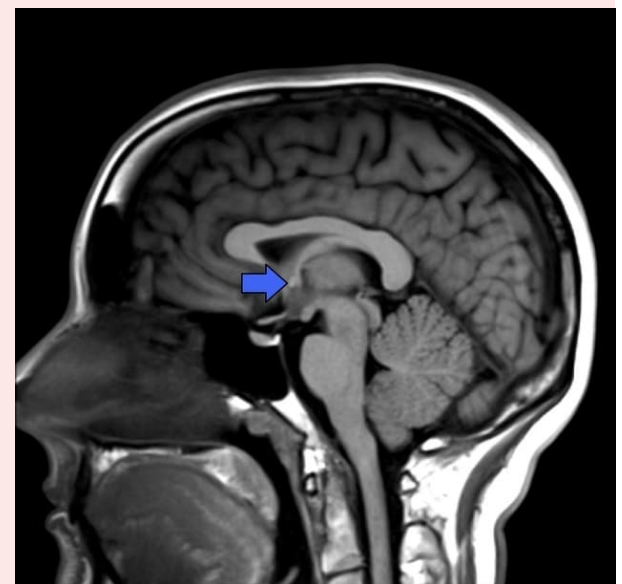
- A. Amygdala
- B. Hippocampus
- C. Hypothalamus
- D. Mammillary bodies
- E. Parietal lobe

▼ **Explanation**

- **Answer is D (Mammillary bodies)**
 - **IMP Clues:**
 - Confused, wondering, unwashed, malodorous, and disheveled lady (probably an intoxicated homeless lady)
 - Told the police she is a prominent physician & member of city council (yah, no)
 - Broad-based gait & nystagmus (ataxia & ophthalmoplegia, screaming Wernicke's)
 - Not oriented to person, place, or time (confused, now we know it is Wernicke's)
 - Negative alcohol & drug screening (excludes other intoxications)
 - **Dx → Wernicke's Encephalopathy**
 - Risk Factors: **Chronic alcohol intoxication [asked on NBME] & Malnourishment (Vitamin B1 deficiency)**
 - Pathophysiology: **Thiamine (Vitamin B1) deficiency → impaired glucose metabolism & ATP production → neuronal death & neurotoxicity**
 - **Mammillary Body** is most affected [asked on NBME]
 - Presentation: **Ataxia, Confusion, and Oculomotor dysfunction**
- Mnemonic "A COW":**

 - **A** = **A**taxia
 - **C** = **C**onfusion
 - **O** = **O**phthalmoplegia
 - **W** = **W**ernicke's
- **Wernicke's is reversible with Vitamin B1 THEN glucose**
 - If untreated → progression to **Korsakoff's Syndrome (ACOW + confabulations + amnesia) which is irreversible**.
 - **Amnesia** is mostly anterograde (in ability to form new memories) but can also sometimes be retrograde (loss of your old memories)
 - **Confabulations** are false stories made to fill in memory gaps (unintentional, of course)

USMLE may show you an MRI in a case of Wernicke's and ask for site of affection:





Thiamine deficiency on the USMLE can present in 1 of 3 ways:

1. **Wernicke's Encephalopathy** (mentioned above)
2. **Dry Beri Beri** (Polyneuropathy & Ophthalmoplegia +/- muscle affection)
3. **Wet Beri Beri** (Dry Beri Beri + Heart Failure)
 - a. Heart Failure of Wet Beri Beri is → **High-Output HF**
 - b. Heart Failure of chronic alcoholism is → **Low-Output HF (dilated cardiomyopathy)**

Alcoholics have nutritional deficiencies in general because alcohol makes them satiated (7kcal/g)

▼ Other Choices

- **Choice A** → the only HY piece of info you need to know is that in some patients with **Herpes Encephalitis** after they get treated, they develop **hyperphagia, hypersexuality, and hyperorality (Kluver-Bucy Syndrome)** → **BILATERAL AMYGDALA LESIONS**
- **Choice B** → Of the top of my mind, I don't remember seeing any HY info about the hippocampus except maybe that the **"Negri bodies" (eosinophilic cytoplasmic inclusion bodies) of Rabies** are found there.
- **Choice C** → Everything would be fucked up. Everything.
- **Choice E** → Depends on the specific cortical area affected but include → sensory impairment, aphasias, hemi-neglect, or **Gerstmann syndrome**



What is Gerstmann Syndrome?

▼ Answer

Angular Gyrus (Parietal Lobe) Stroke, causing:

1. **Agraphia** (cannot write)
2. **Acalculia** (cannot calculate - cannot do simple math)
3. **Finger Agnosia** (cannot recognize/differentiate fingers)
4. **Right-Left Agnosia** (cannot recognize/differentiate right from left)

Q7

A 16-year-old boy is brought to the physician because of a 3-month history of shortness of breath while playing sports. He has no shortness of breath at rest. He says, "Whenever I run around I cough, so I don't want to be on the basketball team anymore." He takes no medications and has no known allergies. There is a family history of hypertension and asthma. He is 165 cm (5 ft 5 in) tall and weighs 68 kg (150 lb); BMI is 25 kg/m². His respirations are 12/min, and blood pressure is 115/75 mm Hg. Cardiac examination shows no abnormalities except for a midsystolic click at the apex. The lungs are clear to auscultation of the chest. Which of the following best explains this patient's symptoms?

- A. Deconditioning
- B. Exercise-induced asthma
- C. Malingering
- D. Mitral valve prolapse
- E. Thyroid disease

▼ Explanation

- **Answer is B (Exercise-induced asthma)**
 - **IMP Clues:**
 - 3-month hx of SOB + cough while playing sports (activity-related)
 - No SOB at rest
 - Family hx of HTN & asthma (V.IMP keyword)
 - Midsystolic click at apex (description of MVP)
 - Clear lungs

- **Dx → Exercise-induced asthma**
 - Tricky Q that most people will **choose MVP (Choice D) which will cause SOB on exercise, but NOT cough**
 - **The family hx of asthma is the key to solve it.** People with family hx of atopy will most likely have atopy.
 - The family hx was most likely “normal” asthma so the vignette said he has *no known allergies*. His **exercised induced asthma** was his “no known allergy”

His vitals & examination are normal because asthma = attacks. He was just fine at the time of examination.

▼ **Other Choices**

- **Choice A → Deconditioning** (you know when you don’t play football for a few months, then when you play you die in the first sprint, yah you are deconditioned) would present at the beginning of starting activity, not just suddenly
- **Choice C →** Nothing supports it.
- **Choice D → MVP** is a normal finding in many people that is asymptomatic usually. If not it would be SOB (yes) but NOT cough.
- **Choice E →** Irrelevant here.

Q8

Diastolic blood pressures are obtained in two groups of 100 asymptomatic men (group X and group Y) above the age of 40 years. Results are shown in the table.

Diastolic Blood Pressure (mm Hg)	Group X Number	Group Y Number
50	8	2
60	12	8
70	32	10
80	18	20
90	12	18
100	10	17
110	8	15
120	0	10
Total	100	100

Compared with group X, which of the following best represents the median and mode of group Y?

Choices	Median of Group Y	Mode of Group Y
A	Higher	Higher
B	Higher	Lower
C	Lower	Higher
D	Lower	Lower
E	Lower	Same
F	Same	Higher
G	Same	Lower
H	Same	Same

▼ **Explanation**

- **Answer is A**
 - **Median of Group Y is 50.5th value which is 90**
 - Formula to find the median of an even list after rearrangement from lowest to greatest is
 - $= (n/2 + (n/2 + 1)) / 2$
 - $(100/2 + 100/2 + 1) / 2 = 50 + 51 / 2 = 50.5\text{th value}$
 - **Mode of Group Y is 80**
 - **Median of Group X is also 50.5th value which is 70**
 - **Mode of Group X is 70**

- So, both the **median & mode of group Y** is higher than group X (Choice A)

Q9

A 55-year-old man comes to the physician because of a 2-month history of fatigue and a 3-day history of nausea and diarrhea. He has had a 5.4-kg (12-lb) weight loss during the past 2 weeks. His temperature is 37.8°C (100°F), pulse is 110/min, respirations are 24/min, and blood pressure is 98/60 mm Hg. Physical examination shows dry skin with hyperpigmentation and delayed capillary refill. Serum studies show:

Na+	125 mEq/L
K+	6.1 mEq/L
Urea nitrogen (BUN)	21 mg/dL
Glucose	60 mg/dL
Creatinine	1.5 mg/dL

Which of the following serum hormone concentrations is most likely decreased in this patient?

- A. ACTH
- B. ADH (vasopressin)
- C. Cortisol
- D. Glucagon
- E. Norepinephrine

▼ Explanation

- **Answer is C (Cortisol)**

- **IMP Clues:**

- Fatigue (A VERY VERY VERY HY SYMPTOM HERE)
- Blood pressure is 98/60 mmHg (Hypotensive)
- Hyperpigmented skin (HY clue)
- Labs: Low Na & High Na

- **Dx → Autoimmune Adrenalitis**

- **Most common cause of Primary Adrenal Insufficiency (Addison's Disease)**
- USMLE can refer to it as *"antibodies against 21- α -hydroxylase"*
- Most commonly affects the **Zona Glomerulosa & Zona Fasciculata**

- Destruction of **Zona Glomerulosa** → **Deficiency of Mineralocorticoids**
- Destruction of **Zona Fasciculata** → **Deficiency of Glucocorticoids**

- **Presentation**

- Deficiency of Aldosterone:**

- Presents as **HIGH K, low Na, low Cl, low pH, low HCO₃, low CO₂**

- **why?**

- Aldosterone **secretes K + H & reabsorbs Na**, so if deficient → **Hyponatremia, Hyperkalemia, Metabolic Acidosis**

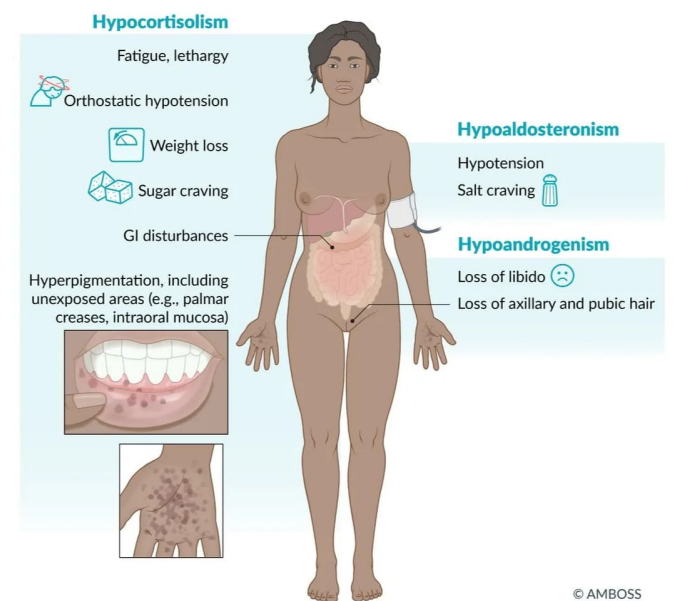
"Neat hack I learned is: Everything follows aldosterone except potassium it is the opposite"

- Deficiency of Cortisol:**

- Presents as **Hypotension, Hypoglycemia, Fatigue & Weakness** (Most underrated HY info), and **Skin Hyperpigmentation**

- **why?**

- Loss of permissiveness on catecholamines ⇒ **Hypotension**
- Stress hormones that counters insulin ⇒ **Hypoglycemia**
- POMC is cleaved into MSH + ACTH; Low cortisol = high POMC → high ACTH + high MSH ⇒ **Skin/Mucous membranes Hyperpigmentation**



! In females, primary adrenal insufficiency presents with *loss of libido & loss of sexual hair (axillary & pubic)*. This is NOT present in males, however, as testes produce the majority of the androgen.

Treatment of this condition is replacement of *glucocorticoids* (prednisone) & *mineralocorticoids* (fludrocortisone).

? What would be the expected renin levels in this patient?
▼ Answer
Increased Renin

▼ Other Choices

- **Choice A** → Decreased ACTH would be seen either in:
 - Hypothalamic lesion (decreased CRH = decreased POMC = decreased ACTH & MSH)
 - Pituitary lesion
 - Adrenal Adenoma (increased cortisol production → negative feedback on ACTH so decreased)
- **Choice B** → **Central DI**; would present as **HIGH** Na, **HIGH** urine output, **HIGH** serum osmolality, **LOW** urine osmolality
 - **Causes of Central DI**: meningitis, trauma, idiopathic
 - **Causes of Nephrogenic DI**:
 - **Lithium** (Q mentions a patient with bipolar disorder + above findings),
 - Demeclocycline
 - **Hypercalcemia** (Q may present it as a patient with hyperparathyroidism+ above findings),
 - **NSAIDs** (NSAIDs cause RPN, so DI can't exert its effects as the renal papillae are necrotized)
- **Choices D & E** → Irrelevant

? Patient on NSAIDs for a long period of time. What would happen to ADH levels & urine osmolality if ADH is given?

▼ Answer
NO CHANGE IN BOTH

Q10

A clinical trial is conducted to compare the efficacy of a surgical procedure versus medical management of gastroesophageal reflux disease. In the study, 800 patients are randomly assigned to either the surgical procedure group or the medical management group; each group consists of 400 patients. Of the patients assigned to the surgical procedure group, 75 do not undergo the operation during the study period. Of the patients assigned to the medical management group, 50 undergo the operation during the study period. In an intention-to-treat analysis, which of the following most accurately represents how many patients would be analyzed in the surgical procedure and medical management groups, respectively?

Choices	Surgical Procedure Group	Medical Management Group
A	325	350
B	375	425
C	400	400
D	425	350
E	450	325

▼ Explanation

- **Answer is C**
 - Last line says, "In an intention-to-treat analysis:
 - Okay, so **intention-to-treat** basically is how the groups **were originally planned / divided**.
 - 2nd line says, "800 patients are randomly assigned to either the surgical procedure group or the medical management group, each group consists of 400 patients"
 - Very simple. What was their "**intention**" plan of assigning patients? **400 in each group (Choice C)**

Q11

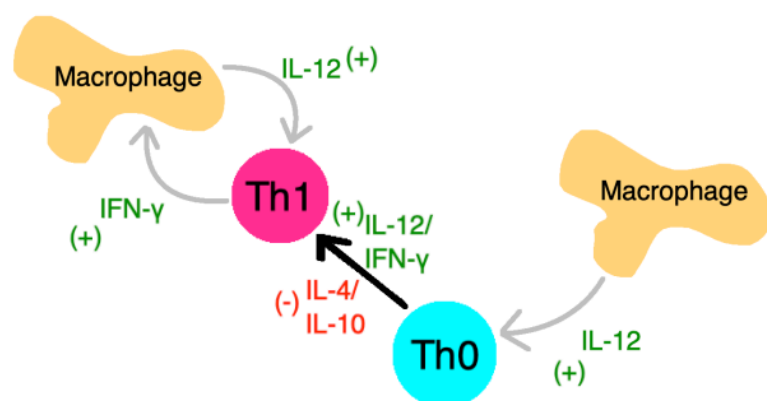
A 4-year-old boy with chronic granulomatous disease is brought to the physician by his parents for a follow-up examination. He has a 2-year history of recurrent catalase-positive fungal and bacterial granulomatous infections that have been inconsistently responsive to trimethoprim-sulfamethoxazole, dicloxacillin, and itraconazole. Physical examination shows no additional abnormalities. Treatment with interferon gamma is begun. Activity of which of the following cells is most likely to be significantly increased in this patient after exposure to this drug?

- A. B lymphocytes producing immunoglobulin
- B. CD4+/CD25+ lymphocytes producing tumor necrosis factor-α
- C. Macrophages producing interleukin-1 (IL-1)

- D. Natural killer cells producing IL-3
- E. T lymphocytes producing IL-4, IL-5, and IL-6

▼ **Explanation**

- **Answer is C (Macrophages producing IL-1)**
 - Q tests a very simple concept:
 - **Th0 is converted into Th1 cells** that produce **INF-gamma which stimulates macrophages**, which in turn produce **IL-12** which further stimulates Th0 conversion into Th1 (**VERY HY LOOP**)



Chronic Granulomatous Disease Rapid Review:

Deficiency of: **NADPH Oxidase** (enzyme that converts O₂ into H₂O₂ to kill organisms after phagocytosis)

Presents as: **recurrent infection with catalase positive microorganisms:**

mnemonic "LC SHAPES"

- L = Listeria
- C = Candida
- S = **Staph aureus** (most commonly tested ~50% of the time)
- H = *H.pylori*
- A = Aspergillus
- P = *Pseudomonas*
- E = *E.coli*
- S = *Serratia*

Diagnosis: **Dihydrorhodamine test**

Q12

A 30-year-old woman comes to the office because she is concerned she may be pregnant. Her last menstrual period was 10 weeks ago. She has been receiving thyroxine (T4) for 2 years because of hypothyroidism and autoimmune thyroiditis. Physical examination shows a uterus consistent in size with a 10-week gestation. Serum studies show thyroid-stimulating hormone (TSH) and free thyroxine (FT4) concentrations that are in the reference ranges for that stage of gestation, and an increased β-human chorionic gonadotropin concentration. The fetus is at greatest risk for which of the following if the mother's TSH concentration increases during pregnancy?

- A. Abnormal brain development
- B. Deafness
- C. Inadequate growth
- D. Pituitary atrophy
- E. Thyroid gland enlargement

▼ **Explanation**

- **Answer is A (Abnormal brain development)**
 - **IMP Clues:**
 - Hx of hypothyroidism & autoimmune thyroiditis + taking T4 as ttt
 - TSH & T4 are normal
 - **Dx → Congenital Hypothyroidism**
 - Q asks what would happen if TSH *increases*?
 - **TSH would increase if T3/T4 decreases.** In other words, Q is asking what will happen to the fetus if the mother develops **HYPOTHYROIDISM**?
 - Well, the baby would develop hypothyroidism ⇒ **Congenital Hypothyroidism**
 - HY Symptoms:

- **Hypotonia**, lethargy, poor feeding
 - **Jaundice** (as bilirubin metabolism is decreased due to decreased T3/T4)
 - **Macroglossia, Umbilical Hernia ("pot belly")**
 - **Constipation**, dry skin, **large fontanelles**
- Complications (if left untreated) → **Intellectual & developmental disability (Choice A)**
- Newborns should be routinely screened for **TSH levels +/- T4**.
 - **Why TSH?**
 - T4 levels may be normal due to maternal T4 in baby's circulation as they can pass the placental barrier.
 - Few weeks after birth, T4 levels drop → Clinical Symptoms.

Q13

A 48-year-old woman comes to the physician because of a 3-month history of fatigue, weakness, loss of appetite, and weight loss. Her serum parathyroid hormone concentrations are increased. X-rays of the skeletal system show generalized osteopenia, with subperiosteal resorption of bone within the phalanges. Which of the following mechanisms is the most likely cause of the skeletal changes observed in this patient?

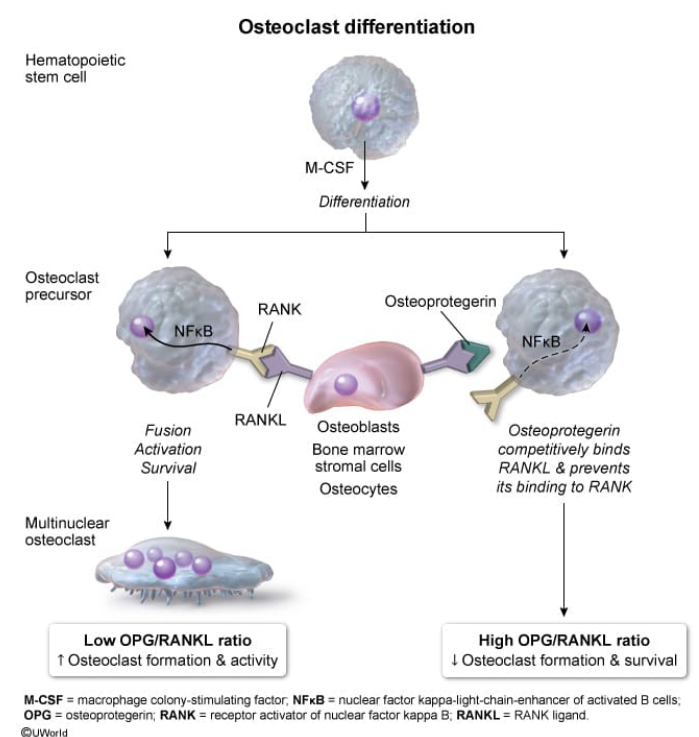
- A. Impaired calcification of preformed osteoid
- B. Paracrine stimulation of osteoclasts by osteoblasts
- C. Parathyroid hormone-mediated induction of calcitonin
- D. Parathyroid hormone-mediated induction of interleukin-1 (IL-1)
- E. Parathyroid hormone-mediated production of transforming growth factor-β1

▼ Explanation

- **Answer is B (Paracrine stimulation of osteoclasts by osteoblasts)**
 - **IMP Clues:**
 - Fatigue, weakness, loss of appetite, and weight loss (some kind of tumor?)
 - Increased serum PTH (some kind of a PTH producing tumor?)
 - Generalized osteopenia & subperiosteal resorption (increased bone resorption 2ry to increased PTH)
 - **Dx → Primary Hyperparathyroidism**
 - Causes of Primary Hyperparathyroidism are **Parathyroid Adenoma (90%) > Parathyroid Hyperplasia > Parathyroid Carcinoma**
 - Increase PTH secretion causes:
 - **Increased bone resorption**
 - **How??**
 - PTH stimulates **osteoblasts** → osteoblasts express **RANK-Ligand** → binds to nearby osteoclasts that express **RANK-Receptor** → **activation of osteoclasts** → bone resorption
 - Now let's rephrase the above sentence → **"paracrine stimulation of osteoclasts by osteoblasts,"** USMLE can also say **"increased osteoclasts maturation & activity"**

Now, Let's review more HY concepts:

- **Renal effects of PTH stimulation:**
 - PTH causes **phosphorus secretion in PCT [asked on NBME]**
 - **Result ⇒ Hypophosphatemia & hyperphosphaturia**
 - PTH causes **calcium reabsorption in DCT [asked on NBME]**
 - **Result ⇒ Hypercalcemia & hypercalciuria**
- Yes, both are hyper-. Increased Ca in blood is filtered above threshold of reabsorption, so Calcium is still excreted by other mechanisms.
- PTH causes **increased 1-alpha hydroxylase activity**



- Result $\Rightarrow$ Increased conversion of 25-OH-Vitamin D into 1,25-OH-Vitamin D (calcitriol)

- PTH causes increased **urinary cAMP**

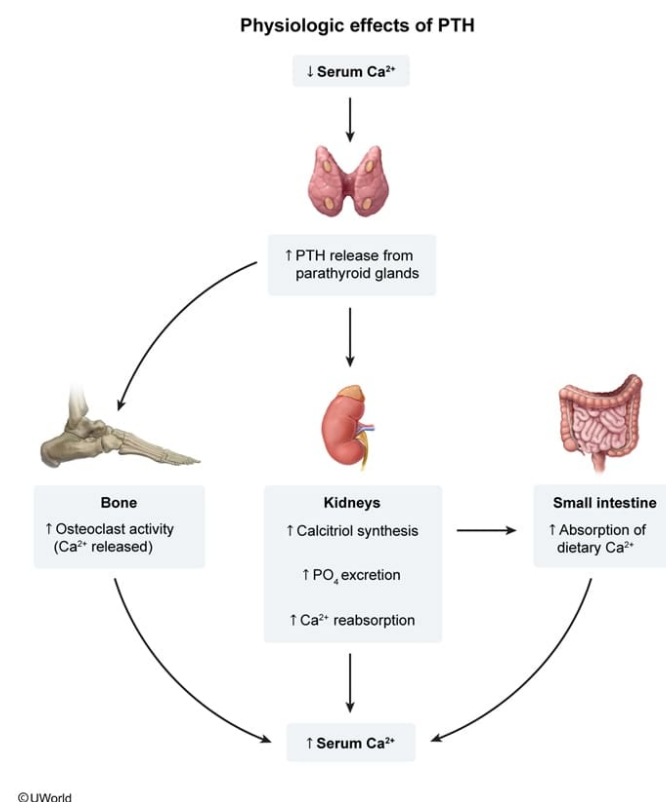
- **Vitamin D effects of PTH stimulation:**

- On **Kidney** $\rightarrow$ **Increased** reabsorption of **BOTH** Calcium & Phosphate
- On **Intestines** $\rightarrow$ **Increased** absorption of **BOTH** Calcium & Phosphate
- On **Bones** $\rightarrow$ **Balances** resorption & mineralization



VITAMIN D INCREASES intestinal absorption of Calcium (and phosphate)

- PTH has **NO DIRECT EFFECT** on intestines



▼ Other Choices

- **Choice A** $\rightarrow$ refers to **Vitamin D deficiency (Rickets)**
- **Choice C** $\rightarrow$ PTH actually opposes calcitonin (calcitonin wants calcium IN, PTH wants it out of bones)
- **Choice D** $\rightarrow$ IL-1 has a role in bone resorption but not in this setting
 - **HY RELATED NOTES**
 - **IL-1 aka osteoclast-activating factor**
 - *Inhibits* **OPG binding to RANK-Receptor** $\rightarrow$ **More RANK-L/RANK-Receptor interaction** $\rightarrow$ more osteoclast activation $\rightarrow$ bone resorption
 - IL-1 is *inhibited* by **Estrogen** $\rightarrow$ **Increase OPG** $\rightarrow$ **Binds to RANK-Receptor** $\rightarrow$ **Less available RANK-Receptors for RANK-L** $\rightarrow$ *decreased* RANK-L/RANK-Receptor interaction $\rightarrow$ *Less* bone resorption
 - Menopause = *less* estrogen = *more* IL-1 = more liable to osteoporosis
 - **IL-1 is increased in Rheumatoid arthritis [asked on NBME]**
- **Choice E** $\rightarrow$ **TGF-B1** DOES NOT play a role in bone resorption

Q14

A 63-year-old man with bladder cancer starts treatment with paclitaxel. Three weeks later, cystoscopy shows a significant decrease in tumor size. Which of the following best describes the mechanism of action of paclitaxel in this patient?

- Bcr-abl-associated tyrosine kinase competitive inhibition
- DNA polymerase competitive inhibition
- DNA polymerase noncompetitive inhibition
- DNA topoisomerase competitive inhibition
- DNA topoisomerase noncompetitive inhibition
- Epidermal growth factor receptor-associated tyrosine kinase competitive inhibition
- RNA polymerase competitive inhibition
- Tubulin polymerization stabilization

▼ Explanation

- **Answer is H (Tubulin polymerization stabilization)**
 - Simple Q which asks about the MOA of paclitaxel:
 - **Taxanes (paclitaxel & docetaxel) $\rightarrow$ hyperstabilize microtubules (prevent disassembly)**

Knowing the drugs that affect microtubule stabilization is super HY:

- **Drugs that stabilize microtubules (prevents disassembly):**

1. Taxanes (**Paclitaxel** & **Docetaxel**)

• **Drugs that inhibit microtubules (causes disassembly):**

1. **Vinblastine** (part of the ABVD regimen for Hodgkin lymphoma) [Neurotoxic]
2. **Vincristine** (part of the CHOP regimen for non-Hodgkin lymphoma)
3. **Griseofulvin** (used in ttt of tinea capitis)
4. **Colchicine** (used in ttt of *acute* gout, pseudogout, and pericarditis)
5. -bendazole (**Mebendazole** is used in ttt of nematodes infections; **Albendazole** is used for ttt of neurocysticercosis)

▼ **Other Choices**

- **Choice A** → refers to **Imatinib** (*bcr-abl tyrosine kinase inhibitor* used in ttt of CML)
- **Choice B** → refers to **Acyclovir/Ganciclovir** (used in ttt of HSV & VZV / CMV)
- **Choice C** → refers to **Foscarnet** (used in Acyclovir/Ganciclovir-Resistant viruses [**due to UL97 gene mutation**])
- **Choice D** → refers to **Etoposide**
- **Choice E** → refers to **Irinotecan/Topotecan**
- **Choice F** → refers to **Erlotinib**
- **Choice G** → refers to **Rifampin** (part of TB ttt regimen)

Q15

A 1-year-old girl is admitted to the hospital because of a fracture of the right femur and bone deformities. She had bilateral clavicle fractures at birth. Oral examination shows six erupted gray-to-translucent, pointed teeth. X-rays of the long bones show generalized osteopenia. Genetic studies show a substitution of an alanine for a glycine residue in type I collagen. Which of the following has most likely occurred in this patient as a result of this mutation?

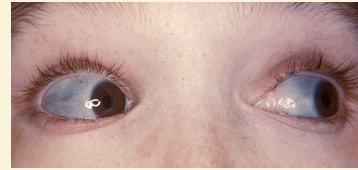
- A. Decreased hydrogen-bond formation between collagen molecules
- B. Decreased proline hydroxylation
- C. Disruption of the secondary structure of collagen molecules
- D. Increased rate of collagen degradation
- E. Weakened interaction between collagen and proteoglycan

▼ **Explanation**

- **Answer is C (Disruption of the secondary structure of collagen molecules)**
 - **IMP Clues:**
 - Fracture of right femur + Bilateral clavicle fractures at birth (Screaming, IO)
 - Erupted gray-to-translucent pointed teeth (teeth are collagen type 1 so affected too in IO)
 - Bone deformities + Long bones shows generalized osteopenia (bone is also type 1 collagen)
 - Genetic studies show a substitution of an alanine for a glycine in type 1 collagen (IO, confirmed)

- **Dx → Osteogenesis Imperfecta**
 - **AD**; mutation in **COL1A1/COL1A2 genes** that cause a defect in **collagen type 1** (eg. Bone, teeth, sclera) caused by substituting **glycine → alanine**.
 - **Glycine** is a small molecule that allows for **collagen's triple helix formation**, giving it its strength
 - When **Alanine** (a much bulkier molecule) is used instead of **glycine**, collagen's triple helix becomes **unstable and loses its strength**.
 - This causes the bones & teeth to be brittle (hence IO is also referred to as brittle bones disease)
 - **Glycine → Alanine = unstable weal collagen triple helix = Disruption of the secondary structure of collagen molecules (Choice C)**

? What amino acid substitution caused the below picture?



▼ **Answer**
Glycine → Alanine
 (Osteogenesis Imperfecta)

This is IO, blue sclera is buzzy but easy. Look for recurrent bone fractures, wormian skull appearance, deformed teeth, hearing loss.

▼ **Other Choices**

- **Choice A** → Hydrogen bond between -NH group & =O group happens **AFTER** the formation of the triple helix.
- **Choice B** → Choose this if the Q is about vitamin C

? 70y old man with toast & tea diet. Physical examination shows follicular hemorrhage & bleeding gums. What is the cause of the mentioned findings?

▼ **Answer**
Decreased Proline Hydroxylation - Scurvy (Vitamin C deficiency)

- **Choices D & E** → These will probably happen, but are downstream processes due to the malformed collagen; however, not the primary causes of IO

Q16

A 30-year-old primigravid woman at 22 weeks' gestation comes to the physician because of a 1-day history of fever, chills, and muscle aches. Her temperature is 39.4°C (102.9°F), pulse is 114/min, respirations are 15/min, and blood pressure is 104/72 mm Hg. Physical examination shows a uterus consistent in size with a 22-week gestation. Fetal heart sounds are heard. Her leukocyte count is 12,000/mm³. Blood cultures grow gram-positive rods. Which of the following is the most likely causal organism?

- A. Bacillus cereus
- B. Clostridium perfringens
- C. Listeria monocytogenes
- D. Staphylococcus aureus
- E. Streptococcus agalactiae (group B)

▼ **Explanation**

- **Answer is C (Listeria monocytogenes)**
 - **IMP Clues:**
 - Pregnant woman (now we think of pregnancy-related infections)
 - Fever, chills, and muscle aches (non specific symptoms)
 - Blood culture grows gram +ve rods (narrows our DD; excludes Choices D & E)

- Dx → *Listeria monocytogenes* infection
 - **Catalase-positive, B-hemolytic, motile, facultative intracellular gram-positive rod.**
 - Transmission: **ingestion of unpasteurized dairy, soft cheeses, and deli meats.**
 - Presentations:
 - Pregnant women: **mild flu-like illness, amnionitis, abortion, or sepsis**
 - Neonates: **Sepsis, meningitis, or granulomatosis infantiseptica** (in CGD patients)
 - Elderly: **Sepsis & Meningitis**



Listeria Movement Pattern:

- Intracellular → Actin rockets
- Extracellular → tumbling motility

Q17

A 40-year-old man is brought to the emergency department 45 minutes after his wife found him unresponsive. His temperature is 37°C (98.6°F). Laboratory studies show:

Hemoglobin	15 g/dL
Arterial blood gases on room air	
Pco2	60 mm Hg
Po2	50 mm Hg
HCO3-	12 mEq/L

Which of the following best describes the acid-base status in this patient?

- A. Metabolic acidosis only
- B. Metabolic acidosis and respiratory acidosis
- C. Metabolic alkalosis and respiratory alkalosis
- D. Respiratory acidosis only
- E. Respiratory acidosis and metabolic alkalosis
- F. Respiratory alkalosis only

▼ **Explanation**

- **Answer is B (Metabolic acidosis and respiratory acidosis)**
 - **IMP Clues:**
 - PCO2 is 60 (normal is 36-44) so → **respiratory acidosis**
 - HCO3 is 12 (normal is 20-28) so → **metabolic acidosis**
 - **Dx → Mixed metabolic & respiratory acidosis.** Simple. Don't overcomplicate it.

Q18

A 47-year-old woman with psoriasis comes to the physician for follow-up care. At her last appointment she was given several topical creams, which must be used in a specified sequence twice daily. No improvement is apparent at this appointment. Which of the following is the most appropriate way for the physician to begin the discussion of this patient's compliance with therapy?

- A. "Did you use the creams twice daily?"
- B. "How many tubes did you use in the last month?"
- C. "How often did you skip treatments?"

D. "Most people find it difficult to stick to a routine. How did you do?"

E. "Using something twice daily can be difficult. I assume you are like most patients who miss at least 10% of treatments."

▼ **Explanation**

- **Answer is D ("Most people find it difficult to stick to a routine. How did you do?")**
 - So first ethics Q of the block. Patient here has psoriasis and the doctor prescribed some topical creams for her but still no improvement. He wants to know if she had been compliant or not.
 - Let's us put some golden ethics rules here:
 - **DO NOT ASSUME**
 - **DO NOT say something intimidating**
 - **DO NOT POINT FINGERS**; you must always start your convos with something like "all of my patients have difficulty in x & y, do you have any difficulties?" to make her feel heard & relatable.
 - Choice D here makes the most sense.

▼ **Other Choices**

- **Choice A** → too direct; why embarrass her
- **Choice B** → same as choice A; why embarrass her
- **Choice C** → just rude. You are assuming she skipped ttt; even if she did, don't be rude
- **Choice E** → Starts really well but then you hit here with the "I assume you are like most patients who miss at least 10% of treatments." okay Mr. smarty pants. WRONG.

Q19

A 42-year-old woman comes to the physician because of a 3-year history of an intermittent facial rash, including the forehead, eyelids, nose, and cheeks. She says that the rash seems to be getting worse since she moved from New York to Florida last year. She notes that she has always blushed easily. Spicy foods also precipitate a flushing reaction that seems to exacerbate the rash. Occasionally, her face burns and stings, and her skin feels dry. Physical examination shows erythema over the nose and cheeks, with scattered telangiectasias and a few papules. Which of the following is the most likely diagnosis?

- A. Acne vulgaris
- B. Carcinoid syndrome
- C. Pityriasis rosea
- D. Rosacea
- E. Seborrheic dermatitis

▼ **Explanation**

- **Answer is D (Rosacea)**
 - **IMP Clues:**
 - Woman
 - Intermittent facial rash on forehead, eyelids, nose, and cheeks
 - She always blushed easily
 - Spicy foods precipitate the flushing reaction
 - Her face burns & her skin feels dry
 - Scattered telangiectasia & few papules

- **Dx → Rosacea**

- Erythema that affects **center of the face** (forehead, eyelids, nose, and cheeks) that affects middle-aged **women more**
- Rash: **papules, pustules, and telangiectasia** (very characteristic)
- Precipitated by: **heat, spicy food, hot drinks, sunlight, stress, or alcohol**
- Associated with: **burning & tingling sensation.**



▼ **Other Choices**

- **Choice A → Acne** is characterized by the presence of **comedones**. Usually affects teenagers or women with PCO or women with androgen hypersecretion
- **Choice B → Carcinoid Syndrome**
 - Appears after carcinoid tumor spreads to the liver or if the origin is non-GI (lung)
 - Carcinoid tumors secrete **serotonin**, which upon arriving to the liver gets cleared out. If it metastasizes to the liver, then serotonin skips the portal circulation into systemic circulation & causes the symptoms.
 - Symptoms are **diarrhea, flushing, diaphoresis, headache, and Tricuspid Regurgitation.**

? 60y old male came to the clinic for episodes of flushing, diarrhea, and headaches. On examination the patient has a pansystolic murmur. U/S shows liver mass. How would you confirm the diagnosis?

▼ **Answer**
Urinary 5-HIAA

- **Choice C →** (the confusing one) **Pityriasis Rosea** is characterized by a **Herald patch** + Christmas tree rash on the trunk.
- **Choice E → Greasy** scales on scalp or eyebrows. Dandruff.



Acne:



Pityriasis Rosea:



Seborrheic Dermatitis:



Q20

A 40-year-old man with type 2 diabetes mellitus comes to the physician for a follow-up examination. Treatment with glyburide and metformin has been ineffective in controlling his disease. The decision is made to try pioglitazone. This drug produces a beneficial effect through which of the following mechanisms of action?

- Blockade of ATP-sensitive potassium channels in the pancreatic β cells
- Increased insulin synthesis by promoting the effect of physiologic insulin secretagogues
- Increased insulin uptake by muscle and adipose tissue, thus making the insulin more effective
- Promotion of insulin action interfering with the synthesis of endogenous antagonists, primarily glucagons
- Stimulation of the peroxisome proliferator-activated receptor γ

▼ Explanation

- Answer is E (Stimulation of the peroxisome proliferator-activated receptor γ)
 - Simple Q that asks about the **MOA of pioglitazone** → activates **PPAR- γ**
- **Thiazolidinediones (pioglitazone, rosiglitazone)** → activate **PPAR- γ** → increased insulin sensitivity
 - Side effects: Weight gain, Edema, Heart Failure
 - mnemonic → “*we have gliter at the PPARtY (party)*”



DON'T GET IT MIXED UP!

Thiazolidinediones → activate PPAR- γ
Fibrates → activate PPAR- α

What drugs do we use in ttt of DM (insulin not included here):

1. Metformin

- MOA → Inhibits **mGPD**:
 - inhibition of glucagon actions → increases glycolysis & **inhibits gluconeogenesis** [asked on NBME]
 - increased peripheral glucose uptake → increases insulin sensitivity
- Side-effects → **Lactic Acidosis**



In what patients are metformin contraindicated?

▼ Answer

Renal insufficiency - due to exacerbation of metabolic acidosis

2. Sulfonylureas (-ide)

you do not need to know which is 1st gen & which is 2nd gen; just know -ide

- MOA → **Closes ATP-gated K⁺ channels** in pancreatic Beta cells → depolarization → **increase Ca influx** → **pushes insulin-containing vesicles** into blood
- Side-effects:
 - 1st gen → **Disulfiram-like reaction** [asked on NBME]
 - 2nd gen → **Hypoglycemia**

3. Meglitinides (-glinide)

- MOA → **Closes K⁺ channels** in pancreatic Beta cells → depolarization → **increase Ca influx** → **pushes insulin-containing vesicles** into blood
- Side-effects → **Hypoglycemia**

4. GLP-1 analogs (-tide)

- MOA → **GLP** is a peptide that normally causes **increased glucose-dependent insulin release**
 - You know why oral glucose's insulin release rate is faster than IV glucose?
 - Yep, it's that GLP-1 peptide.
- Side-effects → **Pancreatitis** [asked on NBME]
- mnemonic → “*stupid kids GULP tide pods all the time*”

5. DPP-4 inhibitors (-liptin)

- MOA → **DPP-4** is a peptide that **breaks down GLP-1**; so DPP-4 inhibitors cause **decreased degradation of GLP-1** → **increased glucose-dependent insulin release**
- Side-effects (LY) → **UTI & RTI**
- mnemonic → “*liptin tea makes you go Do PP(peepee)*”

6. SGLT-2 inhibitors (-flozin)

- MOA → **Blocks SGLT-2 in PCT** → **less Na reabsorption & less glucose reabsorption**

Arrows Q may ask you what would happen to urine Na, glucose, total body water volume?

- **Increased** urine Na (not reabsorbed)
- **Increased** urine glucose (not reabsorbed)
- **Decreased** total body water volume (less Na reabsorbed = less water retention)

- Side-effects → **UTI & vulvovaginal candidiasis** (more sugar in urine = happy bacteria & candida) [asked on NBME]

7. α -glucosidase inhibitors (Acarbose, miglitol)

- MOA → **inhibits intestinal brush border a-glucosidase** → decreased hydrolysis of carbs → decrease glucose absorption (remember that carbs must be broken down to its simplest form to get absorbed)
- Side-effects → **GI upset & bloating**

8. Amylin analog (Pramlintide)

- MOA → **amylin** is a peptide that **gets secreted with insulin** → **decreases glucagon release**
- Side-effects → **Hypoglycemia**

▼ Other Choices

Okay let's review the HY related notes we just spent an hour reading

- **Choice A** → refers to Sulfonylureas or Meglitinides
- **Choice B** → refers to GLP-1 analogs
- **Choice C** → refers to Metformin
- **Choice D** → refers to DPP-4 inhibitors

Q21

A 33-year-old woman, gravida 4, para 4, is admitted to the hospital after she sustained a splenic laceration in a motor vehicle collision. Three units of packed red blood cells are administered. Five hours later, she develops shortness of breath. Her respirations are 29/min. Crackles are heard throughout both lung fields. A chest x-ray shows bilateral lung infiltrates. Arterial blood gas analysis on room air shows a Po₂ of 55 mm Hg. Which of the following is the most likely cause of this patient's condition?

- A. Anaphylactic reaction induced by IgA antibodies
- B. Hemolytic transfusion reaction
- C. Postoperative bronchopneumonia
- D. Pulmonary embolus with pulmonary infarction
- E. Transfusion-related acute lung injury

▼ Explanation

- **Answer is E (Transfusion-related acute lung injury)**
 - **IMP Clues:**
 - Packed RBCs are administered (hx of transfusion)
 - 5 hours later (Time frame is important regarding DD)
 - Shortness of breath, tachypnea (29/min), crackles throughout both lungs, CXR shows bilateral infiltrates, PO₂ 55mmHg (hypoxic) (all of these clues → Respiratory distress symptoms & signs)
 - **Dx → Transfusion Related Acute Lung Injury (TRALI)**
 - Simply put, **TRALI = ARDS-like state post-transfusion**
 - Usually, **< 6 hours post-transfusion**
 - MOA: **Neutrophils in lungs react to cytokines in transfused blood**. Simple.

Other Transfusion Reactions on the USMLE

1. TRALI:

- Discussed above.

2. Transfusion Associated Circulatory Overload (TACO):

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

3. Delayed Transfusion Reaction:

- Hemolysis in a patient post transfusion over a longer period of time usually **days-week** (hence the name "*delayed*")

- MOA → **antibodies against donor's minor RBC antigens** (Rh, Kell, Duffy, Kidd) [so Coomb's +ve]
- Classic Q would be → patient had a blood transfusion for whatever reason then few days after his hemoglobin decreased & labs show increased unconjugated bilirubin (hemolysis) & Coomb's +ve test (which essentially means there are antibodies/antigens involved). Vignettes can also include all sorts of clues to signify hemolysis (increased LDH & decreased Haptoglobin)

4. Hemolytic ABO mismatch:

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

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

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



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

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

Easy? Yes.

▼ Other Choices

- **Choice A** → refers to IgA deficiency
 - VERY HY for STEP 1
 - **Recurrent infections usually Respiratory + giardia infection + atopy (KNOW THIS TRIAD)**
 - MOA → **patients lack IgA** (duh)
 - Blood transfusions in these patients may cause **anaphylaxis**: they lack IgA, donor's plasma have IgA → Anaphylaxis
 - Patients with **IgA deficiency + Celiac disease will have NEGATIVE test results**
 - Celiac is tested for by **IgA tissue transglutaminase (no IgA so negative test)**
 - This association is common because autoimmune diseases go together
- **Choice B** → mention in the HY Related Notes section
- **Choice C** → no fever, no leukocytosis, no sputum. Nothing here yells pneumonia
- **Choice D** → No Chest pain, no hx of DVT or immobility. Bilateral infiltrates & crackles are not findings of PE

Q22

A 47-year-old man is brought to the emergency department by his wife because of severe chest pain for 2 hours. His pulse is 110/min and thready, and blood pressure is 90/70 mm Hg. Pulse oximetry on room air shows an oxygen saturation of 85%. Physical examination shows cold, clammy skin. Crackles are heard

bilaterally on auscultation. An ECG shows 4-mm ST-segment elevation in leads V4 through V6 Cardiac output is 2 L/min (N=4-5). Which of the following is most likely to be decreased in this patient?

- A. Arterial lactate concentration
- B. Hemoglobin concentration
- C. Mixed venous oxygen tension
- D. Pulmonary vascular resistance
- E. Systemic vascular resistance

▼ Explanation

- Answer is C (Mixed Venous Oxygen Tension)
 - IMP Clues:
 - Chest pain + ST-elevation in leads V4-V6 (Anterolateral wall MI)
 - Cold clammy skin + hypotension + tachycardia + decreased CO (Cardiogenic Shock)
 - Dx → Cardiogenic shock 2ry to anterolateral wall MI
 - Left ventricle ischemia = left ventricle dysfunction = heart cannot pump out blood = cardiogenic shock
 - Findings of Cardiogenic shock include:
 - Decreased CO (decreased tissue perfusion, which causes blood decreases oxygen concentration & accumulation of metabolites)
 - Increased Systemic vascular resistance (2ry to body's reflex to maintain BP)
 - Increased PCWP (Retained blood in LV backs up into LA)

▼ Other Choices

- Choice A → Lactate would increase as decreased tissue perfusion = hypoxia = accumulation of metabolites like lactate
- Choice B → Hb concentration most likely would not change
- Choice C → Mixed Venous O2 tension simply means the amount of O2 in blood as it returns from the tissues, decreased CO → decreased perfusion → increased demand → increased O2 extraction → decreased mixed venous o2 tension
- Choice D → Cardiogenic shock = heart cannot pump out blood = blood accumulates in LV = backs up into LA = backs up into pulmonary veins = Pulmonary vasculature constricts in an attempt to stop this, so Pulmonary vascular resistance increases
- Choice E → SVR would increase to maintain the BP (decreased CO causes a decrease in BP)

Q23

An 18-year-old man comes to the physician because of a 2-week history of extreme fatigue. Physical examination shows scleral icterus. Laboratory studies show:

Hemoglobin	9 g/dL
Reticulocyte count	22.5%
Erythrocyte 2,3-bisphosphoglycerate	10,270 nmol/mL (N=4082)
Serum	
Bilirubin, total	10 mg/dL
Indirect	8.5 mg/dL

This patient most likely has a deficiency of the activity of which of the following enzymes in erythrocytes?

- A. Glyceraldehyde-3-phosphate dehydrogenase
- B. Hexokinase
- C. Phosphofructokinase
- D. Pyruvate kinase
- E. Triose-phosphate isomerase

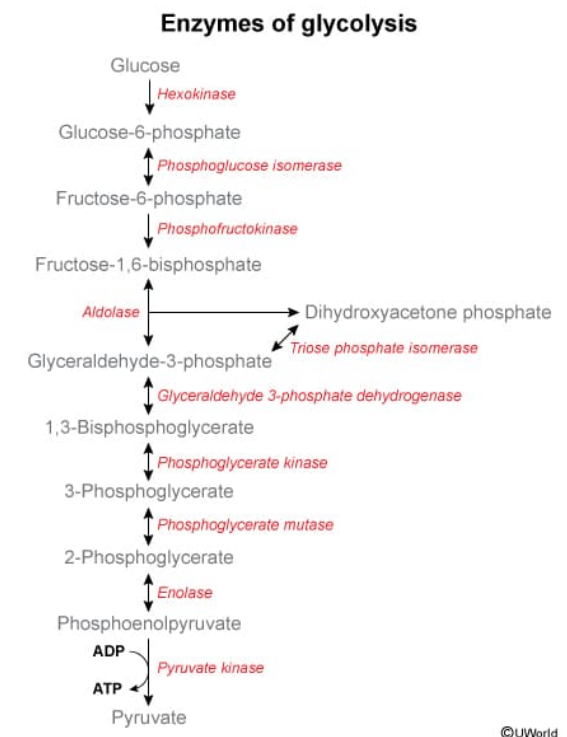
▼ Explanation

- Answer is D (Pyruvate kinase)
 - IMP Clues:

- Scleral icterus (jaundice)
- Reticulocyte count 22.5% (hemolysis responded to by reticulocytosis)
- Erythrocyte 2,3-bisphosphoglycerate 10,270 (elevated, so the enzyme after it is deficient)
- Serum total + indirect bilirubin 10 & 8.5 (so indirect hyperbilirubinemia, aka hemolysis)

• **Dx → Pyruvate Kinase Deficiency**

- **Second most common cause of enzymatic deficiency hemolysis** (after G6PD deficiency)
- Enzyme that carries the last step in glycolysis (PEP → Pyruvate)
- **Decrease PK (enzyme in glycolysis) caused decreased ATP production → decreased Na/K ATPase pump = retention of Na inside the cell → cell swelling & lysis ⇒ Hemolysis**
- To answer the above Q, all you needed to know is that the enzyme that follow 2,3-bisphosphoglycerate is PK, which also is an enzyme deficiency that causes hemolysis



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▼ **Other Choices**

- All of these enzymes are upstream of 2,3-bisphosphoglycerate so their deficiency would not cause an increased 2,3-bisphosphoglycerate.

Q24

A 27-year-old primigravid woman at 39 weeks' gestation is admitted to the hospital in labor. She has a 5-year history of type 2 diabetes mellitus currently treated with insulin. During the pregnancy, she has had difficulty controlling her serum glucose concentration. At a previous examination 1 week ago, her hemoglobin A1c was 8.4%. There is no family history of serious illness. On admission, the cervix is 100% effaced and 7 cm dilated; the vertex is at +1 station. Fetal weight is estimated at 4100 g (9 lb 1 oz). Which of the following is the most likely obstetric complication?

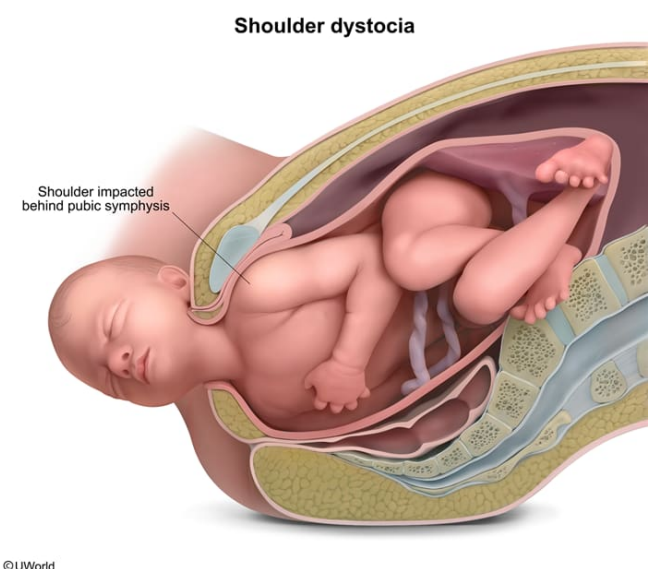
- A. Amniotic fluid embolism
- B. Diabetic ketoacidosis
- C. Preeclampsia
- D. Retained placenta
- E. Shoulder dystocia

▼ **Explanation**

- **Answer is E (Shoulder Dystocia)**
- **Persistence of maternal hyperglycemia causes persistent fetal hyperglycemia, which causes pancreatic beta-islets hyperplasia → fetal hyperinsulinemia**
 - **What happens as a result?**
 - **Inhibition of gluconeogenesis, lipolysis, and protein catabolism** ⇒ Causes **Postnatal hypoglycemia** due to abrupt cessation of maternal glucose supply upon clamping the umbilical cord.
 - **Increases glycogenesis, Fat Storage, and protein anabolism** ⇒ **Macrosomia**, which predisposes to **Shoulder Dystocia (Choice E)**
 - Other features seen are **organomegaly** and **macroglossia**.

? **What glucose transporter is found in the placenta?**

▼ **Answer**
GLUT-1 (The main key transporter)



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Q25

A 50-year-old man with rheumatoid arthritis comes to the physician because of recent worsening of symptoms as well as increasing fatigue 1 month after starting therapy. Laboratory studies show:

Hemoglobin	9.6 g/dL
Hematocrit	29%
Mean corpuscular volume	77 μm^3
Platelet count	200,000/mm ³
Serum	
Iron	30 $\mu\text{g/dL}$
Total iron-binding capacity	150 $\mu\text{g/dL}$ (N=250-400)

Which of the following is the most likely diagnosis?

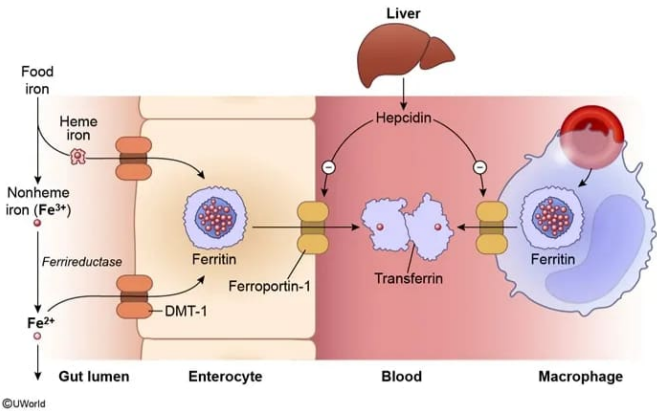
- A. Anemia of chronic disease
- B. Autoimmune hemolytic anemia
- C. Lead intoxication
- D. Sideroblastic anemia
- E. β -Thalassemia minor

▼ Explanation

- **Answer is A (Anemia of chronic disease)**
 - **IMP Clues:**
 - Rheumatoid arthritis (autoimmune disease)
 - Increasing fatigue (usually this = anemia)
 - Okay labs here seal the deal.
 - Low Hb & Hct = anemia
 - low MCV = microcytic anemia
 - Iron is low + TIBC is also low = hence the low TIBC, we know we have enough Iron stores (not IDA). The low serum iron just reflects the body hiding its iron.
 - **Dx → Anemia of Chronic disease**
 - **Autoimmune disease/chronic disease/renal failure** ⇒ think anemia of chronic disease until proven other wise
 - Labs would show:
 - **LOW** circulating iron (*Low Serum Iron, Low transferrin*)
 - **HIGH** iron stores (*High Ferritin, Low TIBC*)
 - **LOW** Reticulocyte count
 - **Why?**
 - The body hides the iron, because infections use body resources to grow
 - Iron is a resource
 - Infection = stress; chronic diseases = stress; **body cannot differentiate.** simple.
 - Mechanism: IL-1 & Hepcidin
 - **Inhibits iron mobilization from stores** (*inhibits release of iron from macrophages*)
 - **Increases storage of iron** (*increased iron sequestration*)
 - **Inhibits intestinal absorption of Iron** (*via inhibition of ferroportin*)

 **Anemia of Chronic disease is a type of BOTH microcytic & normocytic anemia**

- **Normocytic** = MCV 80-100
- **Microcytic** = MCV < 80



 **USMLE can give you this Q and ask you for the cause of the labs, and rephrase the answer as "due to effects of liver-made protein"**

- **Hepcidin is made by the Liver**

▼ Other Choices

- **Choice B** → Low Hb? yes. Normal MCV? No. Anything supporting hemolysis like high LDH, low haptoglobin, high unconjugated bilirubin? NO. Coomb's positive? No.

- **Choice C** → Iron would be actually high + no hx support lead poisoning (paint, chewing on pencils, old homes, lead related occupation)
- **Choice D** → Same findings as Choice C + nothing supports sideroblastic anemia
- **Choice E** → would present in an asymptomatic adult with IDA-like labs refractory to iron therapy

Q26

A 64-year-old woman with type 2 diabetes mellitus and hypertension comes to the physician because of soreness and muscle pain for 3 weeks. She says the pain is in most large muscle groups and usually occurs at night. She began rosuvastatin therapy 4 weeks ago for dyslipidemia. Her medication regimen also includes gemfibrozil, hydrochlorothiazide, losartan, and metformin. Physical examination shows mild tenderness of the quadratus femoris muscle bilaterally. Her serum creatine kinase activity is five times the upper limit of the reference range. The most likely cause of this patient's current condition is an interaction between rosuvastatin and which of the following drugs?

- A. Aspirin
- B. Gemfibrozil
- C. Hydrochlorothiazide
- D. Losartan
- E. Metformin

▼ Explanation

- Answer is B (Gemfibrozil)
 - Fibrates (can be referred to as "*fibric acid derivative*")
 - Stimulates **PPAR-α** → **upregulates LPL** → causes FFA (from TAGs in chylomicrons & VLDLs) to **enter** adipose cells → **decreases TAG serum levels [MAJOR EFFECT]**
 - PPAR-α is a *nuclear transcription factor* which also causes **increases Apo-A I & Apo-A II transcription** → **increases HDL production**.
 - This is why **Fibrates are the most effective drug class in patients with high TAGs & low HDL**
 - Statins + Fibrates = Myopathy with high CK levels (muscles are breaking down)
 - Fibrates + Statins = Rhabdomyolysis
 - Caused by **CYP450 Inhibition**

Fibrates/Statins alone also cause rhabdomyolysis, especially **Gemfibrozil**.

? What are the HY side effects of fibrates?

▼ Answer

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



Don't Get It Mixed-up:

PPAR-α ⇒ Fibrates

PPAR-γ ⇒ Thiazolidinediones (pioglitazone, rosiglitazone)

Q27

A 23-year-old woman comes to the student health center because of a 2-week history of a vaginal sore. She has been sexually active with a new partner, and they use condoms inconsistently. Pelvic examination shows a nontender ulcer on the vulva. Dark-field examination of a scraping of the lesion is positive for spirochetes. Which of the following histologic changes is most likely to be seen on a biopsy specimen of this lesion?

- A. Acute inflammation with abscess formation
- B. Granulomas with caseation and plasma cell infiltration
- C. Granulomas with suppuration
- D. Obliterative endarteritis with lymphocytes and plasma cells
- E. Pyogranulomatous inflammation with edema

▼ Explanation

- Answer is D (Obliterative endarteritis with lymphocytes and plasma cells)

- **IMP Clues**

- Young sexually active woman + unsafe sex + vaginal sore (okay it is an STD)
- Nontender Ulcer (PAINLESS Ulcer, narrows down our DD. Thinking of syphilis rn)
- Dark-field microscopy is positive for spirochetes (confirmed syphilis)

- **Dx → Primary Syphilis**

- Chancre = **painless ulcer**
- Syphilis causes **endarteritis obliterans**. In other words, it obliterates end arteries.
 - **Obliteration of end arteries causes decreased blood supply to tissue (causing ulcers) and peripheral nerves (hence, painless ulcers)**

Let's Review some HY Related Notes:

- If **Primary Syphilis** is left untreated, the **chancre** heals after 3-6 weeks
- **Secondary Syphilis** then develops
 - **Secondary = Systemic disease**
 - **Maculopapular rash** that covers all body **including** palms & soles
 - Condyloma Lata can also be seen (DD Condyloma acuminata of HPV)
- If Secondary syphilis is left untreated, the rash resolves then **tertiary syphilis** develops after years

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

▼ **Answer**

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

- **Tertiary Syphilis**

- **Characterized by:**
 - **Gumma** → **painless** firm necrotic ulcer (granulomatous lesion)
 - **Tree Bark Aortitis** → Ascending aorta aneurysm with tree bark look (due to destruction of vasa vasorum, the blood supply of the aorta)
 - **Tabes Dorsalis** → Destruction of the dorsal column of spinal cord: presents as loss of proprioception & vibration + positive Romberg sign
 - **Argyll's Robertson pupil (aka prostitute's pupil)** → Accommodates but doesn't react

mnemonic: Argyll's Robertson = AR = Accommodate but doesn't React

- Caused by lesion in **pretectal area**
- **Accommodation is intact but light reflex is absent**



HY to know:

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

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

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

- Lastly, Syphilis is one of the **TORCH infections**.
 - **Congenital syphilis causes: Saddle nose, Saber chins, SNHL, and Hutchinson teeth (notched incisors) or mulberry molars**

- **Investigations**

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

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

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

▼ **Answer**

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

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

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

◦ **Treatment → Penicillin**

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

Q28

A 40-year-old woman comes to the physician for an initial examination. She says that she is health conscious and eats only natural organic foods. Fasting serum laboratory studies show a triglyceride concentration of 380 mg/dL; a complete blood count and serum electrolyte concentrations are within the reference ranges. The physician suggests that the patient try taking fish oil and a supplement to treat her dyslipidemia. Which of the following best describes the mechanism of action of the most appropriate vitamin for this patient?

- A. Antagonizes VLDL-cholesterol secretion
- B. Increases catabolism of LDL-cholesterol
- C. Inhibits cholesterol uptake
- D. Inhibits HMG CoA
- E. Stimulates PPAR-α receptors

▼ **Explanation**

- **Answer is A (Antagonizes VLDL-cholesterol secretion)**
 - Simple Q that asks directly for the MOA of the most appropriate "vitamin" for this patient.
 - On the USMLE, the **only vitamin given for dyslipidemia is niacin (Vitamin B3)**

- **Niacin (Nicotinic Acid)** is used as anti-lipid drug via the following mechanisms:
 1. **Decreased VLDL synthesis & export from the liver** (what we have here)
 2. **Inhibits hormone-sensitive lipase** (HSL)
- If USMLE asks you **what increases HDL more than any other agent** → **Niacin**

? What are the HY side effects of Niacin?

▼ Answer

1. Hyperuricemia
2. Insulin Resistance & Type 2DM
3. Flushing (treated with **NSAIDs** not antihistamines)

? What does niacin deficiency cause?

▼ Answer

Pellagra

- **"4Ds": Diarrhea, Dementia, Dermatitis** (Sun-hypersensitivity → hyperpigmented rash on sun-exposed areas), and **Death**
- 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

▼ Other Choices + HY Related Notes

- **Choice B** → refers to **PCSK9 inhibitors (Alirocumab, Evolocumab)**. Sounds like a fighter jet name I know.
 - All you need to know is **PCSK9** is an enzyme that **breaks down LDL receptors**.
 - LDL receptors pick-up cholesterol = less cholesterol in blood = good.
 - so **PCSK9 inhibitors** = less LDL receptors breakdown = more LDL-receptors = more cholesterol picked up from blood = good.
- **Choice C** → refers **Ezetimibe** **inhibits intestinal absorption of cholesterol**, so mainly decreases LDL.
 - Like Bile Acid Sequestrants, **never the correct "lone" drug choice.**
 - HY Side effects: **GI disturbance**

? What transporter on enterocytes is blocked by ezetimibe?

▼ Answer

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

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

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

▼ Answer

mRNA levels of HMG CoA reductase **INCREASED**.

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

- **Choice E** → refers to **fibrates**

A 62-year-old woman is brought to the physician by her husband for a routine follow-up examination. She was diagnosed with dementia, Alzheimer type, 4 months ago and is in the early stages of the disease. She is retired and lives at home with her husband, who is also retired. Which of the following interventions is most likely to help this patient maintain her present functional level for as long as possible?

- A. Instruct the patient to keep notes and lists to help her memory
- B. Suggest that the patient enter individual supportive therapy
- C. Suggest that the couple go to a therapist together
- D. Suggest that the couple move to an assisted living facility
- E. Start the patient on ginkgo biloba

▼ **Explanation**

- **Answer is A (Instruct the patient to keep notes and lists to help her memory)**
 - We have a woman with early stage dementia, lives with her husband who is retired, and asks about how to maintain functional level
 - **Choice A** makes the most sense; keeping notes & lists to help her memory will preserve her functional level & accommodate for her dementia (up to a limit of course)
 - **Choice B** is wrong because an individual support therapy would support her emotionally not functionally
 - **Choice D** is wrong because she is still in the early stages of the disease
 - No idea what ginkgo biloba is but apparently it is some sort of useless herb that is NOT recommended by one so yah also wrong.

Q30

A 5-year-old boy is admitted to the hospital because of recurrent pancreatitis since the age of 2 years. Physical examination shows eruptive xanthomas over the upper and lower extremities and hepatosplenomegaly. His fasting plasma appears turbid. His serum total cholesterol concentration is 235 mg/dL (N<190) and triglyceride concentration is 1875 mg/dL (N<90). After receiving an injection of heparin, his lipoprotein lipase activity is within the reference range. A deficiency of which of the following is the most likely cause of the findings in this patient?

- A. ApoC-II
- B. Cholesterol ester transfer protein
- C. Hormone-sensitive lipase
- D. LDL receptor
- E. Pancreatic lipase

▼ **Explanation**

- **Answer is A (ApoC-2)**
 - **IMP Clues:**
 - Recurrent Pancreatitis (due to hypertriglyceridemia, so type 1 or 4)
 - Turbid plasma & Xanthomas (hinting to hyperchylomicronemia)
 - Lipoprotein lipase activity normal (I guess this is for exclusion)

- Dx → Hyperchylomicronemia
 - Deficiency of **LPL or ApoC-2**
 - Labs: **high chylomicrons**, **high TAGs**, and **high cholesterol**
 - Turbid creamy plasma, pancreatitis, and xanthomas

⚠ 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**

▼ Other Choices

- **Choice B → CETP** transfer cholesterol esters from HDL to LDL & VLDL
 - Deficiency of **CETP** would cause high HDL & low LDLs
- **Choice C → HSL** deficiency would present inability of hormones to liberate TAGs from adipocytes
 - Hormones include **epinephrine, glucagon, and cortisol**
- **Choice D → LDL Receptor** deficiency causes **hypercholesterolemia**
 - Deficiency of **LDL receptor or Apo B100**
 - If **heterozygous** = deficiency → LDL 300-400 & MI in 30-40s
 - If **homozygous** = absence → LDL 700-1000 & MI in teens
- **Choice E → Pancreatic Lipase** deficiency
 - Pancreatic Lipase causes absorption of fats from diet
 - Lipase deficiency would cause steatorrhea & fat-soluble vitamin deficiency

Q31

A 14-year-old boy is brought to the physician by his mother because of daily headaches for 2 months. The headaches are described as a bilateral aching in the temples. His mother states that he also "has not been himself" for the past few months. He seems more confused, often forgetting names, dates, and places, and he is clumsy with frequent falls. His school performance also has declined over the past quarter. Physical examination shows a broad-based, ataxic gait. He is alert and oriented to person, place, and time, but he is slow to answer questions. Chronic abuse of which of the following substances is the most likely cause of this patient's condition?

- A. Cocaine
- B. Ethanol
- C. Inhaled glue
- D. Methamphetamines
- E. PCP (phencyclidine)

▼ **Explanation**

- **Answer is C (Inhaled glue)**
 - **IMP Clues:**
 - 14-year-old boy (being this young makes it harder for him to acquire some drugs)
 - Headaches + "has not been himself" + confused + forgetting names, dates, and places (disoriented & confused)
 - Clumsy + Broad-based ataxic gait (Neurotoxicity)
 - **Dx → Chronic Inhalants abuse**
 - Glue has **toluene**, which is **neurotoxic** causing:
 - **Cognitive decline** (confusion, forgetting, school performance decline)
 - **Cerebellar dysfunction** (clumsiness & ataxic gait)
 - Widely accessible for teens / school-years children unlike some of the other drugs
 - Qs can also mention the finding of "**yellow pieces / crusts on the nares**"
 - boy was just sniffing the glued glitter

▼ **Other Choices**

- **Choice A → Cocaine abuse** would cause *euphoria, sympathetic stimulation, increased activity, and paranoia / hallucinations* up to *stroke & seizures*. **No ataxia** & hard for a child to get their hands on some cocaine.
- **Choice B → Ethanol toxicity** is actually a very solid DD. Chronic Alcohol does cause *Cerebellar degeneration & Cognitive decline*; however, it usually takes years for these symptoms to develop. This makes it unlikely that a 14-year-old had *years* of abuse.
- **Choice D → Methamphetamines** abuse would cause *aggression, paranoia, and hallucinations*. Not ataxia & cognitive decline
- **Choice E → PCP** causes *aggression, nystagmus, and hallucinations*.

Q32

A 66-year-old man is brought to the emergency department because of a 1-day history of fever. He underwent transurethral resection of the prostate 1 week ago. His temperature is 39.5°C (103°F), and blood pressure is 75/40 mm Hg. Physical examination shows no other abnormalities. Blood cultures grow lactose-positive, gram-negative rods. Which of the following best describes the initial event in the development of hypotension in this patient?

- A. Hemolysin lysis of erythrocytes
- B. Induction of histamine release
- C. Invasion of segmented neutrophils
- D. Lipopolysaccharide stimulation of toll-like receptor
- E. Toxic activity of an ADP ribosyltransferase

▼ **Explanation**

- **Answer is D (Lipopolysaccharide stimulation of toll-like receptors)**
 - **IMP Clues:**
 - Fever (infection) + BP is 75/40mmHg (hypotension, so we know this is a septic shock)
 - History of transurethral resection of prostate (we know its of a UTI origin)
 - Lactose-positive, gram-negative rods (DD lactose fermenters)

- **Dx → Septic Shock 2ry to gram negative bacteria (post-op infection)**
 - Gram negative bacteria have **LPS** in their outer membranes
 - The structure of LPS is just bullshit, just know that it includes **Lipid A**
 - **Lipid A (an endotoxin)** binds to **toll-like receptors (CD14)** on **macrophages** → release of cytokines:
 - **IL-1 → Fever**
 - **TNF-a → hypotension [asked on NBME]**



USMLE is also known to ask about the MOA of shock due to super-antigens:

- **Staphylococcus aureus → Toxic Shock Syndrome Toxin (TSST)**
- **Streptococcus pyogens → Exotoxin A (Toxic-shock-like syndrome)**

TSST & Exotoxin A → bridge MHC-2 on macrophages with T-cell Receptor of CD4 T-cells → release of cytokines from macrophages



What are the Lactose-Fermenters on the USMLE? (turn MacConkey agar pink)

▼ **Answer**

1. *E.coli*
2. *Klebsiella*
3. *Enterobacter*
4. *Serratia*



78M + prostatitis + develops hypotension & fever. What is the cause of hypotension?

▼ **Answer**

Increased Synthesis of Nitric Oxide

Patient is septic due to **Lipid A** of **E.coli's LPS** → **TNF-alpha** is released → stimulated **Nitric Oxide Synthase** → increased synthesis of NO → Vasodilation → Hypotension

Q33

A 68-year-old man comes to the physician because of a 1-month history of not being able to sustain an erection for sexual intercourse, although he has no difficulty during masturbation. His wife of 40 years died 2 years ago after a prolonged illness. He began dating recently. He has a multinodular goiter but takes no medications. His serum thyroid-stimulating hormone concentration is 4.0 μU/mL, and serum testosterone concentration is within the reference range. He does not have any symptoms of major depressive disorder. Which of the following pairs of additional findings is most likely to be found on history taking?

Choices	Libido	Nocturnal Erections
A	Decreased	Decreased
B	Decreased	Normal
C	Normal	Decreased
D	Normal	Normal

▼ **Explanation**

- **Answer is D (Normal Libido - Normal Nocturnal Erections)**
 - **IMP Clues:**
 - Cannot sustain an erection however has no difficulty during masturbation (NOT organic, mostly a psychological issue)
 - Wife died 2 years ago + recently started dating (reinforcing that it is mostly psychological)
 - Multinodular goiter + TSH level upper normal limit (trying to throw you off)
 - Serum testosterone is normal (CONFIRMED, no organic causes here)
 - No symptoms of MDD (they have low libido, not interested in sex)
 - **Dx → Psychological Erectile Dysfunction**
 - No organic cause (No Hx of DM, HTN, PVD, Smoking) + Can achieve an erection alone (while masturbating) → Psychological
 - No Organic cause = **Intact Nocturnal Erections**
 - Normal testosterone levels = **Normal libido**

▼ **Other Choices**

- **Answer A →**
 - Low testosterone / hx of MDD
 - Cannot masturbate / hx of organic disease
- **Choice B →**
 - Low testosterone / hx of MDD
 - Can masturbate / NO hx of organic disease

- **Choice C →**
 - normal testosterone / NO hx of MDD
 - Cannot masturbate / Hx of organic disease

? How does hyperprolactinemia present in males vs females?

▼ **Answer**

- **Impotence & Gynecomastia in males**
- **Galactorrhea in females**

Q34

A 33-year-old woman comes to the physician because of fever, malaise, burning on urination, and a scant vaginal discharge for the past 4 days. She has been having unprotected sex with a new partner. She appears acutely ill. Her temperature is 38.3°C (101°F). Pelvic examination shows a swollen labium with multiple, extremely tender vesicles and ulcers. Which of the following is the most likely diagnosis?

- A. Bacterial vaginosis
- B. Candidiasis
- C. Chancroid
- D. Chlamydia trachomatis infection
- E. Condyloma acuminata
- F. Genital herpes
- G. Gonorrhea
- H. Lymphogranuloma venereum
- I. Syphilis
- J. Trichomoniasis

▼ **Explanation**

- **Answer is F (Genital Herpes)**
 - **IMP Clues:**
 - Multiple vesicles & ulcers (this seals the deal, this is herpes)

- Dx → Genital Herpes
 - HSV2 infection
 - dsDNA linear enveloped virus
 - **Painful vesicles & ulcers with inguinal lymphadenopathy**
 - **Tzanck test** → Smear of vesicular fluid showing **multinucleated giant cells** (seen in VZV & HSV)
 - Treatment → **Acyclovir** (HSV/VZV DNA Polymerase inhibitor)

? What is the cause of Acyclovir resistance?

▼ Answer

Altered/Absent Thymidine Kinase

📌 This distinction is Super HY on the USMLE:

- dsDNA enveloped **linear** virus → HSV
- dsDNA enveloped **circular** virus → HBV

? Where does HSV1/2 remain latent at?

▼ Answer

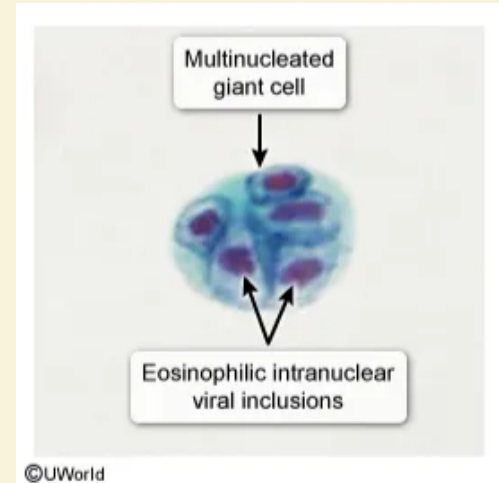
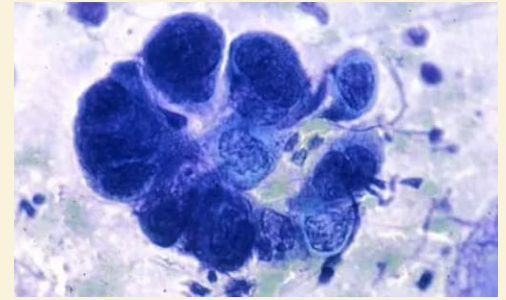
- HSV 1 → **Trigeminal Ganglia**
- HSV 2 → **Sacral Ganglia**

▼ Other Choices

10 Choices???(Sigh)

- **Choice A** → **Bacterial vaginosis** would present as grey-whitish thin discharge + no lesions
- **Choice B** → **Vaginal Candidiasis** would present with cottage cheese like discharge
- **Choice C** → **Chancroid** presents as painful ulcer (not vesicles) with painful inguinal lymph nodes. **Caused by H.ducreyi** (Don't mix this up with Chancer (painless ulcer) of syphilis)
- **Choice D** → Most probably would present as culture negative vaginal discharge specimen + co-infection with gonorrhea. Always treat them together.
- **Choice E** → Genital warts caused by **HPV**. Warts not ulcers and vesicles.
- **Choice G** → **Gonorrhea** causes purulent discharge, PID, Fitz-Hugh-Curtis syndrome, and knee arthritis
- **Choice H** → **Chlamydia L1-L3** presents with painful lymphadenopathy
 - The infection usually starts with *painless* lesions (pustules - papules - vesicles)
 - Then develops into **painful** lymphadenopathy (when the patient usually presents)
 - Then the inflammation turns into fibrosis, causing obstruction of lymph flow.
- **Choice I** → **Syphilis** causes painless chancer
- **Choice J** → **Trichomonas vaginalis** presents with green-yellow fishy smelling discharge with strawberry cervix

 **Tzanck Smear:**



The immunosuppressive agent cyclosporin A (CsA) is a potent inhibitor of T-lymphocyte function that has been successfully used to prevent graft rejection. Graft rejection is most likely prevented by an action of CsA on which of the following steps in T-lymphocyte recognition/activation?

- A. Class I and II MHC protein expression
- B. Costimulatory molecule-dependent signaling
- C. Interleukin-2 (IL-2) gene transcription
- D. Intracellular Ca^{2+} mobilization
- E. Phospholipase C γ -phosphorylation
- F. T-lymphocyte antigen receptor engagement
- G. T-lymphocyte antigen receptor ζ -chain phosphorylation

▼ **Explanation**

- **Answer is C (IL-2 gene transcription)**
 - Simple Q that asks about MOA of cyclosporin
 - Cyclosporin *inhibits Cyclophilin* → *decreases intracellular calcineurin* → *decreases IL-2 transcription*
 - HY Side-effects you must know:
 1. Hypertension
 2. Hyperkalemia 2ry to Nephrotoxicity
 3. Hypertrichosis
 4. Gingival Hyperplasia



KNOW THE DIFFERENCE!

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



Other Related Drugs You Need To Know:

- Okay, so 2 drugs are **calcineurin inhibitors** which **decrease IL-2 transcription**
 1. **Cyclosporin**
 - inhibits **Cyclophilin** → inhibits calcineurin → decreases IL-2 transcription
 2. **Tacrolimus**
 - inhibits **FK506** → decreases IL-2 transcription
 - **Side-effects:**
 - T2DM
 - Hyperkalemia 2ry to Nephrotoxicity
- One other drug **decreases responsiveness** (NOT transcription) of IL-2
 1. **Sirolimus**
 - blocks **mTOR** → decreases RESPONSIVENESS of IL-2
 - **Side-effects:**
 - Dyslipidemia

Q36

A 76-year-old man comes to the physician because of a 2-week history of constant, intense pain of his right arm. There has been no trauma to the arm. Seven months ago, he had a cerebral infarction that resulted in lack of sensation on the right side of the body. Muscle strength and deep tendon reflexes are normal throughout. Sensation to light touch, vibration, pain, and temperature is decreased over the right side of the body. The most likely cause of this patient's pain is damage to which of the following regions of the nervous system?

- A. Left internal capsule
- B. Left postcentral gyrus
- C. Left thalamus
- D. Right internal capsule
- E. Right postcentral gyrus
- F. Right thalamus

▼ **Explanation**

- **Answer is C (Left thalamus)**
 - **IMP Clues**
 - Constant intense pain + hx of cerebral infarction (screaming post-infarction thalamic syndrome)

- No hx of trauma (exclude trauma)
- Normal strength & tendon reflexes (so no motor / LMNL component)
- Decreased right sided sensation (all of them)

- **Dx → Post-infarction Thalamic Syndrome**
 - **CONTRALATERAL PURE SENSORY AFFECTION**

 **VPL nucleus affection = Body**
VPM nucleus affection = Face

▼ Other Choices

- **Choices A & D** → would cause CONTRALATERAL *PURE MOTOR* AFFECTION (I think this is my 4th time reiterating this)
- **Choice B & E** → affection of the primary somatosensory cortex would cause similar sensory affections + would be limited to a certain distribution based on the affected segment (affected homunculus)
- **Choice F** → would cause Left sided symptoms

Q37

A 28-year-old man is brought to the emergency department 30 minutes after the sudden onset of shortness of breath. He has a 3-year history of cocaine abuse. His temperature is 38.1°C (100.6°F), pulse is 100/min, and blood pressure is 150/45 mm Hg. Physical examination shows diminished pulses in the left upper extremity. Crackles are heard over all lung fields. A grade 2/6 diastolic murmur is heard best at the left sternal border. A chest x-ray shows a widened aortic arch. Which of the following is the most likely diagnosis?

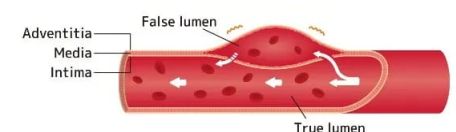
- A. Atherosclerotic aneurysm
- B. Dissecting aneurysm
- C. Mycotic aneurysm
- D. Pseudoaneurysm
- E. Saccular aneurysm

▼ Explanation

- **Answer is B (Dissecting aneurysm)**
 - **IMP Clues:**
 - Hx of cocaine abuse (a very HY cause of dissecting aneurysm)
 - Diminished pulse in left upper extremity (unequal pulses between limbs on USMLE is dissecting aortic aneurysm 3/4 times or subclavian steal syndrome 1/4 times)
 - Crackles in lung fields + Diastolic murmur (Acute Aortic Regurgitation 2ry to dissection spreading to valve)
 - Widened Aortic Arch

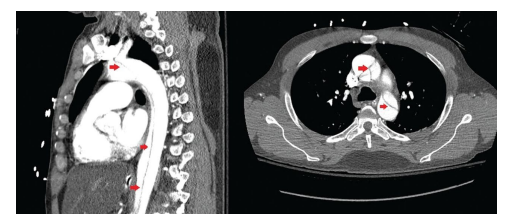
• Dx → Acute Aortic Dissection

- **Aortic Dissection is tear in the intimal layer of the aortic wall, causing blood to flow between → splitting apart the tunica media and intima, creating a "false lumen."**
- Most HY risk factor on the USMLE is → **Hypertension**.
 - Other HY risk factors include **cocaine (the cause here) & Connective Tissue Diseases (Marfan Syndrome & Ehlers-Danlos)**
- Presentations:
 - **Unequal blood pressure between both arms + diminished pulse** (blood pressure is **LOWER in affected arm**)
 - This differentiation is made on a Q on the NBMEs, where *Q has normal/high blood pressure in the right arm and low blood pressure in the left arm. The Q then asks what does the dissection spare/affect?*
 - In this example here, the **spared artery is the brachiocephalic trunk** (which gives the right subclavian artery), so blood pressure is normal/high
 - **Aortic Regurgitation** (if dissection extends to **Aortic Root/Valve**)



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

▼ **Answer**
Beta Blockers



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

▼ Other Choices

- **Choice A** → commonly affect abdominal aorta (specifically aorto-iliac portion) & depending on site can cause different signs & symptoms
 - Most commonly an older man with high BMI
 - Most commonly asymptomatic
- **Choice C** → infected aneurysm
 - A very important complication of IEC
- **Choice D** → aka false aneurysm, just a rupture in the intima & media of the vessel → blood contained by one/two layers (unlike a true aneurysm that is surrounded by all layers of the vessel)
- **Choice E** → aka berry aneurysms, usually found at circle of Willis & at bifurcations

Q38

A 14-year-old girl is brought to the physician for a follow-up examination. She has been regularly undergoing imaging and other studies for approximately 10 years because of a family history of early-onset cancers. Her older brother was diagnosed with a high-grade brain stem glioma at the age of 19 years. Her younger sister was diagnosed with a malignant choroid plexus tumor at the age of 2 years, and a paternal cousin was diagnosed with adrenocortical carcinoma at the age of 7 years. All three individuals have since died from their malignancies. A mutation in which of the following genes is the most likely cause of this family's predisposition to cancer?

- A. APC
- B. BRCA1
- C. RB1
- D. RET
- E. TP53

▼ Explanation

- **Answer is E (TP53)**
 - **IMP Clues:**
 - Family history of early-onset cancers (okay, genetic causes of malignancy)
 - Brother had high-grade glioma + sister had malignant choroid plexus tumor + cousin had adrenocortical carcinoma (these tumors must ring a bell)
 - **Dx → Li Fraumeni Syndrome**
 - **AD mutation in P53 (Tumor suppressor gene)**
 - Causing a wide variety of cancers, most commonly: **Sarcomas, Breast cancers, Leukemias, Adrenocortical tumors**
 - Other really common associated tumors are **glioblastomas, lung cancers, choroidal plexus tumors, and pancreatic tumors**

▼ Other Choices

- **Choice A** → **APC** on the USMLE is most commonly associated with **FAP**
- **Choice B** → **BRCA** mutations cause *recombinant dsDNA repair breaks* which most commonly causes **Breast Cancers**
- **Choice C** → **RB1** mutations cause **Retinoblastoma & Osteosarcomas**
- **Choice D** → **RET** is associated with **MEN2 syndromes & Papillary thyroid carcinoma**

Q39

A 63-year-old woman comes to the physician because of a 5-day history of shortness of breath and swollen legs. Her respirations are 25/min and labored, and blood pressure is 130/50 mm Hg. She has a large subclavian arteriovenous fistula caused by a stab wound to the left supraclavicular area 15 years ago. Physical examination shows 2+ edema of the lower extremities. Which of the following findings is most likely in this patient?

- A. Decreased arterial oxygen saturation
- B. Decreased mixed venous oxygen saturation
- C. Decreased stroke volume
- D. Increased resting cardiac output
- E. Increased systemic vascular resistance

▼ Explanation

• Answer is D (Increased Resting Cardiac Output)

◦ IMP Clues:

- Shortness of breath + Tachypnea + labored breathing (something affecting the lungs, Left side HF?)
- Swollen legs + 2+ edema (Right side HF?)
- Subclavian AV fistula (seals the deal)

◦ Dx → High-output HF

- Essentially what's happening here is there is increased demand by the body, **increased demand → increased CO**.
 - On the long run, **the maintained high output causes the heart to fail.**

• Causes of High-output HF:

◦ Arteriovenous Fistulas (MOST HY)

- AVF = capillaries bypassed → lower resistance → faster return to heart → volume overload → increase in SV → increase in CO

◦ Thyrotoxicosis

- Increased metabolic rate = increased demand

◦ Cirrhosis

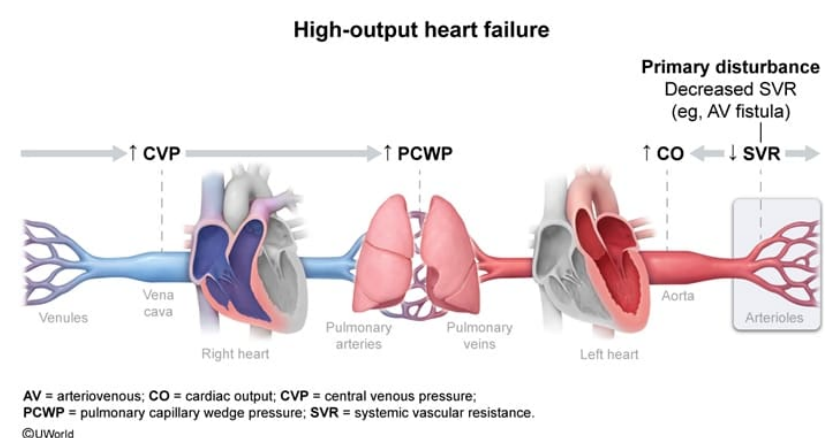
- Splanchnic VD → decreased VR + activation of RAAS → increase in blood volume & CO

◦ Sepsis

- Cytokines (like TNF- α mainly) → systemic VD → compensated by increase in CO
- Fever (caused by IL-1) → increases CO

◦ COPD associated with polycythemia

- chronic hypoxia → EPO production → thicker blood → decreased tissue delivery → compensatory increase in CO



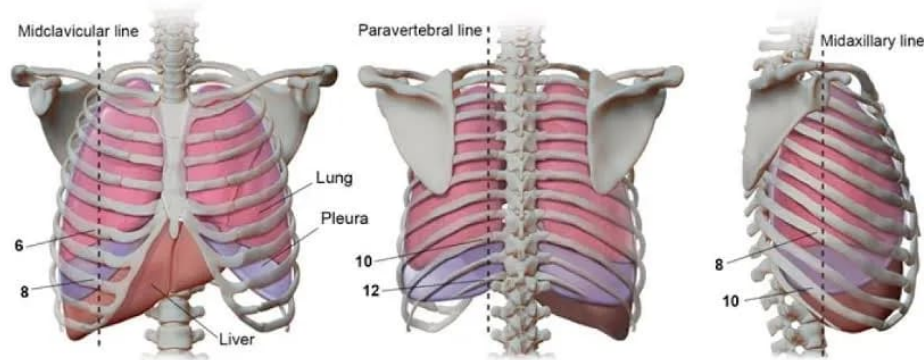
Q40

A 57-year-old woman is brought to the emergency department because of a 6-hour history of increasingly severe shortness of breath. Her temperature is 38.3°C (101.0°F), pulse is 80/min, respirations are 30/min, and blood pressure is 130/70 mm Hg. Pulse oximetry on room air shows an oxygen saturation of 90%. Physical examination shows decreased breath sounds and dullness to percussion on the right. A chest x-ray shows a large pleural effusion on the right. Thoracentesis is planned. With the patient in a seated position, it is most appropriate to position the needle in which of the following intercostal spaces in the midaxillary line?

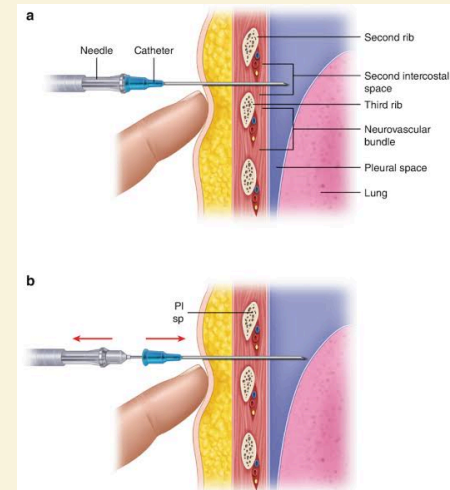
- A. First
- B. Third
- C. Fifth
- D. Seventh
- E. Ninth

▼ Explanation

- **Answer is E (Ninth)**
 - Okay so basically, and this is important for you to learn, thoracentesis sites are:
 - **Midclavicular line** → **6-8th** intercostal space
 - **Midaxillary line** → **8-10th** intercostal space
 - **Paravertebral line** → **10-12th** intercostal space



 **When going in for a thoracentesis always go ABOVE the rib, so that you don't injure the intercostal neurovascular bundle!**



Q41

A 30-year-old woman comes to the office for a follow-up examination. During the past 4 months, she has had a 9-kg (20-lb) weight loss after initiating a low-carbohydrate, low-fat diet. She has no history of major medical illness and takes no medications. She is 157 cm (5 ft 2 in) tall and now weighs 62 kg (138 lb); BMI is 26 kg/m². Her vital signs are within normal limits. Physical examination shows no abnormalities. It is most appropriate for the physician to counsel this patient to include which of the following in her current diet to maintain good nutrition?

- A. Linoleic acid
- B. Oleic acid
- C. Palmitic acid
- D. Palmitoleic acid
- E. Stearic acid

▼ **Explanation**

- **Answer is A (Linoleic acid)**
 - Q is very simple. Asks what should be added to her diet to maintain good nutrition. Well, you must add something that your body cannot make on its own.
 - **Linoleic Acid (Omega 6)** is an **essential** fatty acid.

 **What are the essential fatty acids?**

▼ **Answer**
Linoleic acid (Omega 6) & alpha-linoleic acid (Omega 3)

Q42

A 7-month-old boy is brought to the physician 2 days after his mother felt a lump in his groin while she was bathing him. Physical examination shows a normal-sized penis, but there are no palpable testicles within the scrotum. A hernia is palpated in the right external inguinal ring. Two days later, an operation is done in which the testes are brought down to the scrotum and the hernia is repaired. A fallopian tube and uterus are found within the hernial sac. Morphologic studies of a biopsy specimen of the testes show no abnormalities. Karyotype analysis is most likely to show which of the following in this patient?

- A. 45,X
- B. 46,XX
- C. 46,XY

D. 47,XXY

E. 47,XYY

▼ Explanation

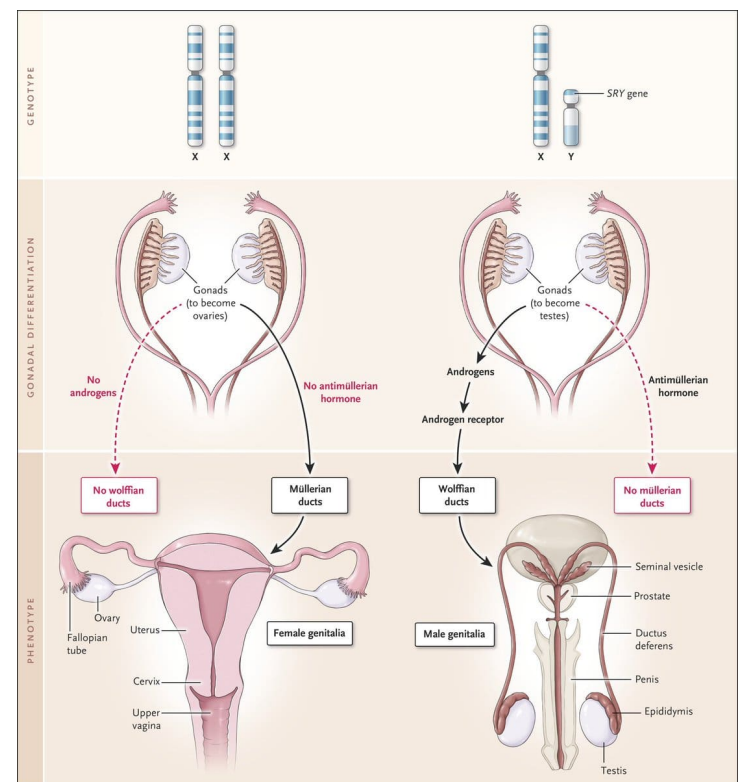
- **Answer is C (46, XY)**

- **IMP Clues:**

- Lump in his groin + no palpable testicles within the scrotum (probably undescended testes)
 - Normal-sized penis + biopsy of testes show no abnormalities (normal internal & external male genitalia)
 - A fallopian tube & uterus are found in the hernial sac (okay, so we have some sort of development issue here)

- **Dx → Persistent Mullerian Duct Syndrome**

- Look, basically what we have here is a **normal male (XY)** with **retained Mullerian duct**.
 - What normally happens, Fetus has **Y chromosome with SRY gene**, which stimulates development of **testes** → testes produce **Mullerian Inhibiting Factor (MIF)** which:
 - Inhibits the development **Mullerian duct** (which go on and form the *fallopian tubes & uterus*)
 - **Wolffian duct** develops via androgen from testes (which go on and form the *epididymis & vas deferens*)
 - In **Persistent Mullerian Duct Syndrome**, the MIF may not be secreted, or the receptors are malfunctioning. **So ⇒ normal male + mullerian duct**.



▼ Other Choices

- **Choice A → Turner Syndrome** - would have no testes or penis. You would find streak ovaries.
- **Choice B → Normal Female** - would have no testes or penis. Would have ovaries too.
- **Choice D → Klinefelter Syndrome** - Would have no fallopian tubes or ovaries. Would have normal testes and when he gets a little older, you'll start seeing the gynecomastia, the tall stature, and the infertility.
- **Choice E → You will never be testes on this, but this is just Jacob's Syndrome**

Q43

A 30-year-old man develops urinary incontinence 2 weeks after successful treatment of a fracture of the left pelvis that was sustained at work. He was pinned against a loading dock by a truck moving in reverse. Physical examination shows a distended bladder. Cystometrography shows absence of micturition reflexes. After the bladder fills to capacity, overflow of urine occurs through the urethra a few drops at a time. This patient most likely sustained additional injury to which of the following during his initial accident?

- A. External urinary sphincter
- B. Hypogastric nerve
- C. Pelvic nerves
- D. Pudendal nerves
- E. Skeletal motor fibers

▼ Explanation

- **Answer is C (Pelvic nerves)**

- **IMP Clues:**

- Urinary incontinence post fracture (incontinence)

- Distended bladder + absent reflexes + fills to capacity then overflows. (Overflow incontinence)

◦ **Dx → Overflow Incontinence**

- Okay so I need you to understand the following concepts:

- **Sympathetic control of bladder → Hypogastric nerve**

- **NO** urination via relaxation of bladder wall (detrusor muscle) & contraction of internal sphincter
- **Pathology here would cause → parasympathetic taking upper hand so always wanting to pee → Urge incontinence**

- **Parasympathetic control of bladder → Pelvic nerves**

- Urination via contraction of bladder wall (detrusor muscle) & relaxation of internal sphincter
- **Pathology here would cause → sympathetic taking upper hand so retention of urine**
 - **Retention of urine = bladder dilation = bladder fills up until pressure inside bladder greater than pressure of sphincter → few drops escape → Overflow incontinence**

- **Somatic Control (voluntary) → Pudendal nerve**

- Urination via relaxation of external sphincter
- **NO** urination via contraction of external sphincter
- **Loss of somatic control = loss of control of external sphincter → Incontinence**

▼ **Other Choices**

- **Choice A** → Would cause the patient to lose voluntary control of urine
- **Choice B** → Would cause Urge incontinence
- **Choice D** → Same as choice A + will cause fecal incontinence too
- **Choice E** → vague but can refer to the skeletal motor fibers of the sphincter which is the external sphincter so same as A

Q44

A 29-year-old woman comes to the physician because of a 10-day history of difficulty walking. Two years ago, she had loss of vision in the left eye, which improved during the next 2 months. Ophthalmologic examination shows decreased visual acuity in the left eye with pallor of the optic disc. There is past pointing on finger-nose testing. She also has a broad-based gait and spasticity. An MRI of the brain shows lesions in the white matter of the cerebellum. Treatment with which of the following agents is most likely to improve the spasticity in this patient?

- A. Atropine
- B. Baclofen
- C. Bethanechol
- D. Mecamylamine
- E. Pyridostigmine

▼ **Explanation**

- **Answer is B (Baclofen)**

- **IMP Clues:**

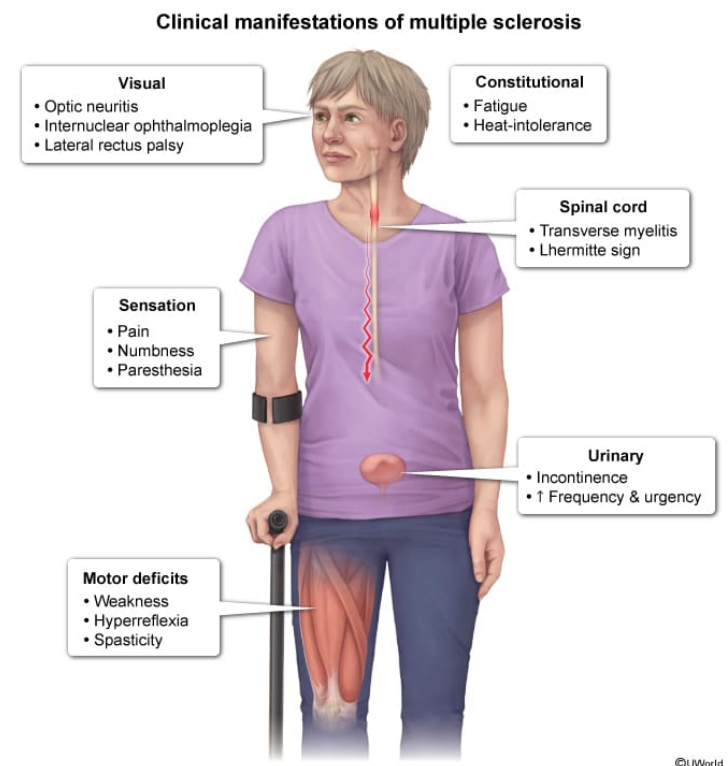
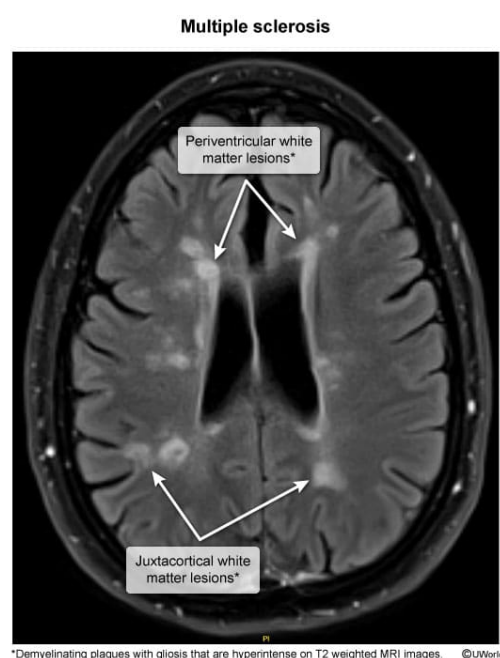
- 29y old Woman
- Loss of vision + decreased VA + pallor of optic disc (optic neuritis)
- Past-pointing on finger-nose test + broad based gait (cerebellum pathology)
- Spasticity (UMNL)
- White matter lesions in cerebellum on MRI (very evidently this is MS)

- **Dx → Multiple Sclerosis**

- Autoimmune disease characterized by **T-cells attacking oligodendrocytes & myelin basic protein → demyelination [asked on NBME]**
 - Periventricular Plaques or white matter lesions

- HY Findings:
 - **Optic neuritis** (present here)
 - Affection of Pons → **Trigeminal Neuralgia-like symptoms**
 - **Intranuclear Ophthalmoplegia**
 - On the USMLE, **Intranuclear Ophthalmoplegia = MULTIPLE SCLEROSIS**
 - Affection of MLF, causing ipsilateral loss of adduction in conjugate eye movement, adduction is still intact if eye is adducted alone
 - **Urge incontinence** [ttt → oxybutynin; M receptor antagonist]
 - **UMNL findings** → Babinski, clonus, spasticity
 - CSF shows **IgG oligoclonal bands**
 - MRI shows scattered upper motor (brain, cerebellum, spinal cord) white matter lesions

- Treatment:
 - **Acute Flares** → IV Steroids
 - **Between Flares** (to reduce recurrence) → INF-B
 - **Urge Incontinence** → Oxybutynin (Muscarinic antagonist)
 - **Spasticity** → Baclofen (GABA-B agonist)



! Multiple Sclerosis is easily confused with Neuromyelitis Optica (Devic Disease)

- Sounds like MS, however, USMLE will tell you:
 - **CSF oligoclonal bands** → **negative**
 - **Antibodies against aquaporin-4**

▼ Other Choices + HY Related Notes

- **Choice A → Atropine**
 - M receptor antagonist
 - Uses on the USMLE
 1. 1st Line ttt for **organophosphorus poisoning** (followed by pralidoxime)
 2. **Acetylcholinesterase inhibitors poisoning**
 - Toxicity (can resent as isolated atropine overdose or as **Jimson weed** overdose) causes anticholinergic syndrome (opposite of "**DUMBELS**," findings of cholinergic syndrome)
 - Constipation, Urine retention, Mydriasis, increase in HR, less bronchoconstriction, dry mouth, dry eyes, dry skin / red / hot
- **Choice C → Bethanechol** is a M receptor agonist used in **flaccid / neurogenic bladder**
- **Choice D** → no ideas what this is, probably a stupid distractor that I have never seen as the right answer
- **Choice E** → *Acetylcholinesterase inhibitor* used mainly in **ttt of Myasthenia Gravis**

Q45

A 28-year-old man is brought to the emergency department after being struck in the right eye by a baseball. He has diplopia, periorbital swelling, and enophthalmos. Upward gaze is impaired, and sensation is decreased over the right zygoma. X-rays of the face show fractures involving the orbital floor. These clinical findings are best explained by entrapment of which of the following muscles within the fracture?

- A. Inferior rectus and inferior oblique
- B. Lateral rectus and superior oblique
- C. Levator palpebrae and superior oblique
- D. Medial rectus and inferior oblique
- E. Superior rectus and superior oblique

▼ Explanation

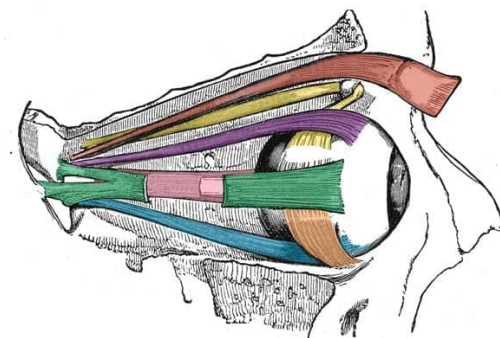
• Answer is A (Inferior Rectus & Inferior Oblique)

◦ IMP Clues:

- Struck in the right eye by a baseball (Eye Injury)
- Diplopia, periorbital swelling, and enophthalmos (Eye muscles are definitely injured)
- Upward gaze is impaired (Either muscles responsible for upward gaze are affected OR the eye is entrapped so cannot move)
- Sensation is decreased over right zygoma (Important clue that I will explain later)
- X-ray of the face show fracture involving the orbital floor (so structures on orbital floor are affected)

• Dx → Orbital Floor Fracture Entrapment

- **Blow-out fracture** (aka Orbital Floor Fracture) is one of the most common eye-injuries.
- What are the structures of the orbital floor?
 - **Inferior rectus muscle**
 - **Inferior oblique muscle**
 - **Infraorbital nerve** (remember the nerve that supplies area over right zygoma? This is it)
- So, injury of orbital floor would cause **entrapment of eye downwards, injury to rectus & inferior oblique muscles, and infraorbital nerve.**



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▼ Other Choices

- **Choice B → Lateral rectus** muscle is found on the lateral aspect of the orbital cavity. Not the floor.
- **Choice C → Superior oblique** muscle is found on the superior aspect of the orbital cavity, while the **levator palpebrae** is found in the eyelids.
- **Choice D → Medial rectus** muscle is found on the medial aspect of the orbital cavity.
- **Choice E → Superior rectus & superior oblique** muscles are found on the superior aspect of the orbital cavity.

Q46

A 44-year-old man is admitted to the hospital because of altered mental status. His blood pressure is 210/145 mm Hg. Funduscopic examination shows papilledema and retinal hemorrhages. Urinalysis shows 15-20 erythrocytes/hpf. A drug with which of the following effects on vascular smooth muscle is most likely to decrease his blood pressure?

- A. Decreasing activity of membrane K⁺ channels
- B. Decreasing cAMP
- C. Decreasing synthesis of nitric oxide
- D. Increasing activity of membrane Ca²⁺ channels
- E. Increasing cGMP
- F. Increasing release of Ca²⁺ from sarcoplasmic reticulum

▼ Explanation

- **Answer is E (Increasing cGMP)**
 - **IMP Clues:**
 - BP is 210/145 + altered mental status, papilledema. retinal hge, and hematuria (HTN Emergency → BP > 180/110 + end-organ damage)
 - Q asks what MOA of a drug would decrease his BP by acting on vascular smooth muscle?
 - Classically the ttt of Hypertensive emergency would be **Na Nitroprusside** (+ others)
 - Decrease BP = **Vasodilation** of vascular smooth muscle
 - Nitroprusside causes **VD by release of NO → activating guanylate cyclase → increase GTP conversion into cGMP → activation of protein kinase G**
→ myosin light chain **dephosphorylation** → relaxation

▼ Other Choices

- **Choice A** → decreasing activity of membrane K⁺ channels would slow down hyperpolarization → slow down relaxation
- **Choice B** → **cAMP** is irrelevant here. The drug the Q asks about doesn't use this pathway.
- **Choice C** → NO causes VD, so decreasing NO would cause less VD
- **Choices D & F** → increased Ca = increased contraction = VC

Q47

The FOXO transcription factor responds to insulin signaling by altering the transcription of several metabolic genes. FOXO can respond rapidly to changes in insulin signaling because it is reversibly modified. Which of the following best describes the reversible ways in which the insulin signaling regulates FOXO activity?

Choices	Nuclear/Cytoplasmic Shuttling	Serine Phosphorylation	Ubiquitin-mediated Proteolysis
A	Yes	Yes	Yes
B	Yes	Yes	No
C	Yes	No	Yes
D	Yes	No	No
E	No	Yes	Yes
F	No	Yes	No
G	No	No	Yes
H	No	No	No

▼ Explanation

- **Answer is B**
 - Okay, this Q looks scary & you have no idea what all of these words mean? Me too.
 - Let's work it out together.
 - Q asks how does insulin signaling regulate FOXO activity?
 - It says in the beginning that FOXO transcription factor responds to insulin by altering transcription of metabolic genes.
 - Okay so we know that essentially, **insulin is anabolic**
 - **Anabolic = more transcription** (aka more DNA → RNA → protein, "anabolism")
 - so, there would be **MORE** nuclear/cytoplasmic shuttling (referring to mRNA → protein)
 - so also know that insulin phosphorylates **ANABOLIC** enzymes (so Serine phosphorylation)
 - Anabolic = **less proteolysis**
 - So, answer should be:
 - **Nuclear/Cytoplasmic Shuttling → YES**
 - **Serine Phosphorylation → YES**
 - **Ubiquitin-mediated proteolysis → NO**

Q48

A 40-year-old African American woman comes to the physician because of a 2-week history of fever, malaise, and dyspnea. Her temperature is 36.7°C (98°F), and respirations are 20/min. Physical examination shows erythema nodosum, parotid enlargement, and hepatosplenomegaly. Her serum calcium concentration is 16 mg/dL. A CT scan of the chest shows bilateral hilar adenopathy. Serum studies are most likely to show an increased concentration of which of the following?

- A. Calcitonin
- B. Cholecalciferol
- C. 1,25-Dihydroxycholecalciferol
- D. 24,25-Dihydroxycholecalciferol
- E. Parathyroid hormone

▼ Explanation

- **Answer is C (1,25-Dihydroxycholecalciferol)**
 - **IMP Clues:**
 - African American (this is classic epidemiology for sarcoidosis)
 - Erythema Nodosum, parotid enlargement, and hepatosplenomegaly (classic associations)
 - Serum Calcium Concentration is 16mg/dl (associated hypercalcemia 2ry to hypervitaminosis D)
 - Bilateral Hilar Adenopathy (cannot be more evident, this is classic sarcoidosis)
 - **Dx → Sarcoidosis**
 - Sarcoidosis is associated with **hypercalcemia secondary to hypervitaminosis D**
 - Sarcoidosis **stimulates macrophages to release 1-alpha-hydroxylase**, which converts 25-OH-Vitamin D into 1,25-OH-Vitamin D.
 - Clinical Features of sarcoidosis include:

Use the mnemonic **"SARCOID LUNGS"**

- **S → Skin** (Erythema nodosum 'Panniculitis T4HS')
- **A → ACE** levels increased & **Arthritis**
- **R → Reticuloendothelial** system involvement (HSM & Adenopathy)
- **C → CD4/CD8 ratio increased (>2:1)**
- **O → Ophthalmic** affection (Uveitis)
- **I → Immune mediated non-caseating granulomas**
- **D → Hypervitaminosis D (hypercalcemia)**
- **LUNGS → Bilateral Hilar Lymphadenopathy & Lung Fibrosis**



What is the greatest risk factor in a patient for sarcoidosis?

▼ Answer
Ethnicity (African Americans)



Sarcoidosis cause **Restrictive** Lung Diseases PFTs!



Sarcoidosis is mainly treated with **corticosteroids**

Q49

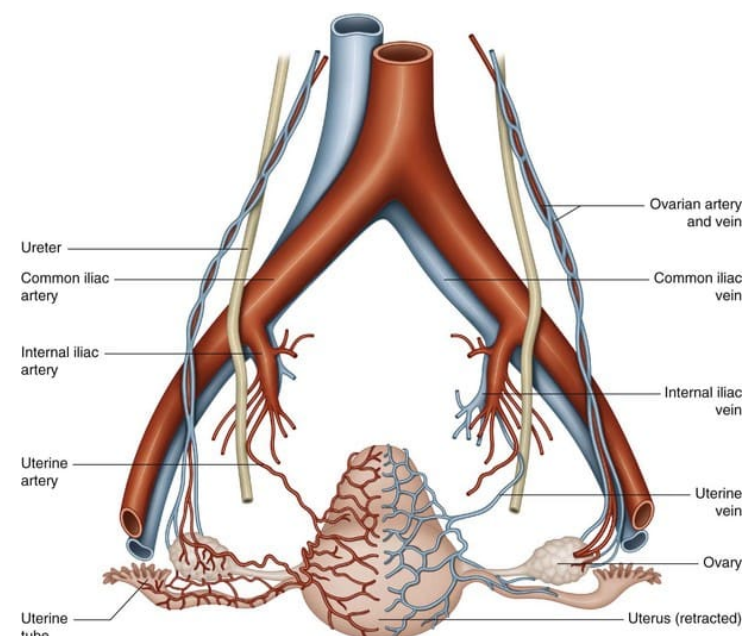
A 22-year-old woman, gravida 1, para 1, is brought to the emergency department because of a 2-day history of fever and severe vaginal bleeding. Four days ago, she delivered a healthy male newborn spontaneously at term. Her temperature is 38.1°C (100.6°F). Pelvic examination shows an open cervix and heavy vaginal bleeding. Ultrasonography of the uterus shows no retained placental tissue or large thrombi. If an operation is required to control the bleeding, ligation of a branch of which of the following arteries is most appropriate?

- A. External iliac
- B. Internal iliac
- C. Internal pudendal
- D. Median sacral
- E. Obturator

▼ Explanation

- **Answer is B (Internal Iliac Artery)**
 - Going into details of postpartum hemorrhage is for STEP 2. This question here tests simple STEP 1 anatomy, so don't complicate it.

- Bleeding uterus & asks what vessel would control the bleeding?
 - **Uterine Artery.**
- Uterine Artery is a branch of **Internal Iliac artery**. Simple.



Q50

An 11-year-old boy has had persistent pain in his right knee since he twisted it in a soccer game 3 weeks ago. Physical examination shows a tender area in the distal femur but no perceptible mass. An x-ray of the femur shows an osteolytic mass that has eroded through the cortex and elevated the periosteum; the mass is surrounded by reactive bone in some areas. Biopsy of the mass shows atypical cells with hyperchromatic pleomorphic nuclei. The cells are surrounded by an eosinophilic matrix, some of which is calcified. This tumor is most likely to spread first to which of the following areas?

- A. Brain
- B. Cervical lymph nodes
- C. Liver
- D. Lung
- E. Vertebrae

▼ Explanation

• Answer is D (Lung)

◦ IMP Clues:

- Persistent pain (persistent pain = bad)
- X-ray shows osteolytic mass + elevated periosteum (okay, now we know what's going on, this is a bone tumor → osteolytic mass in distal femur (mostly metaphysis) + elevated periosteum (just means Codman triangle)
- Surrounded by reactive bone (referring to sunburst pattern)
- Biopsy shows atypical cells with hyperchromatic pleomorphic nuclei (tumor, duh)
- Eosinophilic matrix which is calcified

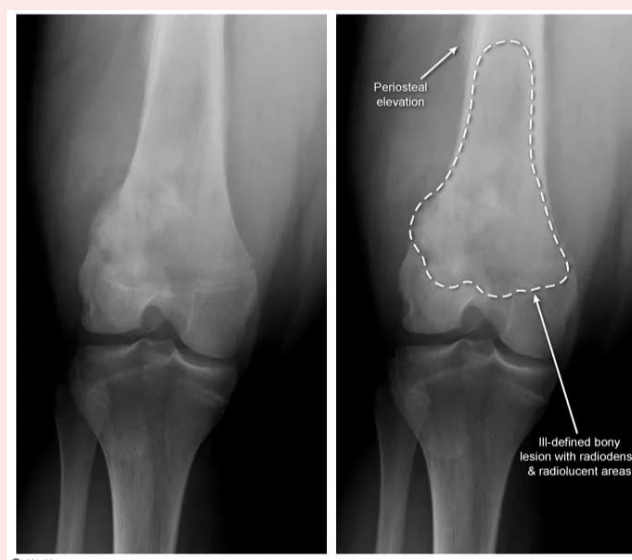
• Dx → Osteosarcoma of bone

- Site → **Metaphysis**
- X-ray → **Osteolytic (moth eaten mass) + Codman triangle & sunburst pattern**
- Biopsy → **Osteoblasts & Osteoid & Woven bone**
- Associated with:
 - **Retinoblastoma (RB1 mutation)**
 - **Li-Fraumeni Syndrome (TP53 mutation)**

• Now Q asks, where would this tumor spread to first?

- **Sarcoma = Blood spread**
 - **Leg → blood (venous) → Lung (Choice D)**

The X-Rays are actually HY, and you being able to recognize the "Codman Triangle" and "Sunburst Pattern" is actually important:

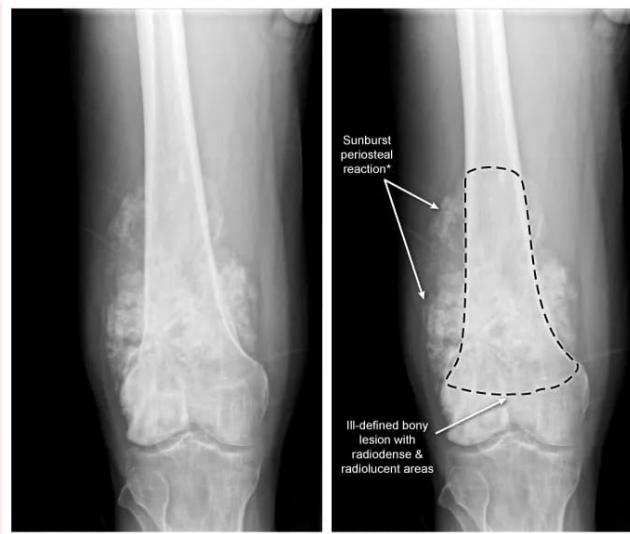


*** The Periosteal Elevation above is another name for "Codman Triangle."



Remember that carcinomas prefer lymphatic spread

- **EXCEPTIONS ARE PRESENT** for example the HY ones are:
 - **Choriocarcinoma** → Blood
 - **Follicular Thyroid Carcinoma** → Blood



▼ Other Choices

- **Choice A** → HY tumors that love spreading to the brain are lung cancer & choriocarcinoma
 - Lesions would be at → grey-white junction
- **Choice B** → Head & Neck SCC LOVE cervical lymph nodes
- **Choice C** → Famously CRC spreads there early. Any GI tumor eventually spreads to the liver due to portal circulation
- **Choice E** → Learn these like your name: Breast, Lung, Prostate. (Super HY)



CHORIOCARCINOMA

- Carcinomas usually prefer Lymphatic spread
 - 2 HY exceptions are: **Choriocarcinoma & Follicular Thyroid Carcinoma**
- Choriocarcinoma LOVES Brain & Lung spread
 - You get a Q on the USMLE where you have a gynecological patient with seizures / pulmonary nodules ⇒ THINK OF CHORIOCARCINOMA



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