



NBME EXPLANATIONS

NBME 22 Block 2

from CrackNBME

22-Block 2

Q1

A 9-year-old boy is brought to the physician by his mother because of a 1-year history of cough productive of mucoid sputum, wheezing, and shortness of breath with exertion. He has a history of recurrent upper respiratory tract and sinus infections since birth. He is at the 25th percentile for height and weight. The mother says that his younger sibling is beginning to develop similar problems. Physical examination shows mild clubbing of the fingers. Laboratory studies show markedly increased sweat chloride and sodium concentrations. A defect of which of the following in this patient's bronchial epithelium is most likely causing these symptoms?

- A. Adrenoreceptors
- B. Membrane receptors
- C. Nuclear receptors
- D. Protein regulation
- E. Protein structure

▼ Explanation

• Answer is E (Protein Structure)

◦ IMP Clues:

- History of recurrent respiratory tract & sinus infection since birth + younger sibling is beginning to develop similar problems (some sort of congenital / hereditary defect)
- Cough productive of mucoid sputum + wheezing + SOB on exertion + clubbing (pulmonology etiology causing chronic hypoxia)
- Increased sweat chloride & sodium concentration (seals the deal, this is CF)

• Dx → Cystic Fibrosis

- **AR** disorder; Classically caused by a **deletion ($\Delta F508$; deletion of phenylalanine)** in the **CFTR** gene on **Chromosome 7**
- **Misfolded CFTR channels** (these are proteins, which are misfolded so defected protein structure) **retained in the Golgi**.

◦ How does the CFTR channels normally work?

▪ CFTR channels in **sweat glands**

- Chloride ions (negative ion) are **reabsorbed into the cell** from the lumen of the gland.
- Sodium ions (positive ion) **follow the Chloride ions into the cells** to balance the charge
- **Water follow Sodium in**, causing the secretions to be **less salty**

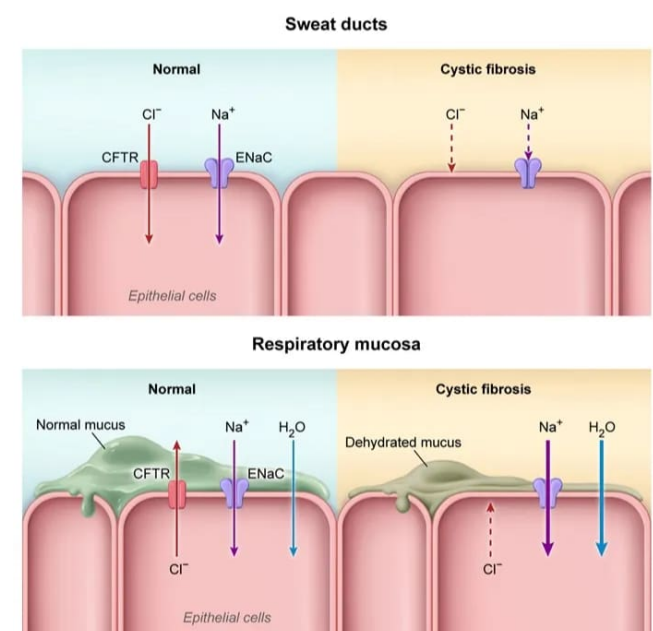
▪ CFTR channels **everywhere else (pancreas, lungs, reproductive system, GI)**

- Chloride ions (negative ion) are **pushed out from the cell** into the lumen of the gland.
- Sodium ions (positive ion) **follow the Chloride ions out into the lumen** to balance the charge
- **Water follow Sodium out**, causing the secretions to be **thin, and the walls to be lubricated**

◦ What happens in CF?

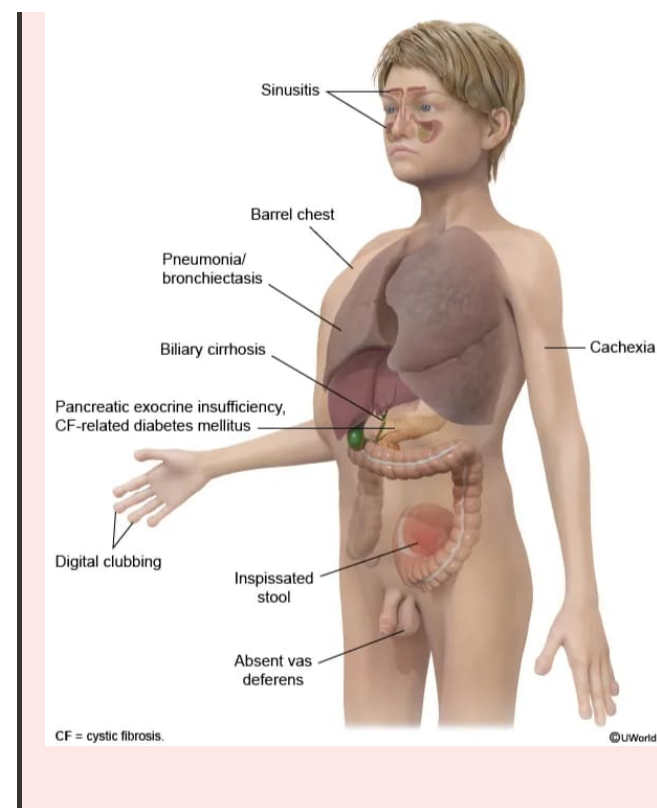
- CFTR channels are **dysfunctional**, so what happens normally doesn't:
- CFTR channels in **sweat glands**
 - Chloride ions (negative ion) **CANNOT BE reabsorbed into the cell** from the lumen of the gland.
 - Sodium ions (positive ion) **CANNOT follow the Chloride ions into the cells** to balance the charge
 - **Water DOESN'T follow Sodium in**, causing the secretions to be **MORE SALTY**.
 - This is the basis of Diagnosis → **Increased Chloride Sweat test**
 - **Increased Chloride in sweat due to inability of CFTR channels to reabsorb Cl into the cell**

 **Cystic Fibrosis is a HY example of Heterogeneity**



Picture below shows complications of Cystic Fibrosis:

- CFTR channels **everywhere else (pancreas, lungs, reproductive system, GI)**
 - Chloride ions (negative ion) **CANNOT** be pushed out from the cell into the lumen of the gland.
 - Sodium ions (positive ion) **CANNOT** follow the Chloride ions out into the lumen to balance the charge
 - **Water DOESN'T follow Sodium out**, causing the secretions to be THICK & IMPACTED
 - This is the basis of **C/P & Complications**
 - **Thick impacted secretions in the PANCREAS**
 1. Pancreatitis
 2. Pancreatic Enzymes insufficiency
 - a. Malabsorption
 - b. Fat-Soluble Vitamins Deficiencies
 - i. Vitamin K → Bleeding Tendency
 - ii. **Vitamin E → Ataxia, Hemolysis, Peripheral neuropathy, Muscle weakness [HY AS FUCKKKK]**
 - iii. Vitamin D → Ricket's & Osteomalacia
 - iv. Vitamin A → Retinitis Pigmentosa, Corneal Ulcers, Night Blindness, Bitot Spots... you get it
- **Thick impacted secretions in the Lungs**
 - Cilia cannot work & push-out debris/infection
 1. Recurrent Sinusitis & Respiratory Tract Infections
 2. Chronic productive cough & SOB & Clubbing
 3. Nasal Polyps & Bronchiectasis
- **Thick impacted secretions in the Reproductive System**
 - Infertility
 - **Congenitally Bilateral Absence of Vas Deferens**
- **Thick impacted secretions in the GI**
 - **Meconium Ileus** (failure of newborn to pass meconium within first 24 hours is highly associated with CF)



Don't forget that regarding RTIs, Staph aureus is the **MOST COMMON** if age less than 20 years, while Pseudomonas **MOST COMMON** if age > 20 years

Q2

A 25-year-old woman is admitted to the hospital because of septic shock. She underwent splenectomy 6 months ago after she sustained traumatic injury during a motor vehicle collision. Her temperature is 39.4°C (103°F), and blood pressure is 80/40 mm Hg. Coarse tubular breath sounds are heard bilaterally, and egophony is heard at the right base. A chest x-ray shows bilateral pulmonary opacities, dense consolidation at the base of the right lung, and a possible right-sided effusion. Which of the following is the most likely causal organism?

- Actinomyces israelii
- Bacillus anthracis
- Klebsiella pneumoniae
- Pseudomonas aeruginosa
- Streptococcus pneumoniae

▼ Explanation

- **Answer is E (Streptococcus pneumoniae)**
 - **IMP Clues:**
 - Septic Shock + 39.4C + BP 80/40 mmHg (she's septic, probably infection)
 - Underwent splenectomy 6 months ago (This is our keyword)
 - Tubular breathing + egophony + CXR shows opacities + consolidation + effusion (fucked up lungs)

- **Dx → OPSI (Overwhelming Post-Splenectomy Infection)**
 - People who undergo **splenectomy (either elective - emergency - or even auto splenectomy in sickle cell anemia patients)** are at risk of something called **OPSI "Overwhelming Post-Splenectomy Infection"**.
 - This patient here had **emergency splenectomy after MVA**, so she should have been *vaccinated & she must be prescribed prophylactic antibiotics*
 - Otherwise, she is at **massive risk of developing sepsis → DIC → Death**
 - The Infection is caused by **encapsulated organisms**.
 - Most Commonly ***Streptococcus pneumoniae***
 - Other common ones include *H.influenza*, *N.meningitides*, and *E.coli*.

Why Post-splenectomy & Why Encapsulated Organisms?

- Normally, **encapsulated pathogens** are opsonized with antibodies and then ***phagocytosed by specialized macrophages in the spleen.***
- **Individuals with asplenia** lack these specialized macrophages, so ***pathogens are able to spread and cause sepsis.***



If you find *Streptococcus pneumoniae* & another encapsulated organism in an OPSI Question, always choose ***Streptococcus pneumoniae*** as it is the MOST COMMON

Q3

A 54-year-old man has an aneurysm in the distal portion of his abdominal aorta. The estimated cross-sectional area of the aneurysm is 2 cm² and the mean velocity of blood flow through the aneurysm is 20 cm/sec. Which of the following best represents the flow rate (in L/min) through the aneurysm?

- A. 1.0
- B. 2.4
- C. 3.2
- D. 3.6
- E. 4.0

▼ Explanation

- **Answer is B (2.4)**
 - Q asks about **Flow Rate**
 - ***Flow Rate = Cross-sectional Area x Velocity***
 - 2 cm x 20cm/sec = 40cm/sec
 - However, he asks for flow in **L/min**. so we need to change the cm → L (x1000) & sec → min (x60)
 - ***(2cmx1000) x (20cm/sec x 60) = 2.4L/min (Choice B)***

Q4

A 66-year-old man develops worsening shortness of breath and swelling of the legs. He had a myocardial infarction 6 months ago. Pulse is 120/min, and blood pressure is 135/82 mm Hg. Examination shows distended jugular veins, bilateral crackles, and pitting edema in the lower extremities. Serum sodium concentration is 129 mEq/L. Which of the following is most likely responsible for the hyponatremia in this patient?

- A. Dilution of serum sodium due to ADH (vasopressin) secretion
- B. Increased urinary sodium excretion due to renal tubular dysfunction
- C. Increased urinary sodium excretion due to secretion of aldosterone
- D. Increased urinary sodium excretion due to secretion of atrial natriuretic peptide
- E. Restriction of dietary sodium intake

▼ Explanation

- **Answer is A (Dilution of serum sodium due to ADH secretion)**
 - **IMP Clues:**
 - SOB + Swelling of the legs / edema + JVD + Bilateral crackles (Lungs + systemic affection = Right + Left HF = Congestive HF)
 - Had a MI 6 months ago (important risk factor for HF)
 - Sodium concentration is 129 (decreased/diluted Na concentration; this means the body is reabsorbing water)
 - Q asks what is responsible for the hyponatremia?

The Effects of RAAS:

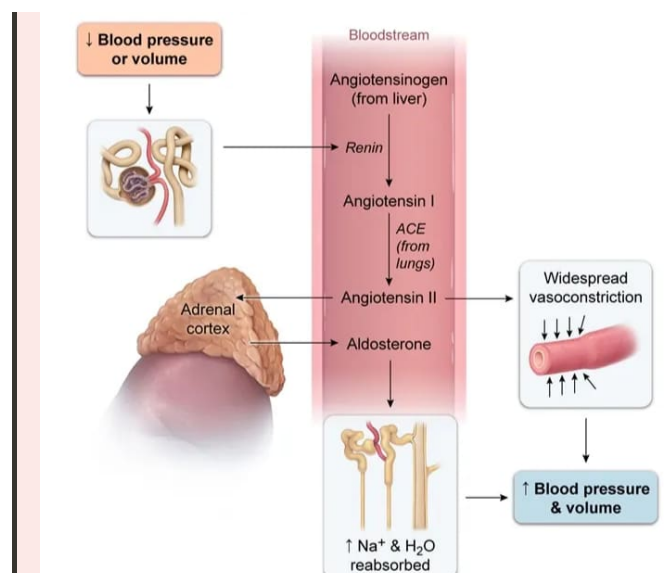
o **Patient has Congestive Heart Failure:**

- **Right Side HF** → Blood stays in systemic circulation & heart can't fill up
 - This causes **JVD & Edema**
- **Left Side HF** → Blood clogs up the lung & heart can't pump blood
 - This causes **Pulmonary edema & decreased COP**
- **The decreased Cardiac Output = Decreased Renal Flow & Decreased Effective plasma volume**
 - **Decreased Renal Flow** ⇒ Activation of **RAAS**
 - **AT-2** → VC of arterioles → increased BP
 - **Aldosterone** → reabsorption of Na & Water retention
 - **Decreased Effective Plasma Volume** ⇒ Release of **ADH**
 - **ADH** causes massive water retention
- **Net Effect of all of that:**
 - **Increased BP**
 - **Some Na reabsorption**
 - **MASSIVE water retention (which then dilutes the Na)** → Hyponatremia (Choice A)

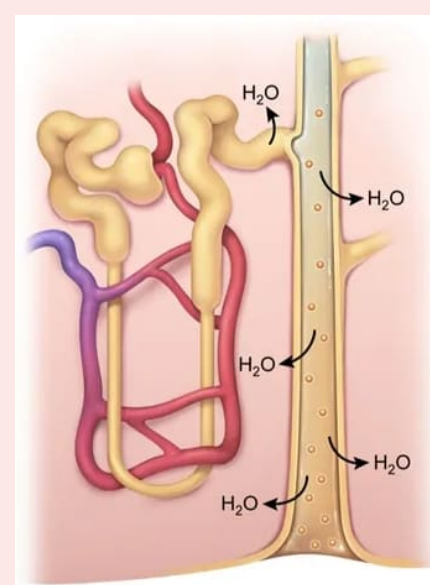


ADH Rapid Review:

Synthesized in: **Supraoptic** nucleus of the hypothalamus
 Stored in: **Posterior** Pituitary
 Action: Binds to **Vasopressin-2 (V2) Receptors** in the **collecting ducts**, causing an **increase in cAMP**, resulting in translocation of **aquaporin-2** water channels to the apical membrane.
 Result: **Increases water permeability**, causing **free water reabsorption**.



The Effects of ADH:



▼ **Other Choices**

- **Choice B** → Increased urinary sodium excretion would cause the water to follow it, this would cause **features of hypovolemia**. Here, we have **HYPERVOLEMIA** (leg edema, JVD, pulmonary edema)
- **Choice C** → Aldosterone causes sodium **reabsorption not excretion**
- **Choice D** → ANP does actually cause natriuresis, however, its effects are **negligible**
- **Choice E** → Nothing in the vignette says his intake was restricted.

Q5

A 30-year-old man comes to the physician because of a 2-day history of blood in his urine, dull flank pain, and voiding large amounts of urine. The patient states that his father died of an unknown kidney disease. His blood pressure is 150/100 mm Hg. Physical examination shows bilateral renal masses. Laboratory studies show proteinuria and gross hematuria. A CT scan of the abdomen shows cystic masses in each of the kidneys; the right mass is larger than the left. A right nephrectomy is done; the surgical specimen is shown. The underlying defect most likely involves which of the following molecules?



- A. Desmocollin-1a
- B. E-cadherin
- C. Laminin receptor
- D. P-selectin
- E. Polycystin

▼ Explanation

- Answer is E (Polycystin)
 - IMP Clues:
 - 30-year-old man (old man)
 - blood in urine + dull flank pain + voiding large amounts of urine (dull pain excludes out stones;)
 - Father died of unknown kidney disease (Hereditary disorder)
 - Blood pressure is 150/100mmHg (Kidneys affected to 2ry HTN)
 - Bilateral Renal masses + Cystic masses in each kidney + pic shows specimen (Cystic Kidneys)

- Dx → Autosomal Dominant Polycystic Kidney Disease (ADPKD)
 - AD condition, caused by mutation of *PKD1 gene* on **chromosome 16**
 - [For Nerds] 15% of cases of ADPKD are caused by a mutation in *PKD2 gene* on **chromosome 4**
 - Affects **Adults**
 - Presentation: **Kidneys grow cysts which compress renal vasculature → RAAS activation → Hypertension**
 - Associated: **Saccular Aneurysm & Hepatic/Pancreatic cysts**
 - **Saccular Aneurysms can cause Subarachnoid Hemorrhage**
 - Q asks about affected protein name, well you can just infer that **polycystin** is the protein affected in polycystic kidney disease, right?



ADPKD vs ARPKD

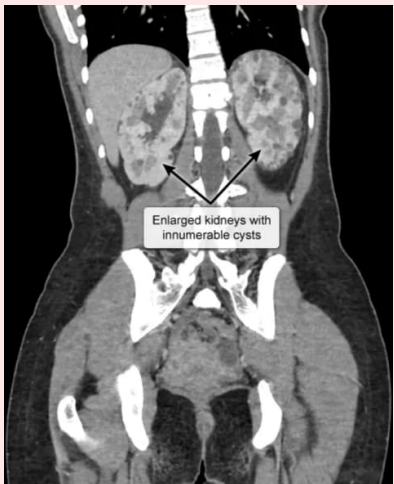
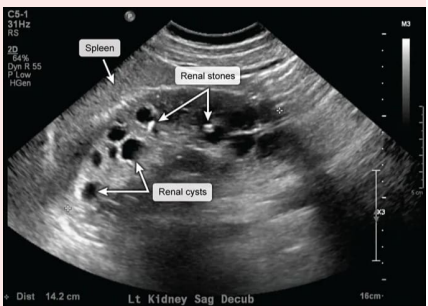
Feature	ARPKD	ADPKD
Age at Presentation	Pediatrics	Adults
Transmission & Chromosome	Autosomal recessive; Chromosome 6	Autosomal dominant; Chromosome 16
Associated Symptoms	Hepatic fibrosis	HTN, Hepatic cysts, Saccular (berry) aneurysms of the circle of Willis

HY Pictures of ADPKD:

Gross Pathology:



Imaging:



▼ Other Choices

- Choice A → “Desmo” means it is related to Desmosomes, which bind epithelial cells to each other
- Choice B → E-cadherin is a calcium-dependent protein that also binds cells together

- **Choice C** → Laminin sounds like Lamina so related to basement membranes
- **Choice D** → P-selectin is involved in leukocytes adhesion & rolling

Q6

A 60-year-old woman comes to the physician because of a 2-month history of shortness of breath and cough and a 2-week history of progressive swelling of her face. The cough is productive of approximately 1/4 cup of mildly blood-tinged, white-to-yellow sputum daily. She has had a 2.3-kg (5-lb) weight loss over the past 4 months. She has a 15-year history of hypertension treated with enalapril. She has smoked 1 pack of cigarettes daily for 45 years. Her pulse is 90/min and regular, respirations are 20/min, and blood pressure is 135/90 mm Hg. Physical examination shows edema of the face and neck and jugular venous distention. Breath sounds are mildly decreased throughout all lung fields, and there are no cardiac murmurs. Her serum sodium concentration is 125 mEq/L. Which of the following is the most likely underlying cause of this patient's facial edema?

- A. Angioedema
- B. Hyperthyroidism
- C. Hyponatremia
- D. Hypoparathyroidism
- E. Lung cancer

▼ **Explanation**

• **Answer is E (Lung Cancer)**

◦ **IMP Clues:**

- SOB + productive blood-tinged, white-to-yellow sputum cough + weight loss + Smoker (Major risk factors/ presentation for lung cancer)
- Progressive swelling of her face + edema of face & neck + JVD + breath sounds are decreased all over lung fields (Compression of mediastinum, notably SVC & main bronchus)
- Sodium concentration is 125 (hyponatremia; lung cancer + hyponatremia = SCLC)

• **Dx → SVC Syndrome due to compression of SCLC**

◦ What is SVC Syndrome?

- **Obstruction OR Compression of the SVC**
- **Presents as:**
 - Progressive Facial Swelling +/- Upper Limb Swelling
 - JVD
 - Engorged face, neck, and UL veins.

◦ What is Small Cell Lung Cancer (SCLC)?

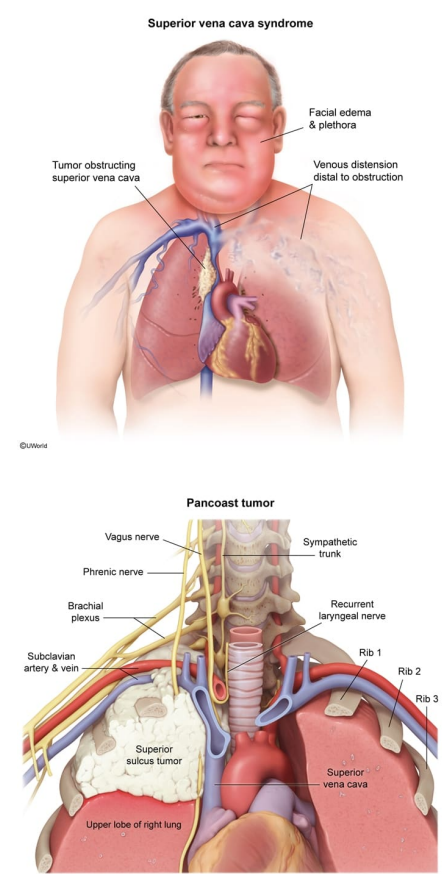
- **Neuroendocrine tumor** of the lung derived from **Kulchitsky cells**
- **Central mass** that most commonly affects **smokers**.
- **Biopsy:** "round cells with little cytoplasm that are twice the size of lymphocytes" is a description used on NBME, "small blue round cells" can also be found
- **Associated paraneoplastic syndromes are:**
 - **SIADH** → **Ectopic ADH secretion** → **hyponatremia (what we have here)**
 - **Cushing's syndrome** → **Ectopic ACTH secretion**
 - **Lambert-Eaton Syndrome** → antibodies against *presynaptic voltage-gated calcium channels*
 - **Neurological Syndromes** → *anti-Hu/Yo*

◦ How can Lung cancers cause SVC Syndrome?

1. Compression of the SVC by a **Pancoast Tumor** (more common in **NSCLC**, **peripheral** tumors)
2. Compression of **Mediastinum** (more common in **SCLC**, **central** tumors)

• Having put all of these things together, I'd look at the presentation:

- **SVC Syndrome** (Progressive swelling of her face + edema of face & neck + JVD + breath sounds are decreased all over lung fields)
- **Lung cancer symptoms** (SOB + productive blood-tinged, white-to-yellow sputum cough + weight loss)



- **Well, Smoker + hyponatremia ⇒ Small-Cell Lung Cancer, which is a central mass**
 - So, this is probably **mediastinal compression**, NOT a Pancoast tumor

▼ Other Choices

- **Choice A** → Angioedema would be recurrent acute attacks of facial swelling + inability to breath +/- pruritic & urticaria. Why would there be hyponatremia or purulent sputum or weight loss?
- **Choice B** → Hyperthyroidism presents as palpitations, nervousness, hypertension, weight loss. No facial swelling or cough or hyponatremia
- **Choice C** → Hyponatremia alone would cause seizures & delirium. Not all of these symptoms
- **Choice D** → Hypoparathyroidism on the USMLE presents either as
 - **Congenital** → **DiGeorge Syndrome**
 - **Acquired** → post-thyroidectomy, the surgeon removed the parathyroid gland accidentally
 - Both would cause **hypocalcemia** & its associated symptoms
 - Seizures
 - Paresthesia & Tingling peri-oral & on extremities
 - Muscle weakness & cramps
 - QT prolongation & Arrhythmias
 - Chvostek & trousseau sign

? What are the Genetics & Features of DiGeorge Syndrome?

▼ Answer

22q11 deletion - this causes failure of **3rd & 4th pharyngeal pouches** to develop

- 3rd pouch → inferior parathyroid glands & Thymus gland
- 4th pouch → superior parathyroid glands

Features of DiGeorge Syndrome

"CATCH22"

- **C** → **C**ongenital Heart Anomalies (TOF, usually on the USMLE)
- **A** → **A**bnormal Facies
- **T** → **T**hymic aplasia (Immunodeficiency of T-cells)
- **C** → **C**left Palate
- **H** → **H**ypocalcemia

Q7

A 57-year-old woman comes to the physician because of episodes of burning, shock-like pain on the left side of her face during the past 4 months. She has several episodes each day, usually caused by chewing. The pain lasts from 5 to 10 seconds. Neurologic examination shows no abnormalities. Which of the following is the most likely diagnosis?

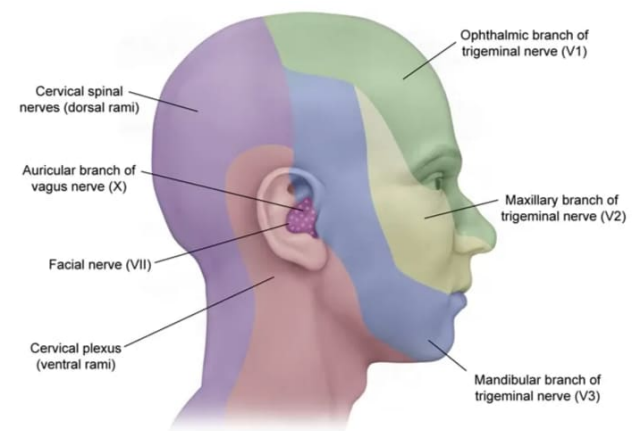
- A. Cluster headache
- B. Migraine
- C. Multiple sclerosis
- D. Temporal arteritis
- E. Trigeminal neuralgia

▼ Explanation

- **Answer is E (Trigeminal Neuralgia)**
 - **IMP Clues:**
 - Burning, shock-like pain on the left side of her face caused by Chewing (DD is MS, Trigeminal neuralgia)
 - Pain lasts from 5-10 seconds (again, MS & Trigeminal Neuralgia can present like this)
 - Neurological Examination shows no abnormalities (this here excludes MS)

- **Dx → Trigeminal Neuralgia**

- Unilateral *Stabbing stitching pain*
 - **Precipitated by stimulation of affected segment** (for example, brushing teeth = cheek pain)
 - Seconds in duration
- Location depends on the affected division of trigeminal nerve
 - **V1 = Ophthalmic + Forehead distribution**
 - **V2 = Maxillary distribution (Most Common)**
 - **V3 = Mandibular distribution**
- Treatment is **carbamazepine** (anti-epileptic that can be used for tonic-clonic seizures & Trigeminal Neuralgia)



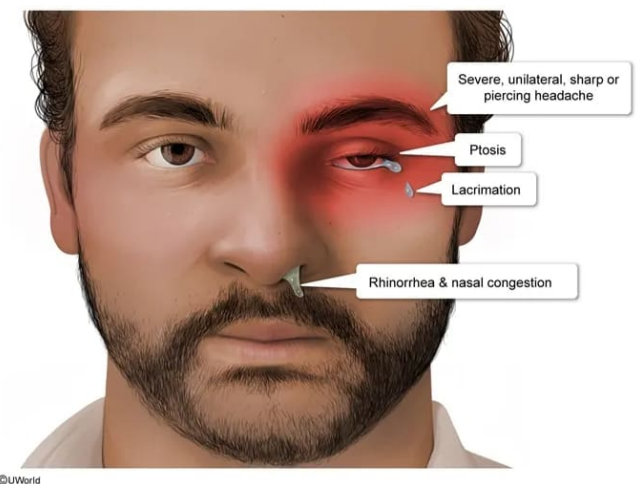
Trigeminal Neuralgia is a very common presentation of Multiple Sclerosis

- USMLE often give you a case of **MS + trigeminal neuralgia** & asks where the pathology is → **PONS**
 - They usually don't give any nerves in the choices
 - But we know that Trigeminal nerve originates from pons. Makes sense.

▼ **Other Choices**

- **Choice A → Cluster Headache**

- Unilateral *Periorbital pain*
- Associated **autonomic manifestations (lacrimation - stuffiness - miosis) [characteristic]**
- mins to hours in duration
- Treatment is **100% Oxygen (Most Effective) or Triptans (Serotonin Agonist)**
- Prophylaxis is **Verapamil**
 - **NOT Beta Blockers [asked on NBME]**



- **Choice B → Migraines**

- Unilateral *Pulsating pain*
- Associated with **"auras" (attacks of visual / sensory manifestations before or after the migraine), nausea, photophobia, or phonophobia**
- Hours to days
- Treatment is **NSAIDs then Triptans, or Ergots**
- Prophylaxis is **Beta Blockers**



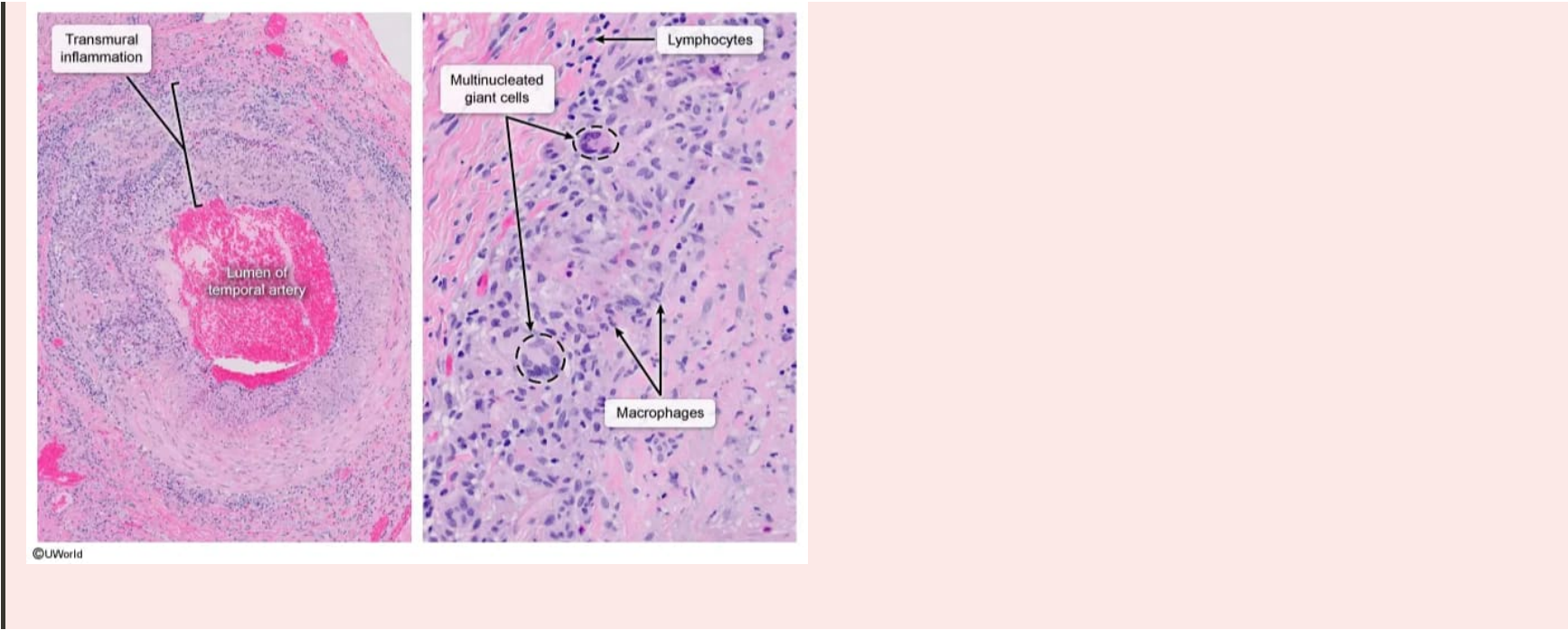
- **Choice C → Multiple Sclerosis**

- There are no neurological symptoms, so this excludes MS, Let's review MS:

- **Choice D → Temporal Arteritis**

- Presents as **temporal headache + intermittent jaw pain +/- proximal muscle pain [Polymyalgia Rheumatica] (NOT WEAKNESS)**
 - Headache is usually **dull aching** not sharp stabbing in character
- How to confirm diagnosis → **ELEVATED ESR**
- FIRST INTERVENTION → **STEROIDS (to prevent blindness)**
- THEN → Biopsy

Granulomatous Transmural Inflammation with multinucleated giant cells & lymphocytes



Q8

A 42-year-old man comes to the physician because of a 1-month history of fatigue, excessive thirst, and frequent urination with large volume. He is 178 cm (5 ft 10 in) tall and weighs 61 kg (135 lb); BMI is 19 kg/m2. His pulse is 96/min, and blood pressure is 104/60 mm Hg. Physical examination shows dehydration. Fasting laboratory studies show:

Serum	
Glucose	normal
ADH (vasopressin)	increased
Osmolality	increased
Urine osmolality	decreased

In addition to a low-sodium diet, which of the following drugs is the most appropriate treatment for this patient?

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

▼ Explanation

- Answer is D (Hydrochlorothiazide)
 - IMP Clues:
 - Excessive thirst, and frequent urination + Dehydrated (okay so electrolytes all messed up)
 - Increased Serum ADH & Increased Serum Osmolality (Doesn't make sense because increased ADH = increased water reabsorption = less osmolality, so something is not right)
 - Urine Osmolality decreased (also doesn't make sense as ADH should increase urine osmolality)
 - Dx → Nephrogenic DI
 - Basically, the patient can synthesize ADH, however, his kidneys don't respond to the ADH.
 - What does ADH normally do?
 - Increases free water absorption in CD by inserting aquaporin channels.
 - This causes urine to have a higher osmolality (less water & more solutes)
 - This also causes the serum to have a lower osmolality (more water & less solutes)
 - What happens in Nephrogenic DI (the opposite)?
 - Despite high ADH levels, water is not reabsorbed from the CD.
 - This causes increased free water in urine → excessive urination & lower osmolality (more water & less solutes)
 - This also causes the serum to have a high osmolality (more solutes & less water) → hypernatremia → Excessive Thirst.
 - Treatment
 - Salt Restriction + Thiazide Diuretic + NSAIDs

- **Hydrochlorothiazide (Choice D)** is a thiazide diuretic

▼ Other Choices

- **Choice A** → Used in *high altitude sickness*. Can also be used as eyedrops for *glaucoma*
- **Choice B** → Used for **Central DI**
 - The problem here is that the **hypothalamus stops producing ADH**. The kidneys are fine. Labs would be exactly the same, but the **ADH levels would be low**
 - Caused by: **Head trauma, Meningitis, Cancer**
 - Treatment: **Replacement (Desmopressin)**
- **Choice C** → Loop diuretic that is used for *fluid overload*
- **Choice E** → Added to loop for hypokalemia prevention, also can be used in *Hyperaldosteronism*.

Q9

A 1-year-old boy is found to have an impairment of the respiratory burst of phagocytes. He has a family history of immunodeficiency. This patient is at greatest risk for infection caused by which of the following organisms?

- A. Enterococcus faecium
- B. Escherichia coli
- C. Haemophilus influenzae
- D. Staphylococcus aureus
- E. Streptococcus pneumoniae
- F. Streptococcus pyogenes (group A)

▼ Explanation

- **Answer is D (Staphylococcus aureus)**
 - Patient has *impairment of respiratory burst* of phagocytes
- **What is a Respiratory Burst?**
 - Phagocytes (Macrophages & Neutrophils) phagocyte bacteria.
 - In phagosomes, "*the burst*" occurs as **NADPH Oxidase** facilitates the conversion of NADPH into **Superoxide (ROS)**, which is used to kill the bacteria
 - **Deficiency of NADPH Oxidase → Chronic Granulomatous Diseases**
 - Superoxide is then converted into H₂O₂ (Hydrogen Peroxide) by Superoxide Dismutase
 - **H₂O₂** then converted into **HOCl (hypochloric Acid, or bleach)** by **Myeloperoxidase (MPO)**, which is a potent bactericidal substance
 - **Deficiency of MPO ⇒ MPO Deficiency**



Chronic Granulomatous Disease Rapid Review:

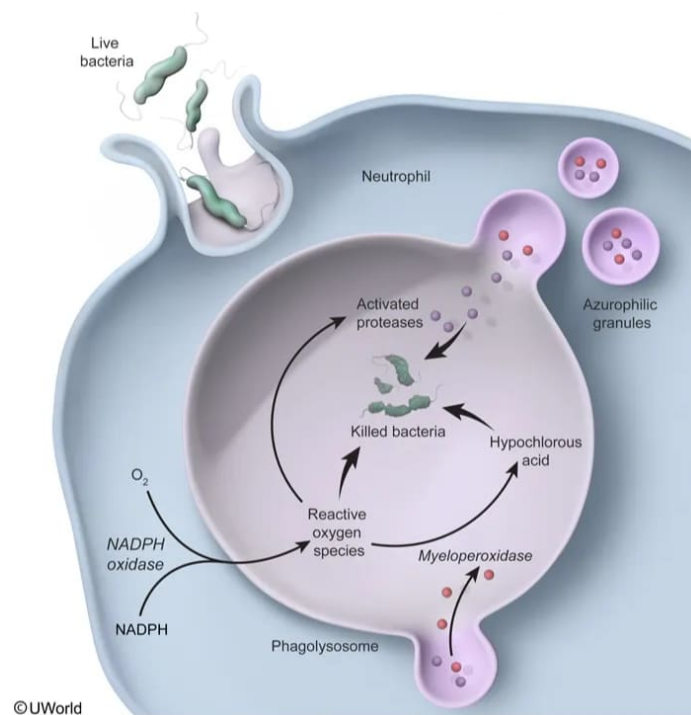
Deficiency: **NADPH Oxidase**

- They can't make Superoxide, so they use the bacteria's own superoxide to form H₂O₂ & then into MPO → kill the organisms
- However, **Catalase positive organisms neutralize their own superoxide**, as a result, the phagocytes can't use the superoxide → can't form H₂O₂ & MPO → Can't kill the organisms.

Catalase-Positive Organisms: "**LC-SHAPES**"

- Listeria
- Candida
- **Sta^{ph}yl^ococcus Aureus (most common & most HY)**
- H. pylori
- Aspergillus & Actinomyces
- Pseudomonas
- E.coli
- Serratia

Diagnosis: Dihydrorhodamine (DHR) Test OR Nitroblue Tetrazolium (NBT) Test



- We have both E.coli & staph aureus in the answer choices and both are catalase positive organism, but if we had to choose, **we'd choose the commonest → Staph Aureus (Choice D)**

Q10

A 13-year-old girl is brought to the physician by her mother for a routine well-child examination. Neither the child nor the mother has any particular health concerns. The patient is doing well in school and participates in soccer and lacrosse in a local recreation league. The physician wants to ask the patient about sexuality and sexual activity. Which of the following actions by the physician is most appropriate?

- Ask the mother to leave the room before asking the patient any questions
- Ask the patient to leave the room and then ask the mother about her daughter
- Ask the questions with both the mother and the patient present
- Give the patient a questionnaire that she can fill out at home
- Tell the patient that some sensitive questions are next and that only she can ask her mother to leave the room

▼ Explanation

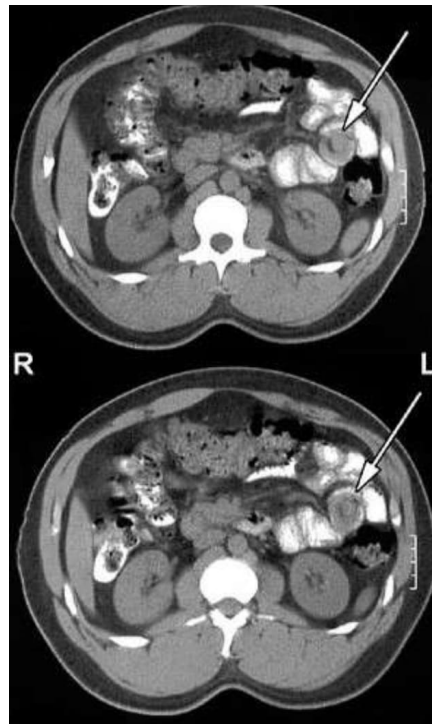
- **Answer is A**
 - **Sex & Drugs** are 2 very hot topics for teenagers.
 - As a doctor, you must explore their **safety, concerns, and explain to them what they need to know for their own benefit**.
 - These topics, however, are *sensitive*, making discussing them in front of parents *uncomfortable* for the children.
 - **Best way is to ask the parents to exit the room, for you and the patient to talk freely without being intimidated by their parents. (Choice A)**

▼ Other Choices

- **Choice B** → What will you gain? You need to talk to the patient. She's old enough now.
- **Choice C** → This would make the patient uncomfortable
- **Choice D** → Not effective, and again, you need to TALK to your patient
- **Choice E** → This puts pressure on the patient, and she may refuse to make her mom leave because she's scared. YOU (the doctor, hopefully) MUST ask the mother to leave.

Q11

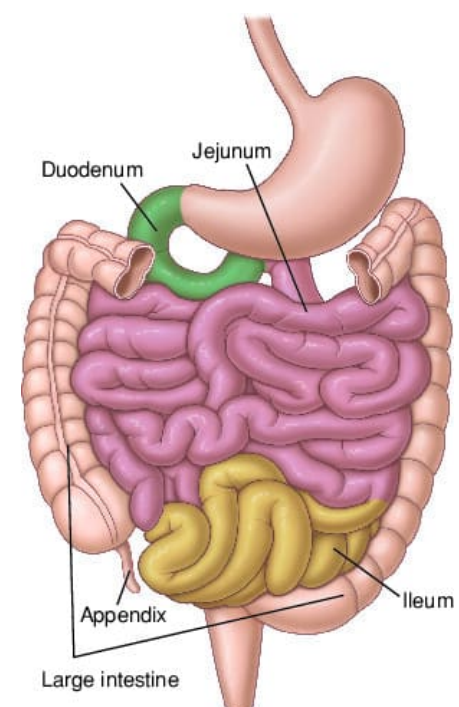
A 28-year-old man comes to the emergency department because of a 6-hour history of cramping and severe left midabdominal pain. He had a single episode of vomiting. His temperature is 37°C (98.6°F). Abdominal examination shows a mass in the mid-abdomen. A CT scan of the abdomen with contrast is shown; the abnormality is indicated by the arrows. Intussusception of which of the following portions of the intestinal tract is the most likely cause of this patient's pain?



- A. Appendix
- B. Cecum
- C. Duodenum
- D. Jejunum
- E. Stomach

▼ Explanation

- **Answer is D (Jejunum)**
 - Patient has intussusception + CT is given with an arrow pointing to the site.
 - It's on the left side, so **not** appendix (A) or cecum (B) or duodenum (C).
 - You can't see the liver, so **not** stomach (E) as they are on the same level
 - Most people easily exclude everything except Duodenum & Jejunum, so to help you differentiate, you must know **that duodenum is on the right side, while the jejunum is on the left side**
 - Picture below shows site of duodenum vs jejunum, so the correct answer is **Jejunum (D)**

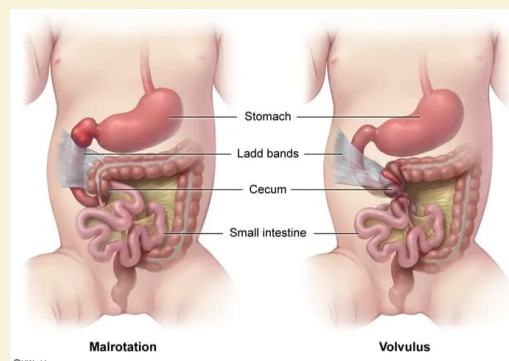


? What if you see the jejunum on the right?

▼ Answer

Midgut Malrotation

- Presents as a **neonate with bilious vomiting & abdominal distention +/- hematochezia**
- Caused by Incomplete Rotation, resulting in:
 - **Duodenojejunal Flexure + Jejunal Loops on the **RIGHT** (instead of the left)**
 - Twisting of intestines (+ presence of Ladd Band's) on SMA ⇒ SMA Syndrome



Q12

An Rh-negative woman, gravida 3, para 2, has had an increasing bilirubin concentration in amniotic fluid obtained between 22 and 29 weeks' gestation. Umbilical cord blood obtained at 29 weeks' gestation had a hematocrit of 6.2%. Transfusion of which of the following types of packed red cells to the fetus in utero should be used to correct the anemia?

- A. A, Rh-negative
- B. A, Rh-positive
- C. AB, Rh-negative

- D. AB, Rh-positive
- E. B, Rh-negative
- F. B, Rh-positive
- G. O, Rh-negative
- H. O, Rh-positive

▼ **Explanation**

• **Answer is G (O, Rh-negative)**

◦ **IMP Clues:**

- Rh-negative woman + para 2 (She's Rh negative so she can only take Rh negative + para 2, means she already may have Rh+ antibodies due to contact of baby blood with hers)
- Umbilical cord blood had Hct of 6.2% (in immediate need of transfusion to save the baby)

◦ Okay what we have here is probably an Rh reaction.

- Mother is **Rh negative**.
- When she had her first 2 babies, she most likely had a Rh-positive child.
- During delivery some baby's blood mix with maternal blood, causing the mother to make Rh antibodies.
- The next time she gets pregnant, Rh antibodies pass the placenta and attack the fetus's RBCs, causing hemolysis

◦ If we are going to give a blood transfusion, we need to worry about 2 things

1. **Rh status:** The mother is *negative*, so we must give **Rh-negative**.
 - If we don't, the mother's antibodies will attack the transfused blood
2. **Blood Type:** No information was given regarding any of the baby's or mother's blood type, so if we had to guess, we would go with the **universal donor (Type O)**.

◦ So best answer is **O (Rh) negative**

Q13

A 35-year-old woman has weakness and fever. When she was 25 years old, she was treated for Hodgkin disease with mechlorethamine, oncovin, procarbazine, and prednisone. She has had a splenectomy. There is no evidence of lymphadenopathy. A peripheral blood smear shows numerous blast forms. Which of the following is the most likely explanation for these findings?

- A. Acute lymphocytic leukemia
- B. Acute myelocytic leukemia
- C. Chronic lymphocytic leukemia
- D. Lymphoma
- E. Recurrence of Hodgkin disease

▼ **Explanation**

• **Answer is B (AML)**

◦ **IMP Clues:**

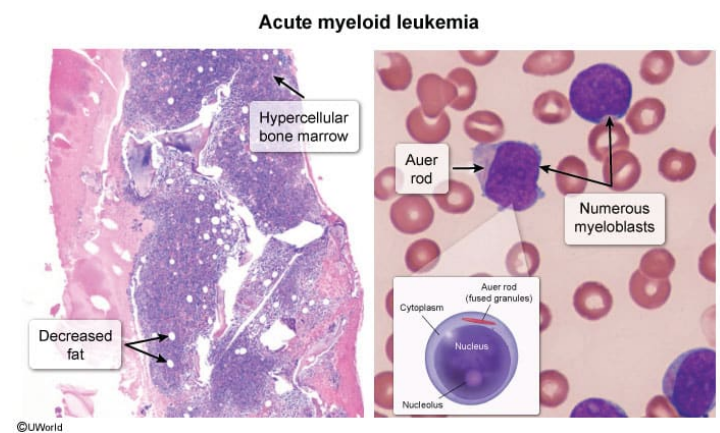
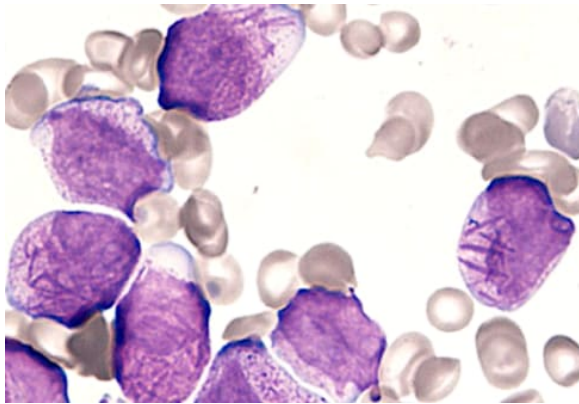
- When she was 25 years old, she was treated for Hodgkin Disease with... (Lymphoma treatment is usually with cytotoxic drugs, which increases risk of leukemia)
- There is no evidence of lymphadenopathy (Excludes lymphoma)
- Peripheral blood smear shows numerous blast forms (basically this is AML)

- **Dx → Acute Myeloid Leukemia (AML)**

- **Adult** with **lots of myeloid blasts**
- Smear shows **Auer rods**, composed of **myeloperoxidase**

Auer rods can be liberated during ttt of AML (leukemic cell lysis) & cause DIC

- Smear used on NBMEs:



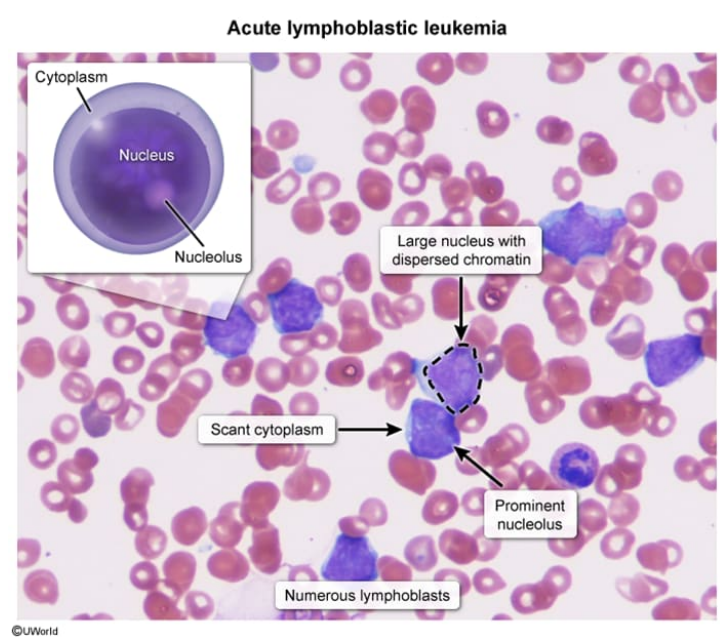
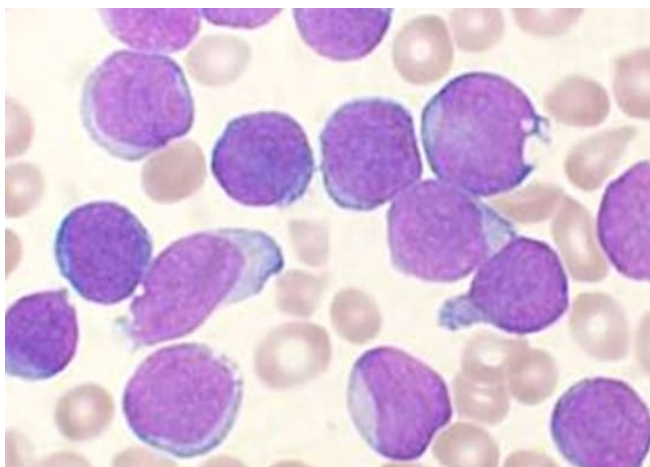
Acute Promyelocytic Leukemia "APL"

- AML type 3 is caused by a **t(15:17) translocation** that can be treated with Vitamin A
 - **Vitamin A causes maturation of blasts into mature granulocytes [asked on NBME]**

▼ Other Choices

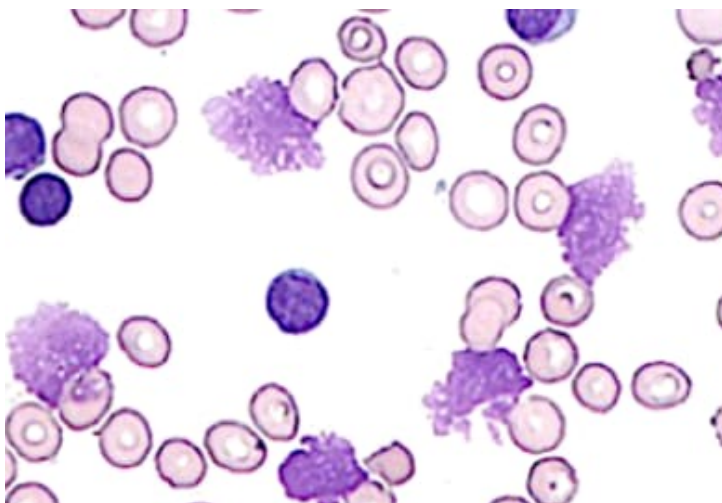
- **Choice A → Acute Lymphoid Leukemia (ALL)**

- **Kid** with **super high WBCs (lymphocytes)**
- Increased risk with **Down Syndrome**
- Markers: **CD10 & TdT positive**
- Smear used on NBMEs:

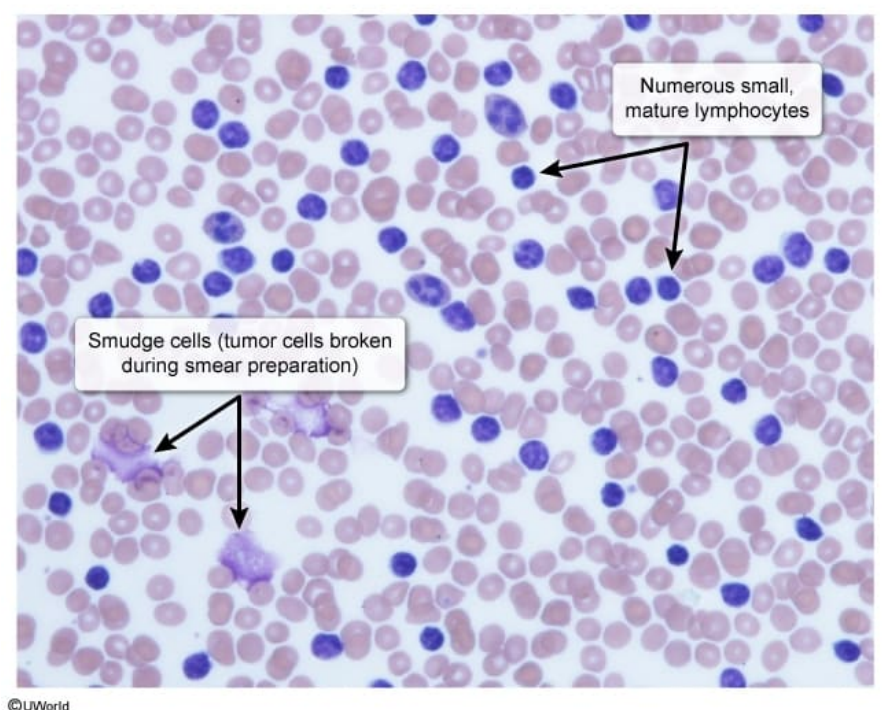


- **Choice C → Chronic Lymphoid Leukemia (CLL)**

- Usually **Elderly** with **super high WBCs (lymphocytes)**
- Markers: **CD5 & CD23**
- Associated with **Warm AHA (IgG against RBCs)**
- Smear shown on NBMEs showing smudge cells:



Chronic lymphocytic leukemia



- **Choice D & E → Hodgkin** is a lymphoma, so automatically these 2 equal one, so both can be excluded. Also, the no lymphadenopathy kinda makes lymphoma unlikely.

Q14

During an experiment, a 22-year-old man receives an infusion of histamine in his left brachial artery. Which of the following sets of microcirculatory changes will most likely occur in his left arm?

Choices	Arteriolar Resistance	Capillary Hydrostatic Pressure	Capillary Filtration Rate
A	↑	↑	↑
B	↑	↑	↓
C	↑	↓	↓
D	↑	↓	↑
E	↓	↑	↓
F	↓	↑	↑
G	↓	↓	↓
H	↓	↓	↑

▼ Explanation

- Answer is F
 - Patient received an infusion of **histamine**.
 - What does histamine cause?
 - **Vasodilation → Decreased Arteriolar Resistance** → *more blood flow* → **higher capillary hydrostatic pressure** → **higher filtration rate** [This is the basis of how histamine causes increased vascular permeability]
 - So, what's the answer?
 - **Choice F**
 - **Decreased Arteriolar Resistance**
 - **Increased Capillary Hydrostatic Pressure**
 - **Increased Capillary Filtration Rate**

Q15

A 25-year-old woman comes to the physician because of easy bruising and bleeding from her gums over the past 2 days. She has been otherwise healthy and has never had abnormal bleeding. Laboratory studies show:

Hemoglobin	13.2 g/dL
Hematocrit	39.6%
Leukocyte count	7000/mm ³
Platelet count	6000/mm ³
Prothrombin time	14 sec (INR=1.2)
Partial thromboplastin time	30 sec

Which of the following is the most likely cause of these findings?

- A. Disseminated intravascular coagulation
- B. Hypersplenism
- C. Immune thrombocytopenic purpura
- D. Iron deficiency
- E. Vitamin C deficiency
- F. von Willebrand disease

▼ Explanation

- Answer is C (Immune Thrombocytopenic Purpura)
 - IMP Clues:
 - Easy bruising and bleeding from gums for past 2 days (bleeding disorder)
 - Never had abnormal bleeding (this excludes congenital disorders like F)
 - Platelet Count 6000 (VERY decreased, normal is between 150,000-450,000)
 - PT & PTT normal (this excludes a clotting disorder, either extrinsic or intrinsic)
 - Dx → Immune Thrombocytopenic Purpura (ITP)

- Antibodies against **Glycoproteins 2b/3a on PLTs (Type 2 Hypersensitivity)**
 - GP 2b/3a** are responsible for PLT **aggregation**
 - GP 1b** is responsible for PLT **adhesion**
- Splenic macrophages **engulf platelets with antibodies**
 - Destroyed PLTs → Isolated decrease in platelet count & increase in Bleeding Time**
 - Clotting Factors not affected → No Change** in PT or PTT
- Precipitated by **Viral infections - post-pregnancy - or even idiopathically**
 - "Most vignettes on the USMLE will be either a female with random bruising and low PLTs or increased BT and no / subtle risk factors present OR a child who had a cough / cold then developed petechia or bruises or epistaxis (some kind of bleeding)"
- Recurr in the presence of an accessory spleen
 - Now if an **accessory spleen is present** and the patient gets an **ITP attack** again, the **tagged platelets will now be destroyed by the accessory spleen.**
 - Causing the above symptoms ⇒ **Thrombocytopenia** (with normal PT and PTT) and **Petechiae**.



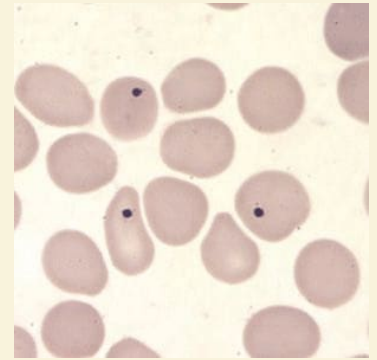
As a result of antibody-coated platelets clearance by splenic macrophages, the decreased platelet count is compensated by an **increase in megakaryocytes in bone marrow.**



Howell-Jolly Bodies:

Howell-Jolly Bodies are **nuclear remnants removed by the spleen.**

- Howell-Jolly bodies are expected to be seen on peripheral smear post-splenectomy.



▼ Other Choices

- Choice A** → DIC would have *Low* platelets, *increased* PT, and *increase* PTT.
- Choice B** → Hypersplenism would cause *Low* platelets and *Anemia*
- Choice D** → IDA would cause *anemia*. *Platelets shouldn't be involved.*
- Choice E** → All labs would be *normal*.
- Choice F** → Von Willebrand disease classically will have *NORMAL* Platelet count as the defect is in **PLT FUNCTION NOT COUNT**. **Factor VIII** will also be affected, so **PTT is expected to be increased** as well.

Q16

An 11-year-old boy has had pain in his right mid-thigh for 2 weeks. Physical examination shows an area of warmth and tenderness around an ill-defined mass. X-ray of the femur shows a solitary mid-diaphyseal osteolytic lesion with permeative margins. The lesion is surrounded by concentric layers of reactive bone. Tissue obtained on biopsy of the mass is composed of poorly differentiated sheets of small, uniform, hyperchromatic cells with a very high nuclear:cytoplasmic ratio, scant stroma, and no visible matrix. Which of the following is the most likely diagnosis?

- A. Chondrosarcoma
- B. Eosinophilic granuloma
- C. Ewing sarcoma
- D. Multiple myeloma
- E. Nephroblastoma (Wilms tumor)
- F. Osteosarcoma
- G. Small lymphocytic lymphoma

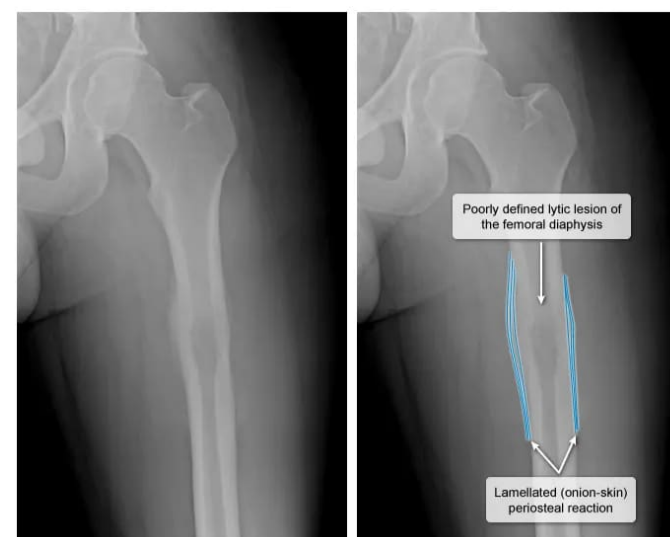
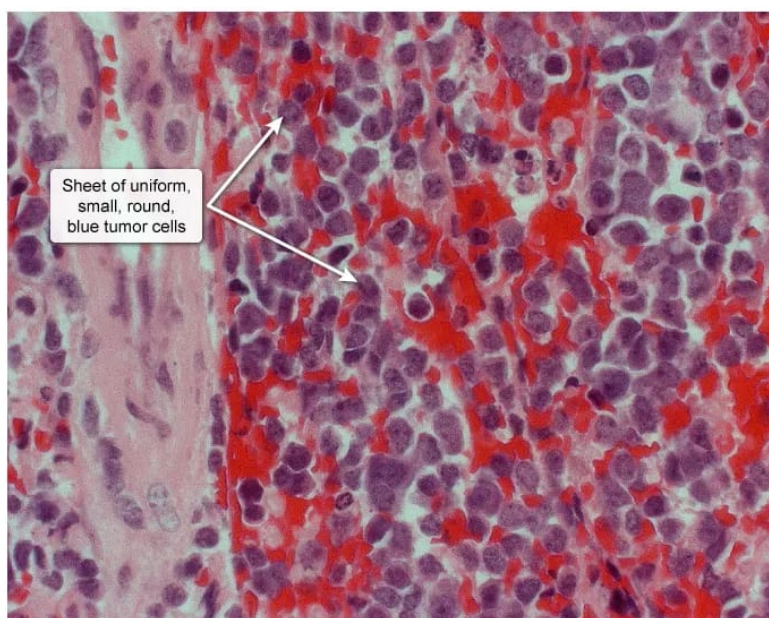
▼ Explanation

- Answer is C (Ewing Sarcoma)**
 - IMP Clues**
 - 11- year-old boy (pediatric)
 - Mid-diaphysis (site is important for exclusion & diagnosis)
 - Osteolytic lesion + surrounded by concentric layers of reactive bone (reactive bone is periosteum so basically osteolytic lesion + concentric periosteum, sounds familiar right?)

- Poorly differentiated sheets of small uniform hyperchromatic cells with high nuclear: cytoplasmic ratio, scant stroma, and no visible matrix (Biopsy findings are characteristic, HY, and repeated on NBMEs so memorize it)

• **Dx → Ewing Sarcoma**

- Origin → **Neuroectodermal cells**
- Epidemiology → **Pediatrics** tumor
- Associated with **t(11:22) → overexpression of EWS-FLI1**
- Site → **Diaphysis**
- XRAY → **Osteolytic lesions + Onion-skin periosteal reaction** (remember the concentric reactive bone?, yah this is the onion skin)
- Biopsy → **Small blue (hyperchromatic cells with high nuclear: cytoplasmic ratio) cells**



▼ **Other Choices**

- **Choices A & F** → Look at below image

BONE TUMORS

Giant Cell Tumor

- * @ the epiphysis (e.g., distal femur).
- * X-ray: Multicystic osteolytic lesions.. (Soap-bubble appearance).
- * Multinucleated giant cells. * RANKL.
- * Risk of malignant transformation.
- * TTT: Surgical resection.

Osteochondroma

- * Most common primary benign bone tumor.
- * Bony protrusion with a cartilaginous cap.
- * Usually asymptomatic. * @metaphysis.
- * X-Ray: Pedunculated or sessile lesion.
- * Rarely progresses to chondrosarcoma.
- * TTT: * Observation if asymptomatic.
- * Resection if symptomatic.

Osteoid Osteoma

- * < 2 cm. * @ diaphysis of long bones.
- * Central nidus produces prostaglandins.
- * Pain relieved by NSAIDs.
- * X-ray: Round lesion + radiolucent nidus.
- * TTT: * NSAIDs if tolerable.
- * Excision if refractory.

Osteosarcoma

- * M/c malignant bone tumor.
- * Bimodal: 10-20 yrs, >65 yrs.
- * M/c @ metaphysis (around the knee).
- * Associated with: Retinoblastoma.
- * X-ray: Sunburst pattern, Codman triangles.
- * Follow positive x-ray by MRI before biopsy.
- * Biopsy: Osteoblasts + osteoid/woven bone.
- * Labs: High ALP, LDH, ESR.
- * TTT: * Surgical resection + Chemo. * usually, radioresistant.

Ewing Sarcoma

- * Arising from neuroectodermal cells.
- * 2nd m/c pediatric bone cancer.
- * M/c in white boys < 15 yrs. * Early metastasis.
- * M/c @ diaphysis of long bones (Femur).
- * Pain & swelling ± B symptoms, leukocytosis.
- * X-ray: Lytic lesions (Moth-eaten), Onion-skin.
- * Biopsy: Small round blue cells. (DD: lymphoma)
- * T(11;22) → Overexpression of EWS-FLI1.
- * Labs: High ESR, High LDH, leukocytosis.
- * TTT: Surgical resection + Chemotherapy.

Chondrosarcoma

- * From mesenchymal cells.
- * > 50 years old. * @GIRDLES.
- * X-ray/CT: Calcification (popcorn), Osteolysis (moth-eaten).
- * Biopsy: chondrocytes filling lobules.
- * TTT: Surgery. ± chemo/radio.

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youtube.com/@OsamaElSawwah

- **Choice B** → **Eosinophilic Granuloma** refers to **LCH**, which causes **osteolytic lesions**, however, it most **commonly affects the skull and spine**.
 - **Biopsy** → **Irregular shaped cells with copious eosinophilic cytoplasm & characteristic horseshoe or kidney shaped nuclei**
- **Choice D** → Multiple Myeloma also causes osteolytic lesions. It affects the skull most commonly, and biopsy shows malformed plasma cells
- **Choice E** → Presents as a painless flank mass. Not a bone lesion.

- **Choice G** → Lymphoma has a similar biopsy findings, however, where is the lymphadenopathy, the fever, the weight loss, the classic lymphoma presentation? The vignette is a classic bones tumor Q.

Q17

A 35-year-old man with bronchial asthma starts taking albuterol. Which of the following changes in second messenger levels is most likely in the cells affected by this treatment?

- A. Decrease in cAMP
- B. Decrease in cGMP
- C. Decrease in inositol 1,4,5-trisphosphate
- D. Increase in cAMP
- E. Increase in cGMP
- F. Increase in inositol 1,4,5-trisphosphate

▼ **Explanation**

- **Answer is B (Increased cAMP)**
 - Q asks what is 2nd messenger of albuterol?
 - We know albuterol is a **beta-2-agonist** → Activates **Gs** → activates adenylate cyclase → increases cAMP



HY Second Messengers

"HAVE 3M&Ms" : Activates **Gq** → activates Phospholipase C → IP3

- H1 - A1 - V1 - M1 - M3

"MAD2" : Activates **Gi** → inhibits Adenylate Cyclase → decreases cAMP

- M2 - A2 - D2

Remaining : Activates **Gs** → activates Adenylate Cyclase → increases cAMP

- B1 - B2 - H2 - V2 - D1

Q18

A 57-year-old woman comes to the physician 2 weeks after finding a lump in her left breast on self-examination. Physical examination shows a 2-cm mass in the upper inner quadrant of the left breast. Carcinoma is suspected. X-rays show multiple lesions in the vertebral column, and metastatic disease is suspected. Which of the following veins draining the breast provides the most direct pathway for malignant cells to travel to the vertebral column?

- A. Axillary
- B. Cephalic
- C. Intercostal
- D. Internal thoracic (mammary)
- E. Lateral thoracic

▼ **Explanation**

- **Answer is C (Intercostal)**
 - This is a HY concept you need to know:
 - **How does breast cancer spread to vertebral column vs Axillary lymph nodes?**
 - 1. Vertebral Column**
 - **Intercostal vein → Azygous vein → Batson's Venous Plexus (of vertebrae)**

2. Axillary Lymph Nodes

- Lateral Mammary L.N → Lateral Thoracic L.N → Axillary L.N

Q19

A 10-year-old boy receives a renal transplant from a living, related donor for cystic renal dysplasia. Three months later, there is tenderness at the site of the graft, and serum creatinine concentration increases from 1.0 to 2.0 mg/dL. Which of the following findings on renal biopsy is most likely to confirm a diagnosis of rejection?

- A. Arteriolar C3 deposition
- B. Dilation of Bowman space
- C. Fibrous scars with plasma cells
- D. Glomerular neutrophils and necrosis
- E. Lymphocytes infiltrating tubular epithelium
- F. Red blood cell casts
- G. Subcortical necrosis

▼ Explanation

- Answer is E (Lymphocytes infiltrating tubular epithelium)
 - IMP Clues
 - Renal transplant (so graft rejection Q or virus reactivation Q)
 - 3 months later (Timing in graft vs host reaction is everything)
 - Tenderness at side of graft + creatinine concentration increased from 1 to 2mg/dl (body is attacking the kidney)
- Dx → Acute Graft Rejection
 - Timing → < 6 months
 - Etiology → Type 4 HS reaction due to cell-mediated (CD8) reaction to donor MHC (CD4 antibodies are also involved, but CD8 dominates)
 - Pathophysiology → Lymphocytic infiltration causing vasculitis

? What are the types of Graft rejection, and what do you know about them?

▼ Answer

Rejection Type	Timing	Etiology	Pathophysiology
Hyperacute	Minutes to hours	Type II hypersensitivity due to preformed antibodies against donor antigens	Complement activation → neutrophil infiltration → vessel ischemia & fibrinoid necrosis
Acute	< 6 months	Type IV hypersensitivity; primarily CD8 ⁺ T cells reacting to donor MHC (CD4 ⁺ cells/antibodies also contribute)	Lymphocytic infiltration → vasculitis
Chronic	Months to years	Type IV hypersensitivity; mixed cell-mediated + humoral response	Progressive fibrosis & vessel obliteration

▼ Other Choices

- Choices A & D → Refers to Hyperacute rejection.
- Choice B → Refers to obstructive uropathy, where for example a stone or cervical cancer compresses the ureter → hydroureter → hydronephrosis, and dilation of Bowman space
- Choice C → Refers to chronic rejection.

- **Choice F** → RBC casts are features of GN. RBC from the glomerulus combines with tubular protein & forms these casts.
- **Choice G** → Subcortical necrosis is seen in cases of severe hypovolemia, which causes hypoxia in tubules as they are most susceptible due to the presence of ATPases.

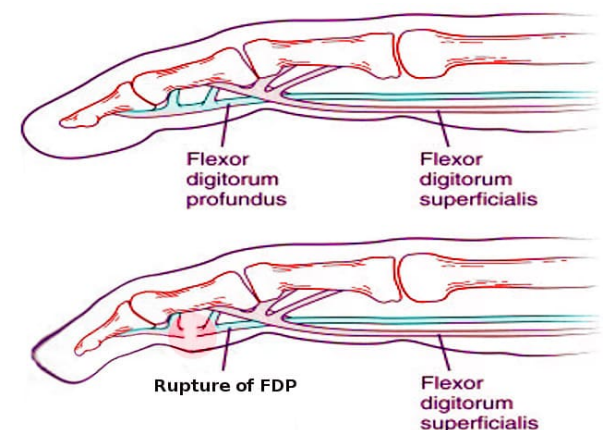
Q20

An 18-year-old man comes to the physician 10 days after injuring his right hand during a game of tag football. He says that he was attempting to tag an opposing player when he inadvertently caught the tip of his ring finger on the other player's jersey. He felt a popping sensation at the tip of his finger and then immediately felt sharp pain localized to the finger. He noticed swelling of the finger several minutes later. Examination of the right hand shows mild tenderness over the palmar tip of the ring finger. He is unable to flex the distal interphalangeal joint of the right ring finger, but he is able to flex the metacarpophalangeal and proximal interphalangeal joints. This patient most likely injured a tendon whose muscle is supplied by fibers from which of the following nerve roots?

- A. C3
- B. C4
- C. C5
- D. C6
- E. C7
- F. C8

▼ **Explanation**

- **Answer is F (C8)**
 - **IMP Clues:**
 - Unable to flex the distal interphalangeal joint of right middle finger (affected FDP)
 - But he's able to flex MCP & PIP joints (intact FDS)
 - Q wants to know the tendon of the muscle injured is supplied by what nerve.
- We can do this in two ways
 1. We know that **Flexor Digitorum Profundus** is what flexes the **DIP**.
 - The **medial half of FDP** (supplies small & ring fingers) is supplied by **ulnar nerve**.
 - What are the roots of the ulnar nerves ?
 - **C8-T1**
 2. By knowing the **myotomes**, we can figure out what nerve roots cause **finger flexion**
 - C4 → Scapula Elevation
 - C5 → Shoulder Abduction
 - C6 → Biceps Flexion
 - C7 → Triceps Extension
 - C7 → Fingers Extension
 - **C8 → Fingers Flexion**
 - T1 → Finger Abduction



? **What muscle causes flexion of DIP?**

▼ **Answer**

FDP - The FDS is responsible for flexion of PIPs & MCPs

▼ **Other Choices**

- **Choice A** → C3 ⇒ Lateral flexion of neck
- **Choice B** → C4 ⇒ Scapula Elevation
- **Choice C** → C5 ⇒ Shoulder Abduction
- **Choice D** → C6 ⇒ Biceps Flexion
- **Choice E** → C7 ⇒ Triceps Extension & Fingers Extension

Q21

A 35-year-old man comes to the physician because of a 6-week history of pain in his right arm and tingling sensation in the fingers of his right hand. Physical examination shows weakness of extension and pronation of the right forearm. The triceps muscle stretch reflex is decreased. Which of the following nervous structures is most likely involved?

- A. C6 nerve root
- B. C7 nerve root
- C. C8 nerve root
- D. Median nerve
- E. Radial nerve

▼ Explanation

- **Answer is B (C7 nerve root)**
 - **IMP Clues**
 - Weakness in extension & pronation of right forearm (Main extensor is triceps & main pronator is pronator ms, both are supplied by radial nerve)
 - Triceps stretch reflex is decreased (reflex is mediated by C6-C7, but with C7 being the main contributor)
 - Q asks what nerve is involved?
 - **Triceps & Pronator muscle** are both injured which might make you think this is definitely the **radial nerve**, however, **radial nerve injury also affects wrist extensors.**
 - So, this must be a *more localized injury*
 - The vignette specifies that the **Triceps Reflex is decreased, which hints to us that C7 is the affected root here.**
 - Yes, **Triceps reflex is C6-C7, but the C7 is the main contributor**
 - Like, the biceps reflex is C5-C6, but with C6 as the main contributor

▼ Other Choices

- **Choice A** → C6 injury would present as inability to flex or supinate arms with decreased bicep reflex.
- **Choice C** → C8 injury would present as loss of sensation in medial forearm & inability to flex fingers
- **Choice D** → Median nerve injury would cause loss of sensation of palmar lateral 3 & half fingers + Thenar atrophy + Ape hand deformity
- **Choice E** → Radial nerve injury would cause Loss of function of Triceps, Pronator, finger extensors, and loss of sensation of Dorsal 3 & half fingers.

Q22

A 27-year-old woman comes to the physician because of swelling in her left arm that began 10 days after a spontaneous abortion in the middle of her second trimester. A radiocontrast study shows axillary vein thrombosis. Laboratory studies show:

Bleeding time	normal
Prothrombin time	increased
Partial thromboplastin time	increased
Thrombin time	normal

Which of the following is the most likely cause of this woman's condition?

- A. Antiphospholipid antibodies
- B. Antithrombin deficiency
- C. Dysfibrinogenemia
- D. Protein C deficiency
- E. Protein S deficiency

▼ Explanation

- **Answer is A (Antiphospholipid antibodies)**

- **IMP Clues:**

- Swelling of left arm + Axillary vein thrombosis (Patient is hypercoagulable)
- Spontaneous abortion in the middle of her 2nd trimester (Most common cause of 2nd trimestric abortion is antiphospholipid syndrome)
- Bleeding time normal (so not a PLT disorder)
- PT & PTT increased (so patient should be “bleedy” not have thrombosis)

- **Dx → Antiphospholipid Syndrome**

- On the USMLE, choose APLS when you see

1. **Thrombus in someone with high PTT**
2. **Recurrent miscarriages**, especially if she has **SLE**
3. **False Positive RPR/VDRL**

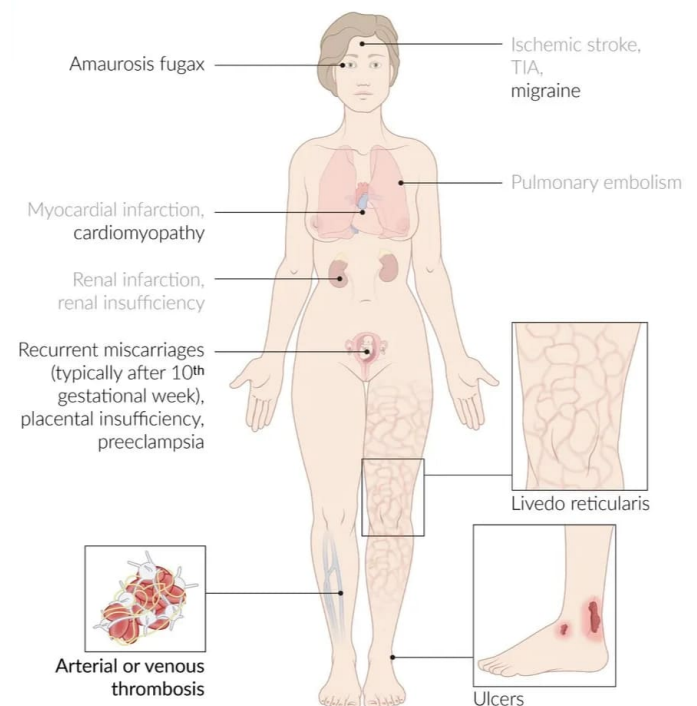
- Associated Antibodies

1. **Anti-Cardiolipin**
2. **B2-microglobulin**
3. **Lupus anti-coagulant**

[For Nerds] Understanding how APLS works!

With **high PTT**, you'd expect **bleeding tendency**
In **APLS**, however, you have **high PTT + Thrombosis**, how?

In **Vitro (lab test tube)**, **phospholipid is added** to the plasma to act as a surface for the clotting cascade, however, in **APLS we have phospholipid antibodies**. They **attack the added phospholipid**, which causes **no clotting**, hence causing a **high PTT**.



▼ **Other Choices**

- **Choice B → Anti-thrombin III deficiency** on the USMLE most commonly presents as a **patient with nephrotic syndrome + DVT/Thrombosis/Varicocele**
 - Anti-thrombin 3 inactivates Thrombin.
 - Anti-thrombin 3 deficiency causes activated thrombin which causes hypercoagulability
 - Patients with nephrotic syndrome, lose the anti-thrombin 3 protein in urine.
- **Choice C → Dysfibrinogenemia** has *increased Thrombin Time*
- **Choice D → Protein C deficiency** is **Skin Necrosis in a patient on Warfarin**
- **Choice E → Protein S** is a co-factor of protein C, so deficiency of Protein S can cause Protein C deficiency

? What drug upregulates Anti-thrombin 3?

▼ **Answer**
Heparin

Q23

The risk for hemorrhagic stroke from drug X is investigated by utilizing a questionnaire about drug use in 702 patients with hemorrhagic stroke and in 1376 control subjects contacted by random-digit dialing. Which of the following best describes this study design?

- A. Case-control study
- B. Cohort study
- C. Cross-sectional survey
- D. Randomized, double-blind experiment
- E. Randomized, single-blind experiment

▼ **Explanation**

• **Answer is A (Case-control study)**

- The participants in the study are sorted as "cases of hemorrhagic stroke" and "controls with no hemorrhagic stroke". They are then contacted to ask about "risk factors" which here is Drug X.

? **What is assessed in Case-Control Studies?**

▼ **Answer**
Odds Ratio

▼ **Other Choices**

- **Choice B** → We'd sort the participants as people who took drug X "the risk factor" & people who didn't take drug X. Then we'd follow up/look back to see if they developed the "result" which is hemorrhagic stroke

▼ **What is assessed for in Cohort Studies?**

Relative Risk

- **Choice C** → Used to measure incidence & prevalence not risk.
- **Choice D & E** → We'd select random people and assign them randomly to a group & we would GIVE them Drug X or Placebo (not just see if they had taken, not an observational study)
 - Double-blinded → neither the doctors nor the patients know who took the placebo from who took the Drug
 - Single-blinded → the patients don't know whether they had taken the placebo or the drug.-

Q24

A 4-year-old boy is brought to the physician by his parents because he has had two bacterial urinary tract infections during the past year. Physical examination shows no abnormalities. Radiologic studies of the urinary tract show marked dilation of the left ureter and renal pelvis, and minimal left-sided renal function. A left nephrectomy is performed. A photograph of the resected specimen is shown. Microscopic examination of the renal parenchyma is most likely to show which of the following?



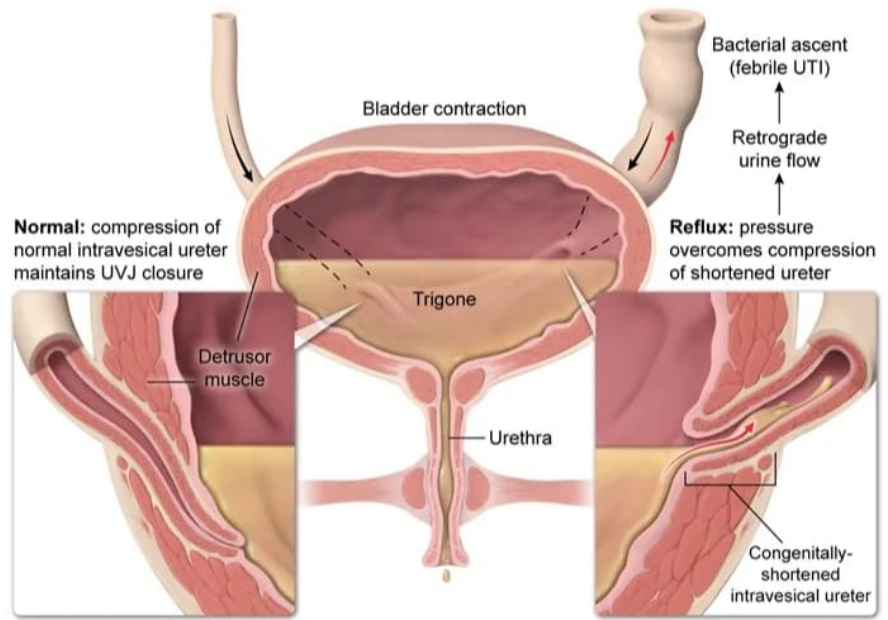
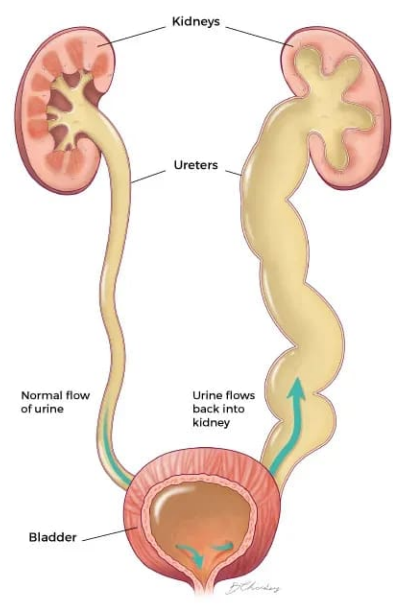
- A. Amyloidosis
- B. Interstitial inflammation
- C. Membranous glomerulonephritis
- D. Nephroblastomatosis
- E. Renal cell carcinoma

▼ **Explanation**

• **Answer is B (Interstitial Inflammation)**

- **IMP Clues**
 - 4-year-old boy (pediatric urology Q)
 - 2 bacterial UTIs in past year (something is causing those recurrent UTIs, especially in a boy with a long urethra)
 - Dilation of Left ureter & renal pelvis & minimal renal function (unilateral obstruction below level of ureter, so most common cause is UVR)
- **Dx** → **Ureterovesical Reflux**

- UVR causes *backflow of urine* through the **incompetent valve** between the ureter and the bladder.
- This causes **dilation of ureter & kidney**.
- This predisposes to **recurrent infections**, which on the long run causes **chronic pyelonephritis**.
- **Chronic Pyelonephritis is characterized by scarring, tubular atrophy, and blunting of renal calyces** (basically the picture you see)



Q25

Which of the following is required for the synthesis of glucosamine from fructose 6-phosphate?

- A. Arginine
- B. ATP
- C. Carbamoyl phosphate
- D. Glutamine
- E. N-acetylglutamate

▼ Explanation

- **Answer is D (Glutamine)**
 - Garbage biochemistry in my opinion. This is the Hexosamine Pathway, which is LYYYY AFFF, so don't bother.
 - Just memorize the fact.
 - **Fructose 6-Phosphate + Glutamine ⇒ Glucosamine.**

Q26

A 25-year-old woman comes to the physician because of a 6-month history of irregular menstrual periods and progressive acne. Menses have occurred at irregular 25- to 42-day intervals. She is 170 cm (5 ft 7 in) tall and weighs 100 kg (220 lb); BMI is 35 kg/m². Her voice is deep. Physical examination shows dark hair over the upper lip and chin, and open and closed comedones over the face, chest, and back. Serum studies are most likely to show which of the following in this patient?

Choices	Fasting Insulin	Testosterone	Luteinizing Hormone
A	Increased	Increased	Increased
B	Increased	Increased	Decreased
C	Increased	Decreased	Increased
D	Decreased	Increased	Increased
E	Decreased	Increased	Decreased

Choices	Fasting Insulin	Testosterone	Luteinizing Hormone
F	Decreased	Decreased	Decreased

▼ **Explanation**

• **Answer is A**

◦ **IMP Clues**

- Irregular menses (hormones fucked up)
- Progressive Acne + comedones + dark hair over upper lips & chin (high androgens)
- Weighs 100kg & BMI is 35 (High BMI is major risk factor for PCOS)

◦ **Polycystic Ovary Syndrome**

▪ Characterized by Triad of:

1. Insulin Resistance
2. High Androgen
3. High LH/FSH ratio

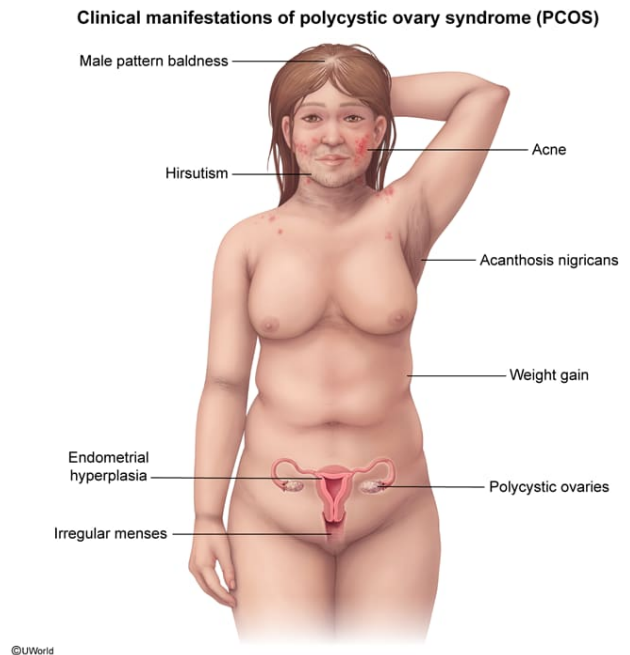
▪ Complications of PCOS

1. Metabolic Syndrome
2. Hirsutism (hair on upper lips, chin, chest) & Acne
3. Irregular menses & Infertility

4. **Endometrial Hyperplasia & Endometrial Carcinoma**

- USMLE tests this concept in cases of **anovulation** (like here in **PCOS**) & cases of **unopposed hyperestrogenemia** (women on **Estrogen-only pills** or **Tamoxifen**)

- Non-ovulatory = no progesterone to offset the effects of Estrogen = **UNOPPOSED HYPER-ESTROGENEMIA ⇒ ENDOMETRIAL HYPERPLASIA**

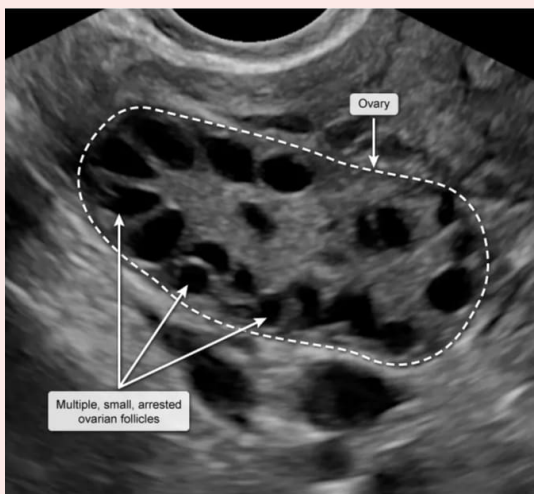


? On the USMLE, you will get an arrows Q with FSH & LH in PCOS. What to choose?

▼ **Answer**

- **HIGH LH**
- **NORMAL FSH** (yes, normal. That's what USMLE wants. Normal FSH not low)

USMLE can be assholes & give you U/S of the ovaries (below) or its "String of Pearls Appearance" or "Necklace pattern" description and ask for the diagnosis/cause/one of the above triad/arrows:



- If they ask for cause of the U/S appearance, the answer is "**chronic anovulation, causing failure of follicles rupturing**"

? USMLE gives you a case of PCOS/Estrogen-Only Pills/ Tamoxifen & asks what is patient at risk of developing

▼ **Answer**

Endometrial Hyperplasia/Carcinoma

Q27

A 56-year-old woman is brought to the emergency department by her husband because she has had headache, confusion, and difficulty speaking and walking for the past 2 days. Mental status shows confusion and memory loss. Her temperature is 38.9°C (102°F). Brudzinski and Kernig signs are absent. Analysis of cerebrospinal fluid shows:

Opening pressure	260 mm H ₂ O
Leukocyte count (mostly lymphocytes)	208/mm ³
Protein	52 mg/dL
Glucose	40 mg/dL

An EEG shows abnormalities in the right temporal lobe and periodic lateralized epileptiform discharges. Which of the following is the most likely diagnosis?

- A. Aseptic meningitis
- B. Bacterial encephalitis
- C. Herpes encephalitis
- D. Neurosarcoidosis

E. Tuberculous meningitis

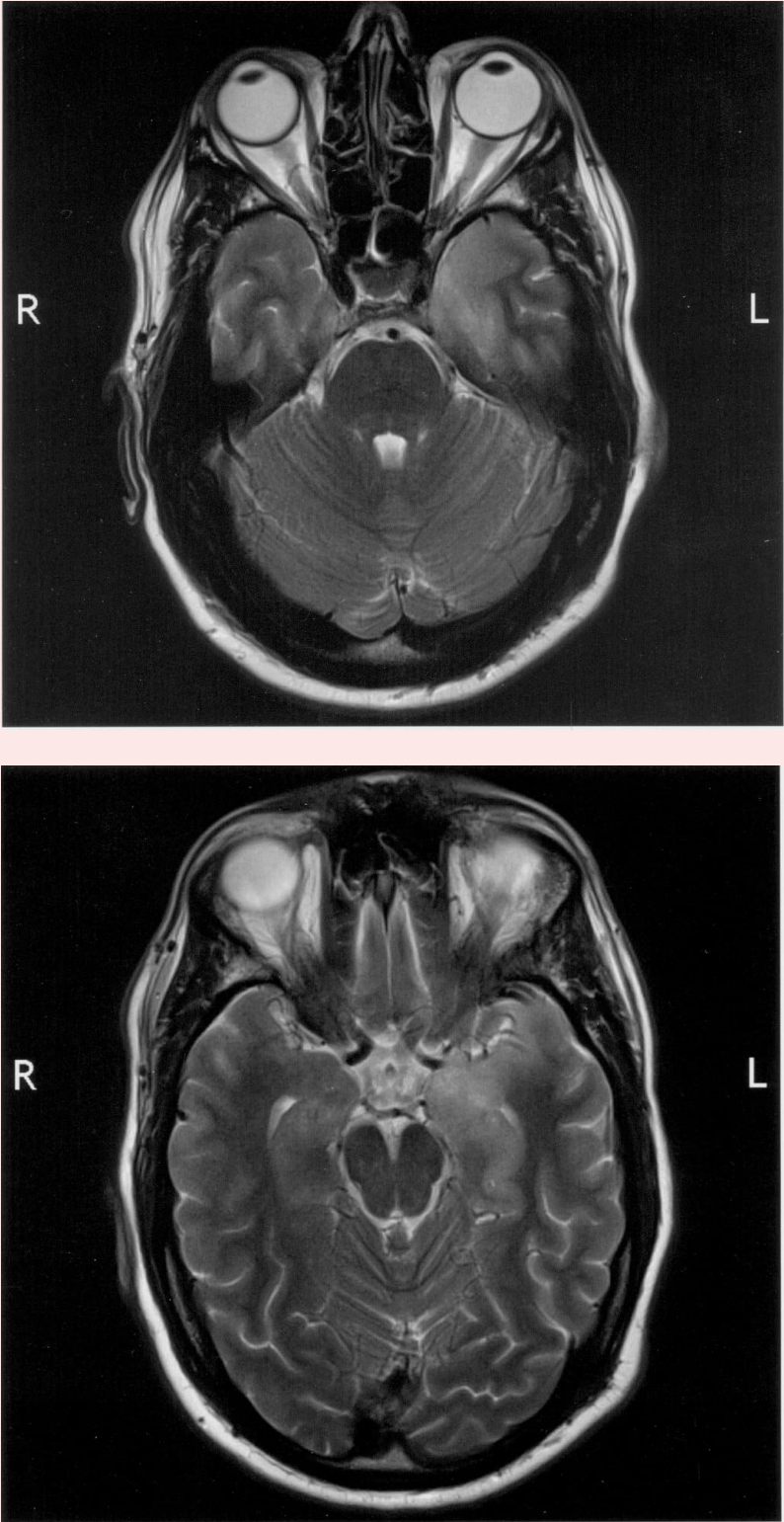
▼ Explanation

- **Answer is C (Herpes Encephalitis)**
 - **IMP Clues**
 - Headache, Confusion, Mental Status shows confusion & memory loss (nonspecific symptoms, nothing yet. Maybe some CNS suspicion)
 - Brudzinski & Kernig Signs are absent (excludes meningitis on the USMLE, on real life their absent don't)
 - CSF analysis shows high opening pressure (so increased ICP is what to blame for the above symptoms)
 - High leukocyte counts mostly lymphocytes (Viral/TB/Fungal etiologies)
 - Normal Glucose & Slightly elevated proteins (consistent with viral etiology)
 - EEG shows abnormalities in the right temporal lobe (bingo, this on USMLE = Herpes Encephalitis)
 - **Dx → Herpes Encephalitis**
 - On the USMLE, **Temporal Lobe involvement on EEG, even despite normal CT findings, is Herpes Encephalitis**
 - [🧠] **RBCs in CSF = Temporal Lobe Bleeding = Herpes Encephalitis**
 - Most common cause of **sporadic encephalitis is HSV1**

CSF findings (like other viruses) → high cells (lymphocytes), normal glucose, normal/slightly elevated protein

Cerebrospinal fluid analysis			
Diagnosis	WBC count (mm ³)	Glucose (mg/dL)	Protein (mg/dL)
Normal	0-5	40-70	<40
Bacterial meningitis	>1,000	<40	>250
Tuberculous meningitis	100-500	<45	100-500
Viral meningitis	10-500	40-70	<150
Guillain-Barré syndrome	0-5	40-70	45-1,000
WBC = white blood cell.			

Below you can see Brain MRIs with LEFT-SIDED Temporal Lobe Hyperintensity (Whiter/Paler than surrounding/Contralateral Brain Matter):



▼ Other Choices

- **Choice A →** Meningitis would have positive Brudzinski & Kernig Signs. Q also mentions abnormality in right “temporal lobe”, yah that’s not meninges.

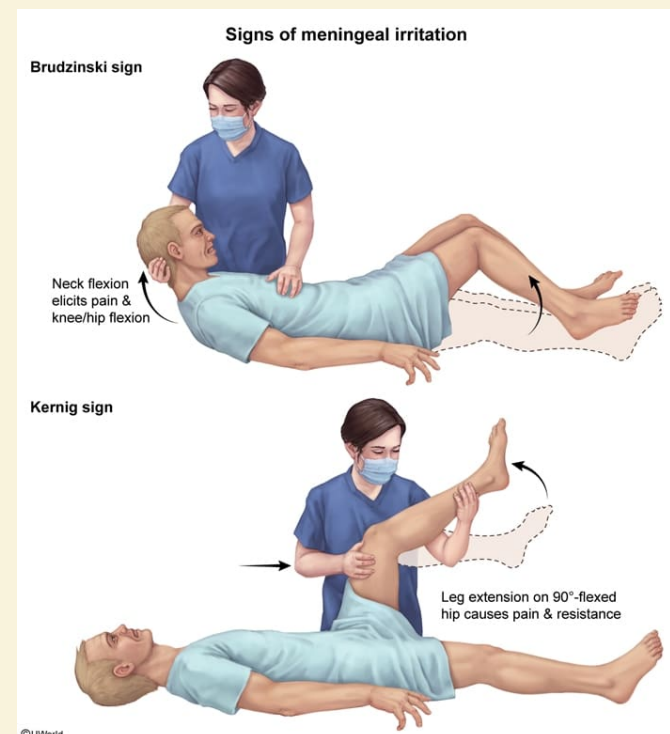
? Can you tell me what are Brudzinski & Kernig Signs?

▼ Answer

Kernig → **Extension of legs** causes stretch on inflamed meninges, which causes severe pain.

Brudzinski → **Flexion of neck** causes stretch on inflamed meninges, which causes severe pain + flexion of hips & legs to decrease stretching.

Mnemonic: To remember which is which, I say "**CurlLeg**" instead of "**Kernig**", which reminds me that its **Kernig's sign** is the one where I use the legs



- **Choice B** → Would have neutrophils + elevated proteins + low glucose
- **Choice D** → Never a correct answer choice, just complete bluff. Neurosarcoidosis is LY & will is not assessed on the USMLE.
- **Choice E** → TB meningitis would have Lymphocytes + elevated protein + low glucose.

Q28

A 66-year-old man comes to the physician because of a 2-month history of the inability to maintain an erection. He also has had fatigue and difficulty sleeping and concentrating during this period. Three months ago, he had a cerebral infarction with right hemiparesis that has gradually resolved. Physical examination shows no abnormalities. Which of the following additional pairs of findings in this patient is most likely on history taking?

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

▼ Explanation

- **Answer is C**
 - **IMP Clues**
 - Inability to maintain an erection (Impotence)
 - Fatigue + difficulty sleeping & concentrating (symptoms of depression)
 - Cerebral infarction with right hemiparesis that has gradually resolved (cause of depression not cause of impotence, for a stroke to cause impotence it must be a "bilateral" which is unrealistic)tence, it must
 - Physical Examination shows no abnormalities (no gynecomastia, which is a very common duo with Impotence in cases of hyperprolactinemia)
- Q asks what is most likely to be found on history taking.
 - **2 Rules to approach any impotence case:**
 1. **Organic causes vs Psychogenic causes**
 - **Organic causes** → cause **loss** of nocturnal erections
 - **Psychogenic causes** (like what we have here, due to depression) → **intact** nocturnal erections
 2. **Libido is related to 2 things**
 - **Testosterone** levels → low levels = **low** libido
 - **Depression** → depression = **no interest** in sex

- Patient here is depressed + No physical exam findings (organic causes) so this is just depression which causes low libido + intact nocturnal erections (Choice C)



Case Scenarios:

1. Patient with wife that died 2 years ago + hyperthyroidism + can't maintain erection when dating but can masturbate alone

▼ Answer

- Libido → **Decreased**
- Nocturnal Erections → **Normal**

Reasoning: Depression causes less libido, can masturbate alone = intact erections

2. Patient that has can't maintain erection + hits people accidentally when walking & hits his toe in furniture at home

▼ Answer

- Libido → **Decreased**
- Nocturnal Erections → **Decreased**

Reasoning: Bilateral hemianopia due to a prolactinoma causes less testosterone which causes decreased libido & erections (organic)

3. Patient with obesity & atherosclerosis presents with inability to maintain erection.

▼ Answer

- Libido → **Normal**
- Nocturnal Erections → **Decreased**

Reasoning: Patient has normal testosterone levels & normal sex drive but atherosclerotic patient = atherosclerosis everywhere, even there. So less blood flow → inability to maintain erection (organic cause)

Q29

A 52-year-old man is brought to the emergency department 1 hour after he was found next to a faulty space heater. He is confused. Physical examination shows reddish-tinged skin. Arterial blood gas analysis on room air shows a Po_2 within the reference range and carboxyhemoglobin concentration of 40% (N=2%). He is intubated and mechanically ventilated with supplemental oxygen. Assuming no further carbon monoxide (CO) exposure, which of the following is the best estimate for the time it will take for the removal of all the CO-carrying erythrocytes from this patient's circulation?

- A. 1 Day
- B. 2 Weeks
- C. 1 Month
- D. 4 Months
- E. 1 Year

▼ Explanation

- Answer is D (4 Months)
 - Q just asks for an estimate of the time for the removal of the CO-carrying erythrocyte from the patient's circulation.
 - **CO poisoning doesn't cause premature death of the cell or hemolysis. It just binds to the hemoglobin instead of Oxygen.**
 - So, cells will live their normal life span, which is about **120 days (4 months)**

Q30

A randomized controlled trial is conducted to assess the effect of diuretic therapy on the risk for cerebral infarction in patients with systolic hypertension. A total of 4736 patients with systolic blood pressure measurements greater than 140 mm Hg and diastolic blood pressure measurements ranging from 50 mm Hg

to 85 mm Hg are randomly assigned to receive diuretic therapy or placebo. After 5 years, results show:

	Cerebral Infarction		
	Yes	No	Total
Diuretic Therapy	123	2242	2365
Placebo	194	2177	2371
Total	317	4419	4736

Which of the following best represents the absolute risk reduction for cerebral infarction in patients receiving diuretic therapy?

- A. $(194/2177) - (123/2242)$
- B. $(194/2371) - (123/2365)$
- C. $(123/2242) / (194/2177)$
- D. $(123/2365) / (194/2371)$
- E. $(194/2177) / (123/2242)$
- F. $(194/2371) / (123/2365)$

▼ Explanation

- Answer is B
 - Absolute Risk Reduction measures how an intervention decreases the risk of an outcome as an absolute percentage.
 - For example, people who take drug X get a 10% risk reduction of developing Disease Y, while people on the placebo drug get a 2% risk reduction.
 - Absolute Risk Reduction = $A - B = 10\% - 2\% = 8\%$
 - Relative Risk Reduction = $ARR / A = 8\% / 10\% = 80\%$
 - Now, let's implement this in this Q, which asks for ARR for cerebral infarction in patients receiving diuretic therapy
 - Patients with cerebral infarction on diuretics = 123
 - Total people on diuretics = 2365
 - Risk B = $123/2365$
 - Patients with cerebral infarction on placebo = 194
 - Total people on placebo = 2371
 - Risk A = $194/2371$
 - $ARR = A - B = (194/2371) - (123/2365)$

? Calculate the Relative Risk Reduction.

▼ Answer
 $(194/2371) - (123/2365) / (194/2371)$

Q31

A newborn has cyanosis, tachypnea, and retractions of the muscles of the chest wall during inspiration. She weighs 2500 g (5 lb 8 oz). Arterial blood gas values while she breathes room air are:

pH	7.04
Pco ₂	65 mm Hg
Po ₂	35 mm Hg
HCO ₃ ⁻	15 mEq/L

Which of the following best describes her acid-base balance?

- A. Metabolic acidosis, uncompensated
- B. Metabolic alkalosis, uncompensated
- C. Respiratory acidosis, uncompensated
- D. Respiratory alkalosis, uncompensated
- E. Respiratory acidosis and metabolic acidosis
- F. Respiratory acidosis and metabolic alkalosis

▼ Explanation

- **Answer is E (Respiratory Acidosis & Metabolic Acidosis)**

- **How to Approach**

1. Look at **pH**

- pH is 7.04 (normal is 7.35-7.45) → **severe acidosis** (makes it more likely to be both respiratory & metabolic acidosis)

2. Look at **Bicarb**

- HCO₃⁻ is 15 (normal is 22-28) → **metabolic acidosis** is present.

3. Look at **Pco₂**,

- if low → compensated, if high → concurrent resp acidosis
- PCO₂ is 65 (normal is 33-45) so high → **Respiratory Acidosis**

- So, patient has **Metabolic Acidosis + Respiratory Acidosis**

Q32

A 42-year-old woman with frequent heartburn has relief of symptoms with ranitidine treatment. The therapeutic effect of ranitidine is most likely mediated by a receptor whose activation increases which of the following in the parietal cells of the stomach?

- Calcium
- cAMP
- cGMP
- Gastrin
- Prostaglandin E₂

▼ **Explanation**

- **Answer is C (cAMP)**

- **Ranitidine** is a reversible competitive **H₂-Blocker** used in treatment of GERD.
- *Remember the mnemonics of G-protein messengers that I mentioned before?*
 - **H₂ → activates G_s, which causes activation of adenylate Cyclase → increase in cAMP → activates Protein Kinase A**

HY Second Messengers Rapid Review:

☐ **"HAvE 3M&Ms"** : Activates **G_q** → activates Phospholipase C → IP₃

- H1 - A1 - V1 - M1 - M3

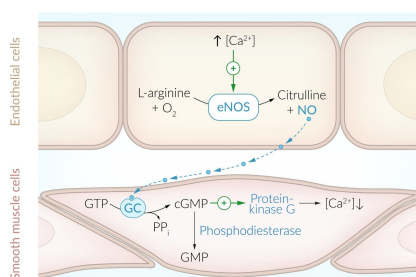
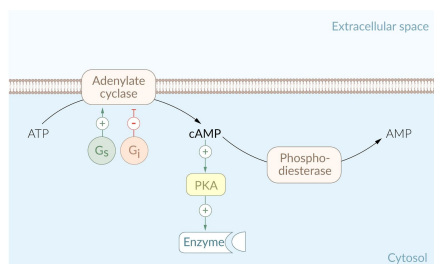
☐ **"MAD2"** : Activates **G_i** → inhibits Adenylate Cyclase → decreases cAMP

- M2 - A2 - D2

Remaining: Activates **G_s** → activates Adenylate Cyclase → increases cAMP

- B1 - B2 - **H₂** - V2 - D1

Just memorize these mnemonics, and you will answer all these Qs right



Let's Review the Entirety of the 2nd Messengers on the USMLE:

1. **Intracellular/nuclear Receptors** ⇒ **Steroid/Cholesterol-derived Hormones AND Thyroid Hormones**

- Examples are **Estrogen, Progesterone, Testosterone, Vitamin D, Cortisol, Aldosterone, AND T3/T4.**

2. **Receptor Tyrosine Kinase** ⇒ **Insulin AND Growth Factors**

- Examples are **Insulin, IGF-1, FGF, PDGF, and EGF**

3. **Non-Receptor Tyrosine Kinase** ⇒ **Acidophils, Cytokines, AND Colony Stimulating Factors**

- Examples are **GH, Prolactin, Interleukins & Interferons, EPO, TPO, and G-CSF**

4. **cGMP (CYTOSOLIC ACTION)** ⇒ **NO, ANP, BNP**

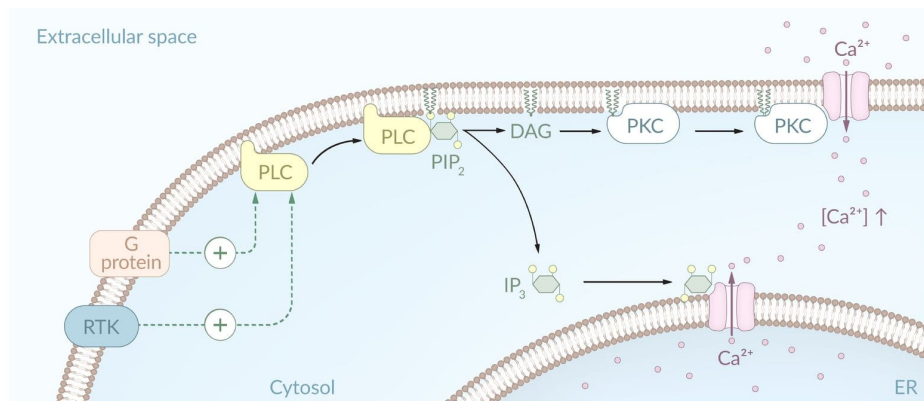
5. **IP₃ (G-Couple Protein Membrane Receptor Action)** ⇒ **Oxytocin, ADH (V1), AT-II, Gastrin, GnRH, TRH, H-1**

6. **cAMP (G-Couple Protein Membrane Receptor Action)** ⇒ **Remaining**

- Examples are **FSH, LH, ACTH, TSH, CRH, hCG, ADH(V2), MSH, PTH, Calcitonin, GHRH, Glucagon, H-2, PGs - LTs**



Despite T3/T4 being peptide hormones, they act via intracellular/nuclear Receptors.



- ! Distinction between **GHRH**, **GH**, and **IGF-1** is very HY:
- GHRH → **cAMP**
 - GH → **Non-Receptor Tyrosine Kinase**
 - IGF-1 → **Receptor Tyrosine Kinase**

- ! Many students tend to mix-up **Oxytocin** for some reason. **Oxytocin is IP3** NOT cAMP.

- ! Glucagon is HY as it increases cAMP, so it is used **as an antidote for BB toxicity**, which causes decreased cAMP.

- ! While Estrogen & Progesterone are Intracellular/nuclear receptors, **b-hCG is cAMP mediated**.

Q33

A physician is unable to communicate 'bad news' to a patient because the patient reminds him of his older brother who always intimidated him. Which of the following terms best describes this reaction?

- A. Conversion
- B. Countertransference
- C. Regression
- D. Splitting
- E. Sublimation

▼ Explanation

• Answer is B (Countertransference)

- **Transference** is when the doctor-patient relationship is affected because the doctor reminds the patient of someone the patient has a history with (father, mother, brother...)
 - For Example, the patient shouts at the doctor because the doctor reminds the patient of his abusing father.
- **Countertransference is the opposite.**
 - It is when the doctor-patient relationship is affected because the patient reminds the doctor of someone the doctor has a history with (father, mother, brother...)
 - This Q is an example of that.

▼ Other Choices

• Choice A → Conversion Disorder

- **Sudden "apparent/reversible" loss of function** due to some kind of **stressor**.
- The patient is **UNBOTHERED BY HIS CONDITION**. [This is so characteristic]
 - USMLE can present it as a hoarseness of voice, blindness, inability to walk, paralysis, cannot move finger or a limb. You get it.

• Choice C → Regression

- **Reverting to an earlier, more primitive and child-like pattern of behavior**
- For example, the patient starts sucking his thumb in response to a stressor

- **Choice D → Splitting**
 - **Viewing other people as either all good or all bad, with no middle ground.**
 - For example, patient sees a surgeon as an egotistic douchebag, and thinks all doctors are inconsiderate & douches.
- **Choice E → Sublimation**
 - **Redirecting unacceptable drives or impulses into socially acceptable activities**
 - For example, patient has an abusive father & starts boxing training.

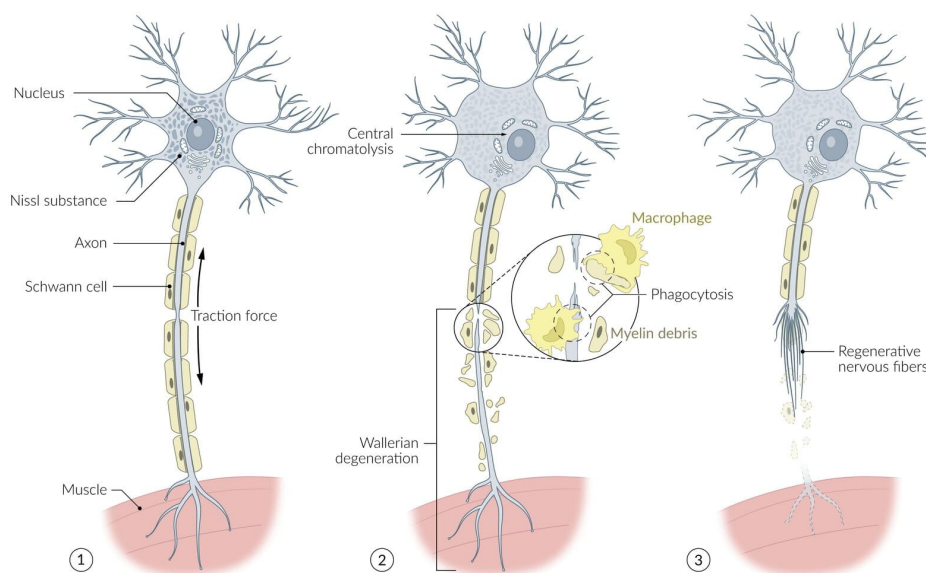
Q34

A 54-year-old man who works in a delicatessen comes to the physician because of decreased sensation of the tip of his right index finger. Six months ago, he severed this finger while slicing meat, and it was successfully reattached by prompt surgical repair. Examination of the finger shows muscle wasting. Which of the following cells is most likely blocking reinnervation of the muscles of this patient's finger?

- A. Fibrous astrocytes
- B. Microglial cells
- C. Oligodendrocytes
- D. Satellite cells
- E. Schwann cells

▼ **Explanation**

- **Answer is E (Schwann Cells)**
 - Q asks what cell is blocking reinnervation of the muscles in his finger.
 - On the USMLE, reinnervation Qs tests all the related concepts of Wallerian Degeneration, so let's go through everything you need to know.
- This patient's finger got cut off, so nerves **in PNS (not CNS)** start process of regeneration:
 1. **Nerves distal so site of injury gets degenerated. (Wallerian Degeneration)**
 2. **Schwann Cells line up to start regenerating the nerve.**



Concept Review:

▼ **What cells are involved in Wallerian Degeneration?**

- **Schwann Cells**

▼ **What cells block reinnervation in Wallerian Degeneration?**

- **Schwann Cells**
 - basically if they don't line up exactly right, nerves don't regenerate
 - "block" is weird, but this is what NBME wants, so just know it.

▼ **What acts as a pathfinding guide for regeneration of the damaged axons?**

- **Schwann Cells / Myelin Sheath**

▼ **What is rate-limiting step of Wallerian Degeneration?**

- **SLOW ANTEROGRADE Axonal Transport**



S100 is cytoplasmic protein that is used as a tumor marker on immunohistochemical staining of cells derived from Neural Crest.

- Associated with malignant melanoma, **schwannomas**, neurofibromas, peripheral neural sheath tumors, and Langerhans cell histiocytosis

HY Diseases Associated with Schwann Cells are:

1. Guillain-Barre Syndrome (GBS)

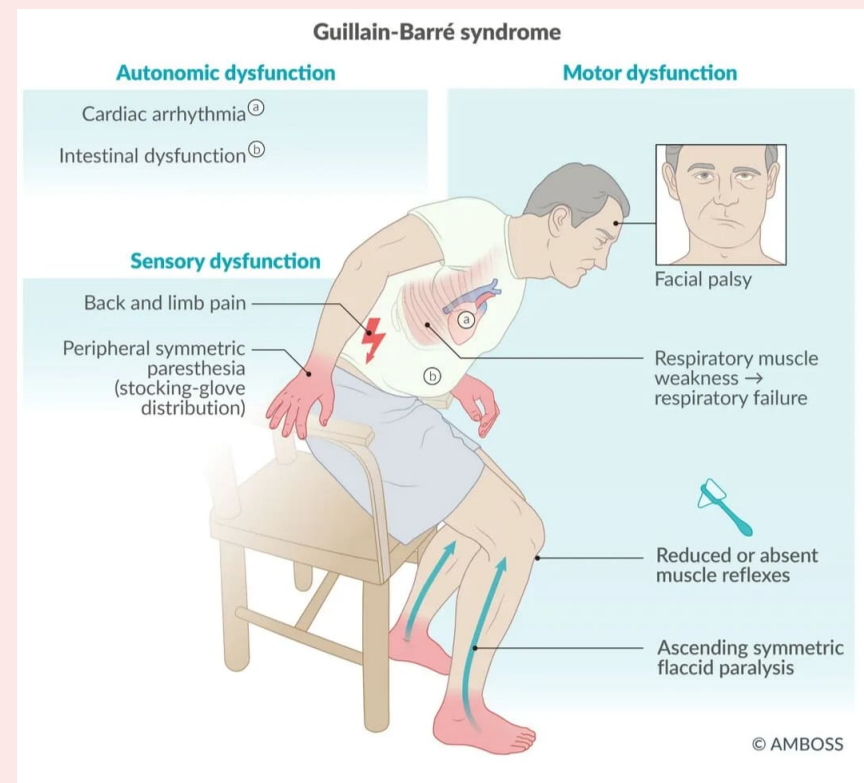
- Schwann Cells are attacked due to **Molecular Mimicry**, where an infectious agent (MC is **C.jejuni**) contains **ganglioside-like substance in its LPS layer**, causing the antibodies formed against this substance to **activate T-cells to "cross-react"/attack the ganglioside component of myelin & Schwann Cells**

2. Acoustic Neuroma (Vestibular Schwannoma)



HY Related Info:

- **Sporadic** Vestibular Schwannomas are usually **UNILATERAL**
- **BILATERAL** Vestibular Schwannomas are a **red flag** and warrant investigation of **Neurofibromatosis-2**
 - **NF-2 gene mutation on chromosome 22**
 - NF-2 gene encodes for **Merlin/Schwannomin Proteins (Tumor Suppressor Proteins)** mutation



▼ Other Choices

Roles of CNS/PNS cells are HY & You will get tested on them, so Let's review them

• Choice A → Astrocytes

◦ HY Functions:

- Uptake of aa (3Gs: GABA, **Glutamate**, Glycine)
- **Scar formation**

◦ How does USMLE test it?

- Patient has a brain abscess and necrosis, 3 weeks a different type of tissue is seen at that site, what cell produced that tissue?
 - Glial Scar tissue, produced by Astrocytes
- They give you bluff Q that mentions glutamate in CNS & asks what cell is related to whatever they say?
 - Astrocytes

• Choice B → Microglial Cells are Macrophages of CNS

◦ HY Functions:

- Phagocytosis
- HIV hides here

◦ How does USMLE test it?

- Patient has stroke & asks what cell clears out necrotic tissue?
 - Microglial Cells (Macrophages of CNS)
- Patient has HIV & asks where can HIV virus be found in CNS

- Microglial Cells (Macrophages of CNS)
- Normally, all around the body they're found in B-cells
- **Choice C → Oligodendrocytes**
 - Function
 - Myelin Formation in CNS
 - How does USMLE test it?
 - What cell does MS attack?
 - Oligodendrocytes, hence the CNS demyelination process of the disease
- **Choice D → Satellite Cells**
 - Not really assessed on the USMLE.
 - Just know that they are found in PNS around in ganglia
 - They support & maintain hemostasis of neurons in PNS

Q35

A previously healthy 28-year-old man comes to the physician's office because of severe abdominal pain accompanied by nausea, vomiting, and blood in the urine. Temperature is 36.7°C (98.1°F), pulse is 100/min, respirations are 20/min, and blood pressure is 140/90 mm Hg. The patient appears to be in distress and occasionally writhes in pain. Abdominal examination shows a flat abdomen with hypoactive bowel sounds. There is mild tenderness on palpation of the right middle and right lower quadrant of the abdomen and the right flank; there is no rebound or guarding. The testes are normal, and no hernia is palpable. Which of the following is the most likely diagnosis?

- A. Acute cortical necrosis
- B. Acute papillary necrosis
- C. Acute tubular necrosis
- D. Cystitis
- E. Glomerulonephritis
- F. Hypernephroma
- G. Interstitial nephritis
- H. Nephrolithiasis
- I. Pyelonephritis

▼ Explanation

- **Answer is H (Nephrolithiasis)**
 - **IMP Clues**
 - Severe abdominal pain + nausea + vomiting (DD are plenty, maybe surgical maybe medical)
 - Blood in urine (okay, renal system is affected)
 - Temperature is 36.7 (rules out infection)
 - Writhes in pain (veryy buzzy for renal stones)
 - Flat abdomen with hypoactive bowel sounds (excludes GI causes)
 - Mild Tenderness on palpation of the right middle & lower quadrants & right flank (course of ureter, so probably a renal stone)
 - No Rebound or guarding (excludes peritonitis)
 - Normal testes & no hernia (exclude torsion & incarcerated hernia or hernia in general)
 - **Dx → Nephrolithiasis**
 - Guy was perfectly healthy & got sudden abdominal pain + gross blood in urine, then this is most probably just a renal stone.
 - Most common type of renal stones → **Calcium Oxalate stones**.
 - Can be idiopathic in etiology like here

▼ Other Choices

- **Choice A →** Acute Cortical Necrosis is just ATN that extends diffusely into the cortex. Commonly seen in massive hemorrhages, like obstetrics
- **Choice B →** Acute Papillary Necrosis is caused by **subacute/chronic ischemia**. Common HY causes include *NSAIDs & Sickie Cell*

- **Patient with Sickle Cell + Red Urine = APN**
- **Patient with Sickle Cell + Protein Urine = FSGS**
- **Choice C** → ATN is caused by **acute ischemia**. HY common causes are *acute HF, AFib or arrhythmias, hypotension, Trauma, or surgery*.
 - Other causes include
 - Drugs like **Aminoglycosides**, Cisplatin, and IV contrast
 - *Rhabdomyolysis* (HY causes include trauma, marathon runs, McCardle's, Statins & Fibrates concurrent intake)
- **Choice D** → Cystitis presents as fever + **suprapubic pain** + dysuria + frequency + urgency
- **Choice E** → Glomerulonephritis urine analysis would show blood Casts + dark urine + PAINLESS
- **Choice F** → Hypernephroma/RCC presents in old **smoker** + hematuria + painful flank mass +/- paraneoplastic syndromes (increased EPO or Hypercalcemia)
- **Choice G** → Interstitial nephritis presents as **Rash + Fever + Eosinophils/WBCs in urine + painless**.
 - Caused by **NSAIDs, B-lactams, and cephalosporins**
- **Choice I** → Pyelonephritis presents as fever + **costophrenic angle tenderness** + casts.

Q36

A 29-year-old woman comes to the physician because of a 5-week history of fatigue and a 4-day history of heart palpitations and anxiety. She has primary hypothyroidism treated with triiodothyronine. She says that she has doubled the dose of the medication over the past week because of fatigue. Her pulse is 112/min, and blood pressure is 126/70 mm Hg. Physical examination shows a fine motor tremor of the hands. Deep tendon reflexes are brisk. Thyroid function testing is most likely to show which of the following sets of serum concentrations?

Choices	Thyroid-stimulating Hormone	Free Thyroxine	Free Triiodothyronine
A	Increased	Increased	Increased
B	Increased	Increased	Decreased
C	Increased	Decreased	Increased
D	Decreased	Increased	Increased
E	Decreased	Increased	Decreased
F	Decreased	Decreased	Increased

▼ **Explanation**

- **Answer is F**
 - **IMP Clues:**
 - 5 weeks of fatigue & 4 days of palpitations & anxiety (hypo then hyperthyroidism?)
 - She has 1ry hypothyroidism managed with T3 (key to answer Q)
 - She doubled the dose of the med over past week (explains the switch from hypo to hyperthyroidism symptoms)
 - Pulse 112/min + fine motor tremors + brisk tendon reflexes (signs of hyperthyroidism)
- Q asks what is expected serum concentrations.
 - **First, you must know that:**
 - Hypothalamus → TRH → pituitary → TSH → Thyroid Gland → T4 → peripheral tissue → T3
 - **Second, T4 is converted to T3** via 5-deiodinase enzyme **but not from T4 back to T3**.
 - So, if I give T3 (Triiodothyronine), this will cause feedback inhibition on TSH, which will decrease T4.
 - Only T3 will increase as it is given externally.
 - **Final Findings: High T3 - Low T4 - Low TSH**

? Patient with hypothyroidism treated with Levothyroxine + she doubled the dose last week + now has tremors & palpitations. What is expected serum concentrations?

▼ **Answer**

- *Decreased TSH*
- *Increased T4*
- *Increased T3*

T4 is given externally so increased. T4 is then converted to T3 peripherally, so also T3 increases. The increase in T3/T4 causes feedback inhibition and decrease in TSH.

Q37

An 81-year-old man comes to the physician for ongoing management of hypertension of 20 years' duration. His temperature is 36.8°C (98.2°F), pulse is 80/min, respirations are 20/min, and blood pressure is 200/110 mm Hg. To reconfirm the patient's blood pressure, the physician places his index finger over the radial artery while inflating the sphygmomanometer cuff to just above the previously measured systolic blood pressure level. At this point, the radial artery becomes non-pulsatile but remains easily palpable even as the cuff is further inflated. Which of the following best explains this phenomenon?

- A. Atherosclerosis
- B. Connective tissue disease
- C. Left ventricular hypertrophy
- D. Thrombosis
- E. Vasculitis

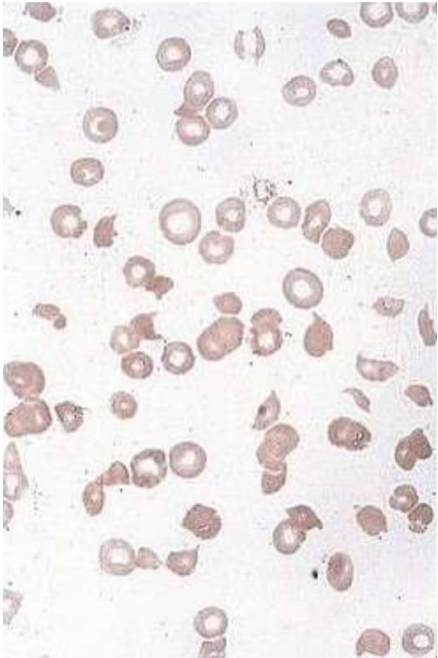
▼ Explanation

- **Answer is A (Atherosclerosis)**
 - This is **Monckeberg Medial Calcific Sclerosis of the Elderly** or **Advanced Atherosclerosis**
 - As people grow, they become more liable to get atherosclerosis & calcification of arterial walls.
 - This causes the arteries to **feel stiff & “rope-like” (Osler Sign)** and also **decreases compliance**.
 - Normally, vessels are compliant, so when the cuff is inflated → no blood → vessel collapse & becomes **not** palpable.
 - In advanced atherosclerosis or Monckeberg Medial Calcific Sclerosis, the calcification causes the vessel to **stay palpable** even when the cuff is inflated.

Q38

A previously healthy 45-year-old woman has had fever, confusion, and decreased urine production for the past 2 days. Her temperature is 38.3°C (101°F). Laboratory studies show: A peripheral blood smear is shown.

Hemoglobin	9 g/dL
Hematocrit	27%
Leukocyte count	10,500/mm ³
Neutrophils	65%
Lymphocytes	25%
Monocytes	8%
Eosinophils	2%
Reticulocyte count	8%
Mean corpuscular volume	95 μm ³
Platelet count	18,000/mm ³
Prothrombin time	12.8 sec (INR=1.0)
Partial thromboplastin time (activated)	32 sec
Fibrinogen	245 mg/dL (N=200-400 mg/dL)
Fibrin split products	<10 (N=<10)



Which of the following is the most likely cause of these findings?

- A. Aplastic anemia
- B. Disseminated intravascular coagulation
- C. Fulminant liver failure
- D. Thrombotic thrombocytopenic purpura
- E. Vitamin B₁₂ (cobalamin) deficiency

▼ Explanation

- **Answer is D (Thrombotic Thrombocytopenic Purpura)**
 - **IMP Clues:**
 - Fever (Important component)

- Decreased urine production (renal dysfunction)
- Hemoglobin 9 + MCV 95 (Normocytic anemia)
- Retics 8% (hemolytic with preserved production)
- Platelet count 18,000 (Thrombocytopenia)
- Smear shows schistocytes

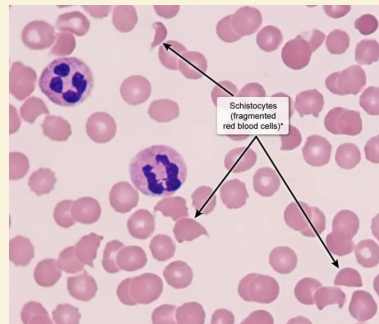
• **Dx → Thrombotic Thrombocytopenic Purpura (TTP)**

- Characterized by Pentad of:
 1. **Thrombocytopenia**
 2. **Hemolytic Anemia with Schistocytes**
 3. **Renal Failure**
 4. **+/- Fever**
 5. **+/- CNS dysfunction**
- Pathophysiology:
 - **Antibodies against/Mutation in a protein called ADAMTS13** (which is a metalloproteinase that breaks down vWF multimers)
 - **ADAMTS13 Deficiency → Excess vWF → microthrombus formation → blockage of small vessels → RBC Fragmentation (Hemolysis & Schistocytes) and End-Organ Damage.**
- Triggers: include **infection, drugs**, or even **idiopathic**

? What would this patient's peripheral blood smear show?

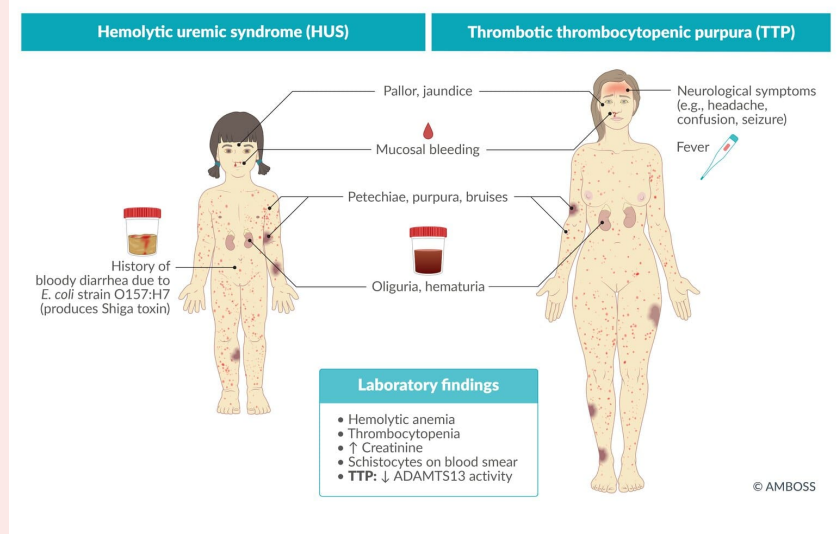
▼ **Answer**

Schistocytes
(Helmet Cells)
(Fragmented RBCs)



Differentiating between TTP & HUS is HY:

- **Thrombotic Thrombocytopenic Purpura** is caused by **ADAMTS13 protein mutation/antigenic destruction**
 - Presents as: **Thrombocytopenia, Renal Failure, Hemolytic Anemia with schistocytes +/- Fever & Neurological Dysfunction (AMS)**
- **Hemolytic Uremic Syndrome** is caused by **Shiga-like Toxin producing E.coli (EHEC O157:H7)**
 - Presents as: **Thrombocytopenia, Renal Failure, and Hemolytic Anemia with schistocytes**



▼ **Other Choices**

- **Choice A** → Aplastic anemia would have Low Reticulocyte Count + Smear will not show Schistocytes
- **Choice B** → DIC would have high PT & PTT + Low PLTs + LOW fibrinogen & HIGH Fibrin split products
- **Choice C** → Acanthocytes / Spur Cells would be seen on smear in patients with FLF. If it was a Hepatology Q, they would've included Lab values of Liver enzymes.
- **Choice D** → We would have MCV > 100, a macrocytic anemia with smear showing Hypersegmented neutrophils & large RBCs

Q39

A 39-year-old woman with rheumatoid arthritis comes to the physician for a follow-up examination. Treatment with multiple medications, including prednisone and methotrexate, has not been effective at slowing the progress of her condition. The most appropriate next step in pharmacotherapy is a drug that blocks the effects of which of the following cytokines?

- Interferon gamma
- Interleukin-2 (IL-2)
- IL-4
- IL-10
- Tumor necrosis factor- α

▼ Explanation

- Answer is E (Tumor Necrosis Factor-alpha)

- IMP Clues

- Rheumatoid Arthritis + treated by prednisone & MTX has not been effective at slowing progress (PROGRESS IS KEYWORD, RA has 2 arms of treatment: one for pain, and one for disease progression)

- Dx → Rheumatoid Arthritis

- Treatment of RA has 2 arms

1. Relief of Pain

- First Line → **NSAIDs**
- In cases where NSAIDs are not sufficient (patient still in pain), then we switch to Second Line → **Corticosteroids**

2. Slowing Disease Progression (DMARDs)

- First Line → **Methotrexate**
- In cases where MTX is not sufficient (disease still progressing), then we switch to Second Line → **Biologics**
 - Most Commonly used biologics are **TNF-alpha blockers**
 - Adalimumab - Infliximab - Certolizumab Pegol - Golimumab - Etanercept
 - Other commonly assessed drugs include **Leflunomide** (Dihydroorotate dehydrogenase inhibitor)

? HY Related Qs:

1. What is the MOA of MTX? What are some drugs with the same MOA? What are the HY side effects of MTX?

- ▼ Answer

- MOA → **Dihydrofolate Reductase Inhibitor**
- Drugs with the same MOA → **Trimethoprim & Pyrimethamine**
- HY Side effects → **Neutropenia, Pulmonary Fibrosis, Hepatotoxicity**

2. What is the Odd TNF-alpha blocker & why?

- ▼ Answer

Etanercept - TNF-alpha recombinant receptor

- Etanercept can bind to and mop up soluble TNF-alpha floating around in the plasma.
- Remaining TNF-alpha blockers are **monoclonal antibodies**



USMLE can differentiate between RA and OA by site of hand nodules:

- RA ⇒ **Spare**s DIPs and 1st CMC
- OA ⇒ **Affect**s DIPs and 1st CMC

Let's Review Rheumatoid Arthritis:

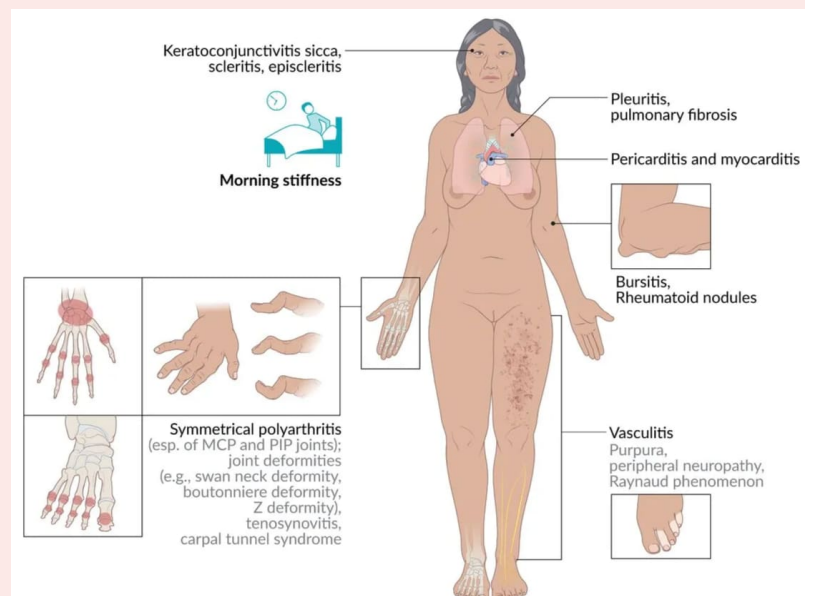
- Autoimmune disease characterized by **CD4 T-cell activation** in response to **antigen-antibody complex deposition**, causing release of cytokines that induce **pannus formation** (synovial hyperplasia by proliferative granulation tissue)
 - This results in **erosion of articular cartilage and bone**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

? Patient has joint pain, fatigue, low-grade fever, and lower limb edema. What else is expected on physical examination?

- ▼ Answer

Splenomegaly - This is **Felty Syndrome** (one of the extraarticular manifestations of RA)

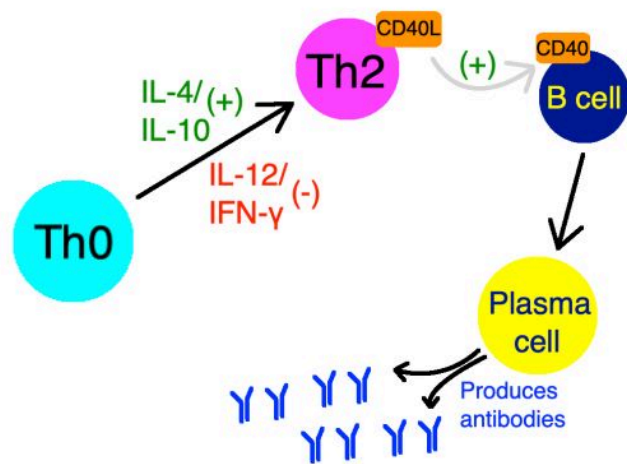
- Mnemonic is **"SANTA"** → **S**plenomegaly, **A**nemia, **N**eutropenia, **T**hrombocytopenia, **A**rthritis
 - Joint pain → **Arthritis**
 - Fatigue → **Anemia**
 - Low-grade fever → hinting to **neutropenia**
 - Edema of lower extremities → Chronic inflammation of RA causes **decrease in albumin & pre-albumin (negative acute phase proteins)** → decreased oncotic pressure → **Edema**



▼ Other Choices

- **Choice A** → INF-gamma is what activates macrophages.
 - **HY to know that INF-gamma is used in CGD & IL-12 deficiency**
- **Choice B** → IL-2 is a T lymphocytes stimulator

- **Choices C & D** → IL-4 & IL-10 play a role in stimulation of Th0 → Th2 to bind to B-cells & produce plasma cells



Q40

A 57-year-old woman comes to the office because of a 5-week history of progressive weakness in her arms and legs. She says the weakness is most apparent when she tries to lift dishes out of overhead cupboards and when she walks up and down flights of stairs. Muscle strength initially improves upon repetitive manual motor testing. Sensation is intact in all extremities. Which of the following mechanisms best explains this patient's weakness?

- A. Autoimmune downregulation of Ca^{2+} channels of the presynaptic terminal
- B. Blockade of nicotinic acetylcholine receptors at the neuromuscular junction
- C. Blockade of sodium channels at the nodes of Ranvier
- D. Impaired excitation-contraction coupling of the muscle
- E. Increased activation of muscle K^{+} channels

▼ Explanation

- **Answer is A (Autoimmune downregulation of Ca channels of the presynaptic terminal)**

◦ IMP Clues

- Progressive weakness in her arms and legs (okay, so we have to figure out the etiology)
- Weakness most apparent when she tries to lift dishes out of overhead cupboard or walks up & down flight of stairs (This is proximal muscle weakness, Hips/Shoulders)
- Strength initially improves upon repetitive manual motor testing (**BIGGG CLUE**, this is very HY differentiating point between diseases)
- Sensation is intact in all extremities (pure motor affection)

• Dx → Lambert-Eaton Syndrome

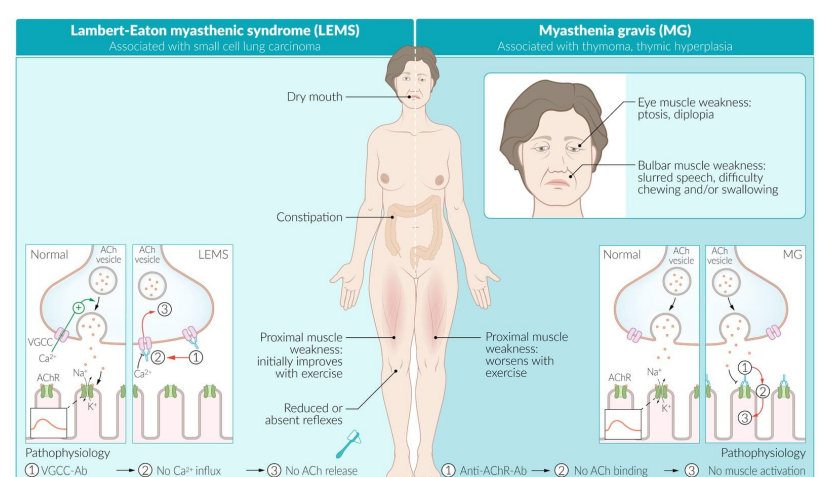
- Etiology → Antibodies against **pre-synaptic** voltage-gated **calcium** channels
- Associated Tumor → **SCLC**
- Behavior → Weakness **improves** with **repeated movements**
- Response to Tensilon test (edrophonium) → **NO** improvement

? Compare Lambert-Eaton Syndrome with Myasthenia Gravis

▼ Answer

Myasthenia Gravis

- Etiology → Antibodies against **post-synaptic Ach receptors**
- **Associated Tumor** → Thymoma
- Behavior → Weakness **improves** with **rest**
- **Response to Tensilon test (edrophonium)** → **Improvement**



▼ Other Choices

- **Choice B** → Refers to MG, which we just discussed
- **Choice C** → This can refer to many things, but notably **pufferfish which contains tetrodotoxin**. It blocks Na channels & causes **paralysis, sensory manifestations** (numbness, tingling), up to respiratory insufficiency & cardiac arrest

- **Choice D** → Refers to **Malignant Hyperthermia**
 - History of **Succinylcholine / Halothane / Sevoflurane** use
 - **Fever, muscle rigidity, acidosis, and tachycardia**
 - Caused by **persistent activation of Ryanodine calcium channels** on the Sarcoplasmic reticulum.
 - Calcium keeps flooding into the cell → **Muscle contraction & Rigidity**
 - Massive amounts of ATP are consumed
 - Metabolic pathways in the body are pumped-up to keep with the increasing demand → Fever, Hypoxia, and Acidosis
 - **Treatment** → **Dantrolene** (Binds to & inhibits Ryanodine Calcium channel Receptors)
- **Choice E** → Garbage & LY.

Q41

A 26-year-old woman comes to the physician 5 weeks after the birth of her first child. She worries constantly that the infant is ill and wakes him 10 to 14 times every night to make sure he is well. She has had no crying spells or problems with appetite. She is worried that she will infect the infant with her germs and washes her own hands 30 times per day. For 2 months prior to the delivery, she worried about people breaking into her house and checked the lock on the front door three to four times every night. She is not breast-feeding. Which of the following is the most appropriate pharmacotherapy?

- A. Alprazolam
- B. Haloperidol
- C. Lithium carbonate
- D. Methylphenidate
- E. Phenelzine
- F. Sertraline

▼ **Explanation**

- **Answer is F (Sertraline)**
 - **IMP Clues**
 - Worries constantly that the infant is ill (the obsession)
 - Wakes him 10-14 times every night to make sure he is well (the compulsions)
 - She is worried that she will infect the infant with her germs (the 2nd obsession)
 - Washes her hands 30 times per day (the 2nd compulsion)
 - She worried about people breaking into her house (the 3rd obsession)
 - Checked the lock on the front door 3-4 times every night (the 3rd compulsion)
- **Dx → Obsessive-Compulsive Disorder (OCD)**
 - Made up of 2 things
 - **Obsessions** → Unwanted and intrusive thoughts, images, or urges that cause significant anxiety or distress
 - **Compulsions** → Repetitive behaviors a person performs in response to an obsession
 - In OCD, the patient **hates** that he/she is OCD (they are aware that they have these obsessions & compulsions, and they **HATE IT**)
 - Treatment → **SSRIs & Clomipramine** (a TCA)
 - Sertraline is an SSRI

? Which of the following agents are SSRIs? (check all that apply)

- | | |
|-------------------|----------------|
| A) Citalopram | E) Fluoxetine |
| B) Desvenlafaxine | F) Milnacipran |
| C) Duloxetine | G) Paroxetine |
| D) Escitalopram | H) Sertraline |
| | I) Venlafaxine |

▼ **Answer**

Citalopram - Escitalopram - Fluoxetine - Paroxetine - Sertraline

The remaining are SNRIs

▼ **Other Choices**

- **Choice A** → Benzodiazepine
- **Choice B** → Typical Antipsychotic, used in schizophrenia, acute psychosis, or Tourette's Syndrome (yes, the one with the tics)

- **Choice C** → Mood stabilizer, used in bipolar disorder
- **Choice D** → Stimulant, used in ADHD
- **Choice E** → Monoamine Oxidase inhibitor

Q42

A 5-year-old boy is brought to the physician because of a 4-day history of red cheeks and rash over his arms and legs. He also has a 1-week history of fever. He has received all of the scheduled childhood immunizations. His vital signs are within normal limits. Physical examination shows malar erythema and a red, lacy rash over the upper and lower extremities. His hemoglobin concentration is 10 g/dL (N=11–15). Which of the following is the most likely cause of this patient's anemia?

- A. Antibody-mediated destruction of erythrocytes in the peripheral circulation
- B. Destruction of erythrocytes in the peripheral circulation by an infectious agent
- C. Interruption of erythrocyte production
- D. Loss of erythrocytes caused by occult gastrointestinal bleeding
- E. Sequestration of erythrocytes in the spleen

▼ Explanation

- **Answer is C (Loss of Erythrocyte production)**

◦ IMP Clues:

- Red Cheeks / malar rash & Rash over his arms & legs / red lacy rash (Slapped cheeks rash + lacy rash are buzzy for Fifth Disease)
- 1 week history of fever (fever is also a feature)
- Hemoglobin concentration is 10 g/dl (anemic)

- **Dx → Erythema Infectious (Fifth Disease)**

- **Parvovirus** Infects **erythroid precursor cells in bone marrow** & causes **interruption of erythrocyte production, resulting in Transient Aplastic Anemia** [asked on NBME]
 - Usually asymptomatic / mild in healthy children (causes Fifth Disease), but can be life-threatening in children with **sickle cell anemia/Thalassemia/Hereditary Spherocytosis → Aplastic Crisis**
- Erythema Infectiosum (Fifth Disease) presents as **Slapped Cheeks rash in children, that then descends causing a lacy reticular rash**.
 - The Rash appears **after** the fever.
- Other HY Presentation of Parvovirus:
 - **Aplastic Crisis:** in patients with SCD, Thalassemia, or Hereditary Spherocytosis
 - **Hydrops Fetalis:** TORCH infection in pregnant women.
 - **Simple Arthralgia:** in adults.



? Characteristics of Parvovirus?

▼ Answer

Single-Stranded DNA Naked Virus

USMLE Can give you a picture similar to the one above, so know how the reticular/lacy rash looks like:



*Due to parvovirus B19 infection.

©UWorld



Parvovirus is the **SMALLEST DNA virus** known!

▼ Other Choices

- **Choice A** → refers to Autoimmune Hemolytic Anemia, which could be Warm AHA (IgG) or Cold AHA (IgM)
- **Choice B** → refers to either **Malaria** (if vignette mention travel outside the USA) or **Babesia** (if vignette doesn't mention travel outside USA)
- **Choice D** → No mention of GI bleeding + would cause IDA not aplastic anemia
- **Choice E** → No mention of splenomegaly & hypersplenism, usually associated with thrombocytopenia as well, so bleeding tendency & petechiae

Q43

An 8-year-old boy is brought to the physician by his parents because they are concerned about his weight. His father has a BMI of 27 kg/m², and his mother has a BMI of 25 kg/m². The patient is at the 75th percentile for height, above the 95th percentile for weight, and above the 95th percentile for BMI. Physical examination shows no other abnormalities. Which of the following is the most likely explanation for the obesity in this patient?

- A. Calorie consumption that exceeds energy expenditure
- B. Decreased leptin production
- C. Diet with a high fat content
- D. Diet with a high glycemic index
- E. Increased cortisol secretion
- F. Increased insulin production

▼ Explanation

- **Answer is A (Calories consumption that exceeds energy expenditure)**
 - **IMP Clues**
 - Father has a BMI of 27 & Mother of 25 (Father is overweight & mother is borderline overweight, just an overweight household)
 - Patient has above 95th percentile for weight & BMI (Obese patient as well which is expected)
 - Physical examination shows no other abnormalities (excludes pathological causes like syndromes or endocrinal disorders)
 - Q asks what is most likely explanation?
 - Well, considering that his parents are overweight, the child will most likely also become overweight/obese due to the *eating patterns of the family*, so **Calories consumption that exceeds energy expenditure** (Choice A) makes the most sense.
 - **Eating more & moving less = Fat gain**

▼ Other Choices

- **Choice B** → Leptin is produced by adipose cells & makes you want to eat less. The more fat cells you have, the more leptin you produce. This child is obese, so he has increased leptin levels.
- **Choice C & D** → We don't know for sure & we're just guessing. If you chose C, then it might have been D, and if you choose D, it might have been C. It could be a mixture of both, we can't say for sure.
- **Choice E & F** → Increase hormones will most likely be associated with "physical exam" findings. IR would have acanthosis nigricans, while cortisol secretion might have cushingoid appearance.

Q44

A population of vegetarians is surveyed to investigate the association between garlic/onion consumption and serum cholesterol concentration. The following results are found:

Garlic/Onion Consumption	Mean Serum Cholesterol (mg/dL)
High	159
Low	208

Which of the following tests should be used to determine whether the means are statistically different?

- A. Chi-square
- B. Rank correlation
- C. Sign test
- D. t-Test

▼ Explanation

- Answer is D (t-Test)
 - Here we are dealing with “means” so **numerical variables**.
 - We also have **2 groups**, High consumption vs Low consumption
 - So best test is **t-Test**



Comparing Variables:

1. Numerical?

- a. 2 groups → **t-Test**
- b. 3+ groups → **ANOVA**

2. Categorical?

- a. Small sample size → **Fisher's**
- b. Large sample size → **Chi-square**

Mnemonic: “Tests Are Fucking Confusing”

Q45

A 60-year-old woman comes to the physician because of a 1-year history of episodes of involuntary rhythmic jerking of her right leg and foot. These episodes last approximately 3 minutes. Neurologic examination shows an increased right ankle jerk reflex. A Babinski sign is present on the right. An MRI of the brain shows a 2-cm, round, enhancing lesion within the interhemispheric fissure in the region of the central sulcus. Which of the following is the most likely diagnosis?

- A. Astrocytoma
- B. Lymphoma
- C. Meningioma
- D. Metastatic carcinoma
- E. Oligodendroglioma

▼ Explanation

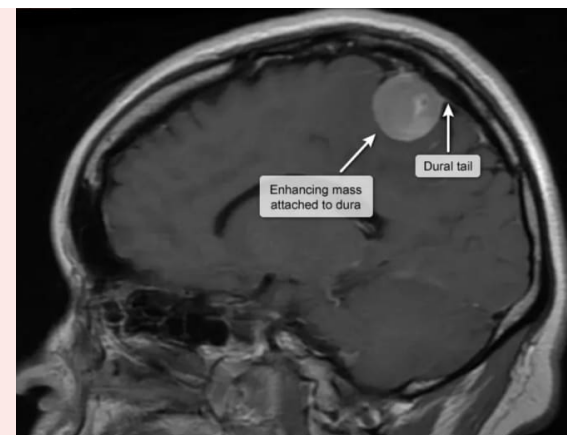
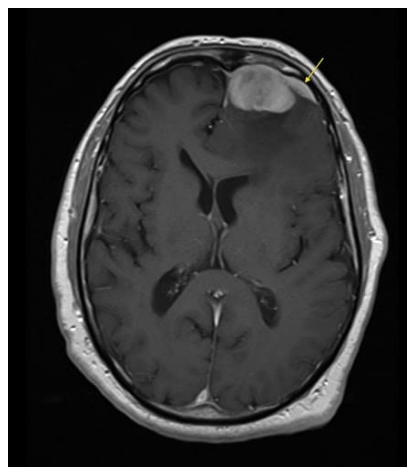
- Answer is C (Meningioma)
 - IMP Clues:
 - Involuntary rhythmic jerking of her right leg & foot (localized seizure, so left upper/medial lobes affected)
 - Increased right ankle jerk reflex + Babinski sign is present on the right (UMNL, Babinski + hyperreflexia, so we know it's something from the cortex to before the AHCs)
 - MRI shows 2cm, round, enhancing lesion within the interhemispheric fissure in the region of the central sulcus (enhancing = meninges, and site explains symptoms)
 - Dx → Meningioma
 - MNEMONIC: “Men have problems with PSA”
 - Meningioma
 - Psammoma Bodies (Seen on biopsy)
 - Spindle Cells (Seen on biopsy)
 - Arachnoid origin **[asked on NBME]**

Picture below shows another Meningioma with its buzzy Dural Tail:

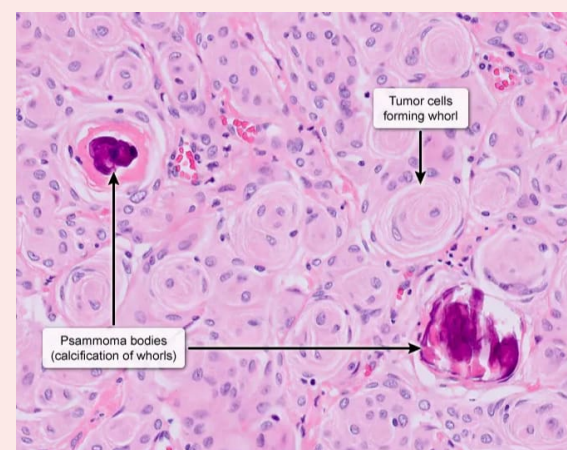
- The rise from **meninges** so they are always *near the surface*
- Meningiomas **enhance** (appear white) on imaging & have these “**dural**” tails (yellow arrow below).

? What conditions are associated with meningiomas?

▼ **Answer**
MEN1 - NF2- NF1



Picture below the Psammoma Bodies on Histological biopsy:

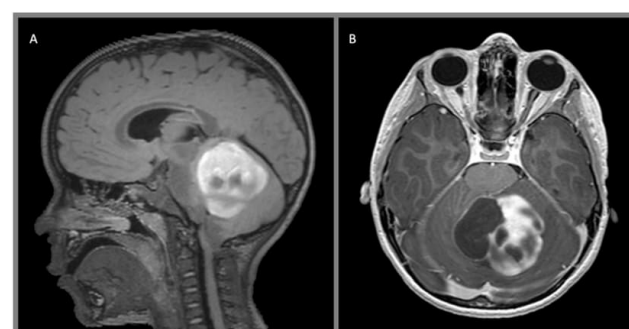


▼ Other Choices

- **Choice A** → Astrocytoma refers to any tumor that originate from astrocytes. The 2 main HY ones for you to know are:

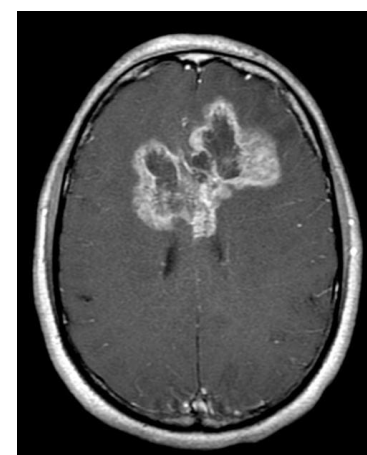
1. Pilocytic Astrocytoma

- Most Common brain tumor in pediatrics
- Solid (White) & Cystic (Black) Components
- Histology → **Rosenthal Fibers (Eosinophilic Corkscrew Filaments)**



2. GBM

- Grade 4 Fibrillary Astrocytoma
- Heterogenous mass because of necrosis & hemorrhage
- **Midline Mass that invades corpus callosum**
- Histology → **Pseudo-Palisading Cells**



- **Choice B** → CNS Lymphomas are enhancing lesions. On the USMLE the Qs will be as follows:

▼ **HIV patient with brain enhancing lesion**

→ Think Toxoplasmosis

▼ **HIV patient with brain enhancing lesion thought to be Toxo & ttt is started, but patient got worse & lesion got bigger**

→ Think Lymphoma

▼ **HIV patient with brain enhancing lesion + prophylaxis of PJP**

→ Think Lymphoma

Prophylaxis of PJP is the same as the Prophylaxis of Toxo

▼ Patient with hx of autoimmune disease + brain enhancing lesion

→ Think Lymphoma

- **Choice D** → Metastatic Carcinoma would be **multiple lesions** not one, and they would be at **grey-white junctions**.
- **Choice E** → Oligodendroglioma
 - Origin → Oligodendrocytes (myelinates CNS nerves)
 - Histology → **Fried Egg appearance + Chicken-wire capillary pattern**

Q46

A 6-year-old boy who recently emigrated from Russia is brought to the physician by his parents because of unstable gait and incoordination for 2 weeks. He has had frequent pale, bulky stools for 4 years and two episodes of bacterial pneumonia and chronic cough since the age of 1 year. He is below the 3rd percentile for height and weight. Increased rhonchi are heard over both lung fields. Neurologic examination shows ataxia, absence of deep tendon reflexes, and loss of proprioception. Stool analysis shows an increased fat concentration. Which of the following vitamins is most likely deficient in this patient?

- A. Biotin
- B. Niacin
- C. Vitamin C
- D. Vitamin D
- E. Vitamin E

▼ Explanation

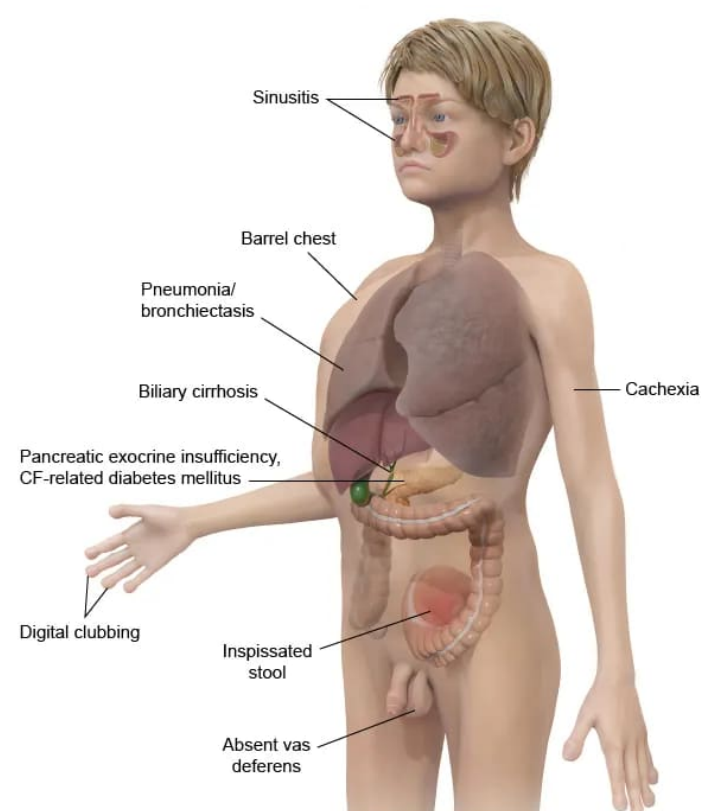
- **Answer is E (Vitamin E)**
 - **IMP Clues:**
 - Unstable gait & incoordination (could be cerebellar cause or dorsal column)
 - Pale Bulk stools + Stool analysis shows increased fat concentration (Steatorrhea & Fat-malabsorption)
 - Bacterial pneumonia recurrence & chronic cough (PUL + STEATORRHEA = CF)
 - 3rd percentile for height & weight (due to malnutrition)
 - Ataxia, absence of deep tendon reflexes, and loss of proprioception (buzzy triad of Vitamin E deficiency)

• **Dx → Cystic Fibrosis**

- **AR disorder**; Classically caused by a **deletion ($\Delta F508$; deletion of phenylalanine)** in the **CFTR** gene on **Chromosome 7**
- **Misfolded CFTR channels** (these are proteins, which are misfolded so defected protein structure) **retained in the Golgi**.

◦ **C/P & Complications**

- **Thick impacted secretions in the PANCREAS**
 1. Pancreatitis
 2. Pancreatic Enzymes insufficiency
 - a. Malabsorption
 - b. **Fat-Soluble Vitamins Deficiencies**
 - i. Vitamin K → Bleeding Tendency
 - ii. **Vitamin E → Ataxia, Hemolysis, Peripheral neuropathy, Muscle weakness [HY AS FUCKKKK]**
 - iii. Vitamin D → Ricket's & Osteomalacia
 - iv. Vitamin A → Retinitis Pigmentosa, Corneal Ulcers, Night Blindness, Bitot Spots... you get it
- **Thick impacted secretions in the Lungs**
 - Cilia cannot work & push-out debris/infection
 1. Recurrent Sinusitis & Respiratory Tract Infections



- a. **Staph aureus MOST COMMON if age less than 20 years, while Pseudomonas MOST COMMON if age > 20 years**

2. Chronic productive cough & SOB & Clubbing
3. Nasal Polyps & Bronchiectasis

▼ Other Choices

- **Choice A** → Vitamin B7 (Biotin) deficiency is caused by ingestion of raw **egg whites**, which contain avidin. Avidin binds biotin and prevents absorption.
- **Choice B** → Niacin (Vitamin B) deficiency is caused by **Hartup disease**, in which **loss of tryptophan (and other amino acids) in PCT causes Pellagra (Diarrhea - Dementia - Dermatitis)**
- **Choice C** → Scurvy
- **Choice D** → Ricket's / Osteomalacia

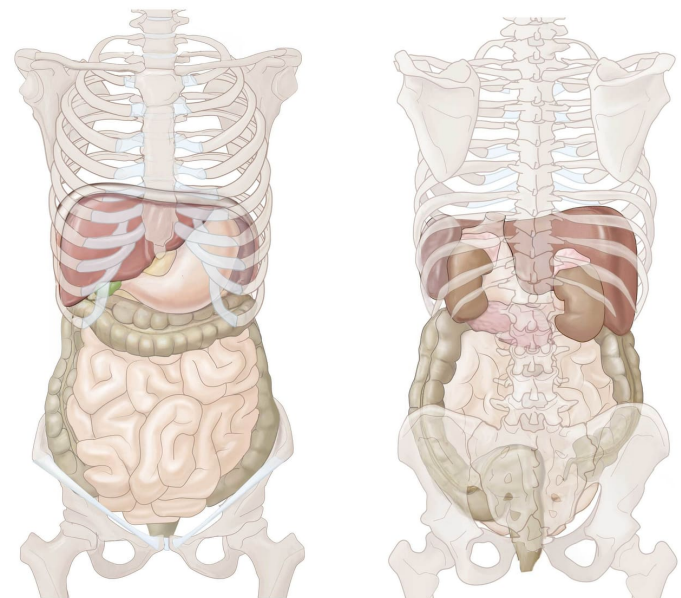
Q47

A 27-year-old man who is a construction worker is brought to the emergency department 30 minutes after he fell from a ladder approximately 14 feet onto a pile of boards from a demolished house. A long, sharp piece of wood penetrated his left side, immediately inferior to the middle of the body of his left 12th rib. A CT scan shows that the wood sliver has grazed the inferior pole of the left kidney and its tip is resting in the structure immediately anterior. This structure is most likely which of the following?

- A. Body of the pancreas
- B. Duodenum
- C. Splenic flexure
- D. Stomach
- E. Suprarenal gland

▼ Explanation

- **Answer is C (Splenic Flexure)**
 - **IMP Clues**
 - Penetrated his left side (this excludes duodenum)
 - Graved the inferior pole of the left kidney & its tip is resting in the structure immediately anterior (okay, so anterior to inferior pole of left kidney. This excludes, A, D, and E)
 - Easy Anatomy Q
 - Let's exclude to get there:
 - **Choice A** → Body of pancreas is a little far, can be related to anterior surface of kidney but not inferior
 - **Choice B** → Duodenum is on the Right
 - **Choice D** → Related to anterior border of SUPERIOR pole of left kidney
 - **Choice E** → SUPRA-renal, so not related to inferior pole.
 - Picture above shows relations of different structure to the Left Kidney.
 - Note how the **splenic flexure** is positioned in relation to the kidney (Anterior to inferior pole)



Q48

During a clinical study, 15 patients with renal allografts volunteer to undergo treatment with Drug X. This drug is converted to a purine antagonist that interferes with the synthesis of nucleic acids and is toxic to dividing cells. Drug X is most likely which of the following?

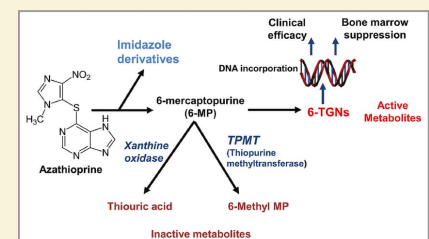
- A. Azathioprine
- B. Cyclosporine
- C. Methylprednisolone
- D. Rapamycin
- E. Tacrolimus

▼ Explanation

- **Answer is A (Azathioprine)**
 - Azathioprine is metabolized into **6-MP**, which in turn **inhibits PRPP-amidotransferase** (rate-limiting enzyme in de novo purine synthesis)
 - Inhibiting Purine synthesis would affect proliferation of *all rapidly dividing cells nonspecifically*, causing:
 - **LOW B-cells**
 - **LOW T-cells**
 - **LOW Immunoglobulin levels**
 - **LOW IL-2 activity.**

? What drugs cannot be given with Azathioprine or 6-MP?

- ▼ Answer
- Xanthine Oxidase Inhibitors** - Allopurinol & Febuxostat



▼ Other Choices

- **Choice B → Cyclosporin**
 - MOA: **Inhibits Cyclophilin** → **decreases** intracellular **calcineurin** → **decreases IL-2 transcription**
 - Side Effects: **Hypertension, Hyperkalemia (Renal Failure), Hypertrichosis, Gingival Hyperplasia**

? What are HY drugs that cause gingival hyperplasia?

- ▼ Answer
1. Cyclosporin
 2. Phenytoin
 3. Verapamil

- **Choice C → Methylprednisolone**
 - It is a **corticosteroid**; a potent type often used in **acute settings as IV** (used commonly for MS flares or severe asthma exacerbations)
 - MOA: **Binds to intracellular (cytoplasmic) receptors** → translocates to nucleus → **gene transcription**
 - **Inhibits Phospholipase A2** → decreases Arachidonic acid → decreases COX & LOX activity → decreases PGs & LTs
 - **Inhibits Cytokines production**
 - **Apoptosis of T-cells**
 - Side Effects: **Immunosuppression, Diabetogenic, Osteoporosis & Avascular necrosis, Hypertension, Adrenal suppression, and cushingoid features**
- **Choice D → Rapamycin (Sirolimus)**
 - MOA: **Inhibits mTOR** → **DOESN'T decreases** intracellular **calcineurin** (all it does is block its signaling) → **decreases response to IL-2**
 - Side Effects: **Dyslipidemia**
- **Choice E → Tacrolimus**
 - MOA: **Inhibits FK506** → **decreases** intracellular **calcineurin** → **decreases IL-2 transcription**
 - Side Effects: **Hyperkalemia (Renal Failure), Type 2 DM**

Q49

A 42-year-old woman is brought to the emergency department by her husband after having a generalized tonic-clonic seizure. She tells the physician that she smelled a foul odor for several seconds immediately before the seizure. Her husband did not perceive the odor. From which of the following regions of the brain did the seizure most likely arise?

- A. Brain stem
- B. Frontal lobe
- C. Occipital lobe
- D. Parietal lobe
- E. Temporal lobe

▼ Explanation

- **Answer is E (Temporal Lobe)**
 - **IMP Clues**
 - Generalized tonic-clonic seizure
 - Smelled a foul odor immediately before the seizure that her husband didn't smell (basically, an olfactory "aura")
 - **Dx → Temporal Lobe Seizure**
 - Originates from the **medial temporal lobe**
 - **Most common site of seizure origin**, so if USMLE gives you a vignette without any details about the tonic-clonic seizure, choose temporal lobe
 - **Often preceded immediately by auras**
 1. **Visual Aura** (temporal lobe contains *inferior optic radiation*) so excessive neuronal discharge affects the radiation → visual symptoms
 2. **Olfactory Aura** (medial temporal lobe contains the *uncus*, which has the *primary olfactory cortex*), so excessive neuronal discharge affects the uncus → olfactory symptoms
 3. Other common auras include **fear & Deja Vu**.

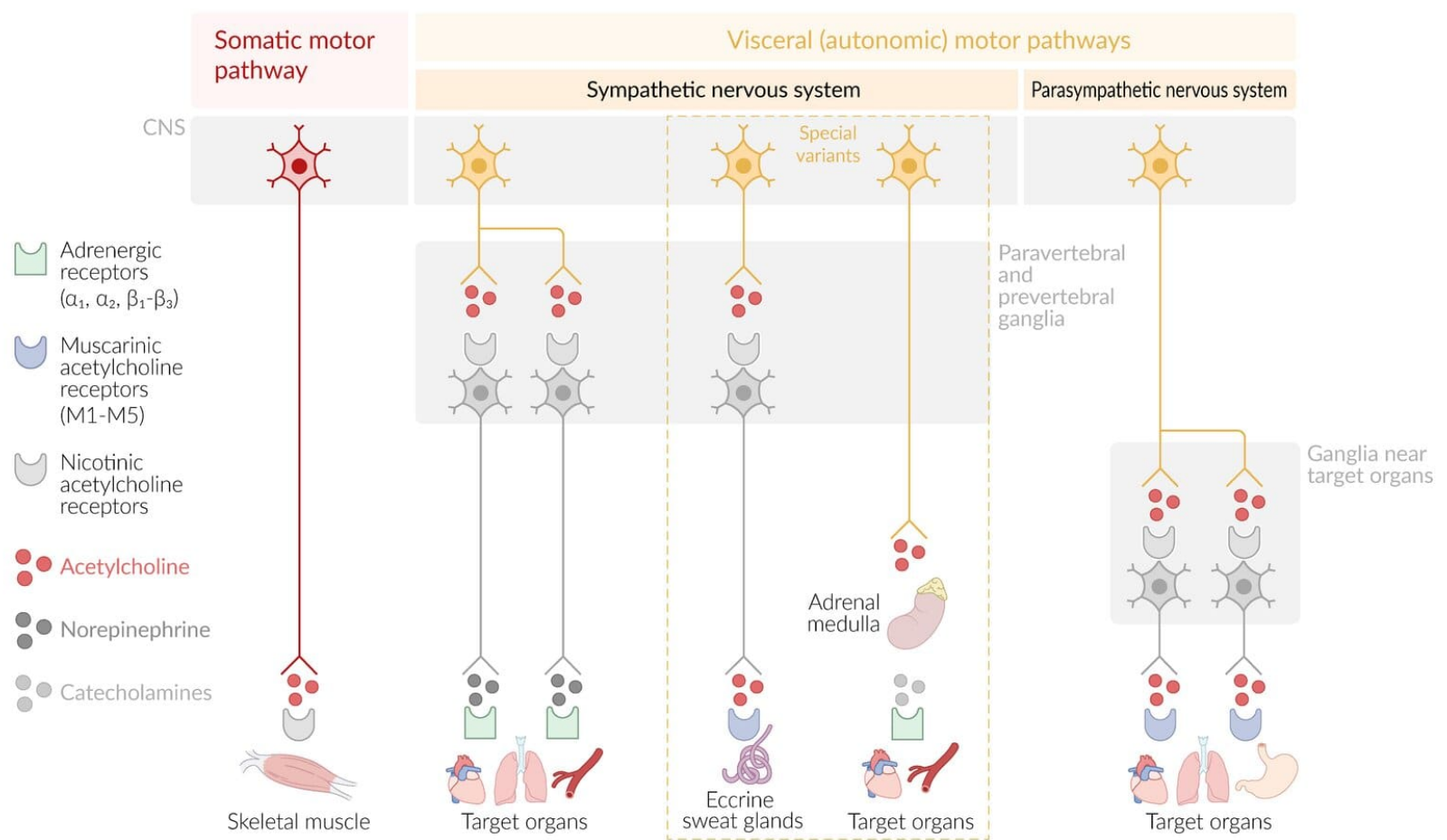
Q50

A 35-year-old man is brought to the hospital after a diving accident. Evaluation shows complete transection of the spinal cord superior to the level of sympathetic nervous outflow. Which of the following responses will most likely occur if he develops a systemic infection?

- A. Alteration of the thermostatic set point
- B. Cutaneous vasoconstriction
- C. Diaphoresis following aspirin ingestion
- D. Generalized involuntary shivering
- E. Heat production by brown fat

▼ Explanation

- **Answer is A (Alteration of the thermostatic set point)**
 - **IMP Clues**
 - Complete transection of the spinal cord superior to level of sympathetic nervous outflow (Now we have no sympathetic system, and loss of all sympathetic functions)
 - Q asks what would happen if the patient develops a systemic infection?
 - Let's go through the answer choices
 - **Choice A → Alteration of the thermostatic set point**
 - Infection causes production of cytokines (IL-1, IL-6, TNF-alpha) → **PGE2 production in hypothalamus** → raises temperature set point → Fever
 - No role of sympathetic system in fever
 - **Choice B → Cutaneous Vasoconstriction**
 - In fight/flight responses, **sympathetic system is activated**, which causes **cutaneous VC** which *raises blood pressure, and diverts blood/oxygen to more vital organs*.
 - **Cutaneous Vasoconstriction is mediated by sympathetic system**
 - **Choice C → Diaphoresis**
 - Sweat glands produce sweat by **stimulation of sympathetic cholinergic fibers** (not adrenergic).



■ **Choice D → Shivering is mediated by motor neurons.**

- Hypothalamus senses that the body is below the new temperature set point
- It then sends impulses via the **descending motor fibers** into the spinal cord.
- If the spinal cord is transected, the motor fibers are interrupted = loss of shivering.

■ **Choice E → Brown fat thermogenesis** is mediated by **B3 adrenergic stimulation**, which is carried by the sympathetic system



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