



NBME EXPLANATIONS

NBME 20 Block 2

from CrackNBME

NBME 20 - Block 2

Q1

A 12-year-old girl is brought to the physician for a follow-up examination. Three months ago, she sustained a complex fracture of the left tibia, which required cast immobilization. The cast is removed. Examination of the left calf shows that it is smaller than the right calf. Which of the following processes in this patient's myocytes is the most likely cause of these findings?

- A. Anaerobic glycolysis
- B. Fatty acid degradation
- C. Glycogenolysis
- D. Oxidative phosphorylation
- E. Polyubiquitination

▼ Explanation

- **Answer is E (Polyubiquitination)**
 - **IMP Clues**
 - Patient had a complex fracture that required cast immobilization (we expect the affected muscles to be atrophied due to disuse)
 - Examination shows that the left calf is smaller than the right calf (yes, due to disuse atrophy)
 - *Q asks which process in the patient's myocytes caused these findings (ie the atrophy)*
 - Muscles require energy to function. If you're not using these muscles (like in cases of cast immobilization), then the body breaks them down to decrease energy wasting. Simply, if you don't use it, you lose it.
 - **Protein degradation in muscle atrophy happens mainly via 2 pathways:**
 1. **Ubiquitin-Proteosome Pathway** → *Ubiquitin* "tags" the to-be digested proteins, for the *proteosomes* to come in after and break them down.
 2. **Autophagy-Lysosome Pathway** → *Autophagosomes* phagocytose cell organelles, fusing then with *lysosomes* → digestion of contents

▼ Other Choices

- **Choice A** → Glucose breakdown in cytosol in absence of oxygen. No protein degradation involved.
- **Choice B** → Lipolysis. Again, no protein degradation involved.
- **Choice C** → Glycogen breakdown. No protein degradation involved.
- **Choice D** → ATP production. No protein degradation involved.

Q2

A 56-year-old man is brought to the emergency department 30 minutes after the onset of severe chest pain while mowing his lawn. His pulse is 110/min, respirations are 20/min, and blood pressure is 105/70 mm Hg. Physical examination shows cool, clammy, diaphoretic skin. Two hours after admission, pulmonary catheterization shows a pulmonary artery pressure of 40/25 mm Hg; the left atrial pressure is 25 mm Hg. Compared with a healthy person, which of the following sets of pulmonary pressure changes is most likely in this patient?

Choices	Capillary Hydrostatic	Interstitial Hydrostatic	Interstitial Oncotic
A	↑	↑	↑
B	↑	↑	↓
C	↑	↓	↑
D	↓	↑	↑
E	↓	↑	↓
F	↓	↓	↑

▼ Explanation

- **Answer is B**
 - **IMP Clues**
 - Severe Chest pain (MI, easy)
 - Pulse is 110/min + RR is 20/min + BP is 105/70mmHg (Patient is tachycardic, tachypneic, and hypotensive. Expected with MI)
 - Examination shows cool clammy diaphoretic skin (MI causing low CO, so might be Cardiogenic Shock)
 - Pulmonary artery pressure is 40/25 mmHg + LA pressure is 25mmHg (Okay, so basically MI → LV dysfunction → decreased CO and blood pools into LV → blood backs up into LA & increases the pressure → backs up into lungs causing pulmonary edema & increase PA pressure)
- **Dx → Cardiogenic Shock**

- Q asks for expected arrows:

- As I said above, MI → LV dysfunction → **decreased CO** and blood pools into LV → blood backs up into LA & increases the pressure → backs up into lungs causing **pulmonary edema** & increase PA pressure.
- Blood backing up into lung vasculature causes **high** capillary hydrostatic pressure → fluid leaves capillaries and escapes into interstitial space (causing the pulmonary edema) → **high** interstitial hydrostatic pressure & **low** interstitial oncotic pressure.
 - Low oncotic pressure is relative as the ratio of fluid to solutes increases:
 - Fluid increases → **Increased hydrostatic pressure**
 - Solutes decrease → **Decreased oncotic pressure**



What are expected arrows for Cardiogenic Shock? [CO - SVR - PCWP]

▼ Answer

- **LOW** Cardiac Output
- **HIGH** Systemic Vascular Resistance
- **HIGH** PCWP (Pulmonary Capillary Wedge Pressure = LA pressure)



Most HY cause of cardiogenic shock on the USMLE is **acute MR**, caused by **papillary muscle rupture** 2-7 days post-MI.

Q3

A 92-year-old woman who was recently admitted to a nursing home because of progressive dementia has large purpuric lesions over the dorsa of both forearms and hands. Her family states that she has had similar lesions on and off for years and that, to the best of their knowledge, these lesions occur in the absence of trauma. The woman appears well cared for and has no other indications of recent or remote injury. Her platelet count is normal. Which of the following is the most likely explanation for the purpura?

- A. Abuse by a family member
- B. Atrophy of dermal collagen
- C. Autoimmune disease
- D. Hereditary hemorrhagic telangiectasia
- E. Platelet dysfunction

▼ Explanation

- Answer is B (Atrophy of dermal collagen)

- IMP Clues

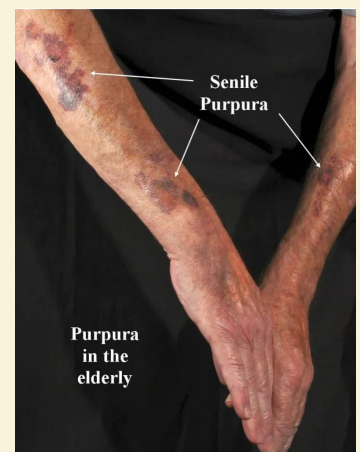
- 92-year-old woman (Age is important here)
- Large purpuric lesions over dorsa of both forearms and hands (site is important as bilaterality makes abuse unlikely, and them being confined to UL makes PLT dysfunction unlikely too)
- These lesions occur in absence of trauma (again, excluding PLT dysfunction / trauma / abuse)
- Woman appears well cared for + no other indication of recent or remote injury (excludes abuse)
- Her PLT count is normal (excludes PLT disorder, yes the problem might be function not number, but diagnosis is overwhelmingly not PLT related)

- Dx → Senile Purpura

- Also known as **Actinic Purpura** (**NOT** Actinic keratosis) or **Solar Purpura** (**NOT** Solar Keratosis)
- As we get older, our collagen **starts to lose its elasticity and tensile power**.
 - **Atrophy of dermal collagen:**
 - Makes the skin weak, wrinkly, and thin
 - **Increases vessel fragility**
 - This makes likelihood of blood extravasation & the appearance of purpura much more likely.
 - Dermal Atrophy is exacerbated by **sun exposure "solar elastosis"**; this is why the extensor surface of the forearms and hands are the most common sites for senile purpura. They are the most exposed to the sun.
- They are usually **harmless and resolve spontaneously**. This means that they are also **recurrent** (as mentioned in the vignette)
- **How to differentiate them from other causes of purpura/ecchymoses?**
 - They are **painless** (vs vasculitis, which are usually painful & palpable)
 - **Labs are normal** (vs coagulopathies & thrombocytopenia, where PT, PTT, PLTs are abnormal)
 - **No hx of meds** (vs steroid-induced dermal atrophy) **[asked on NBME]**
 - USMLE gives you a patient with some sort of **skin allergy/eczema**, where the patient applies **local steroids for a very long period of time** + comes to the physician due to **skin thinning & purpuras**. What is cause? Answer is **Steroids causing dermal thinning**.



Senile Purpura:

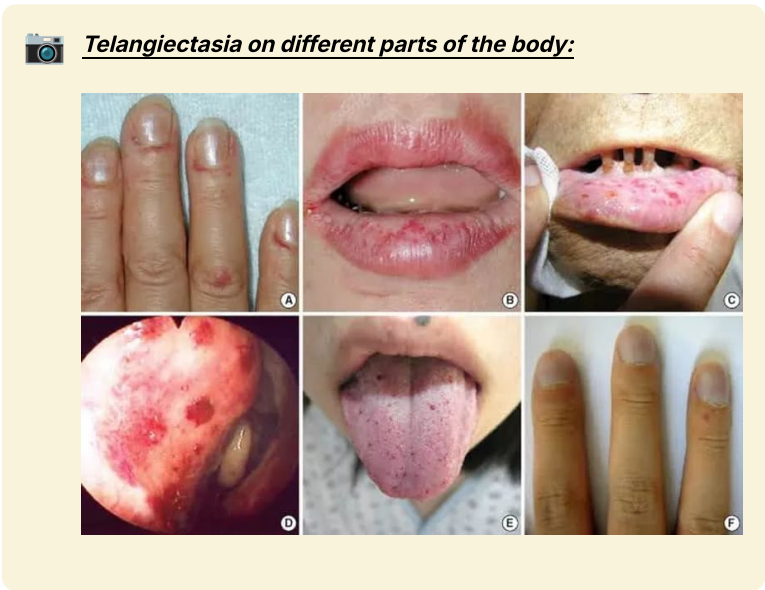


▼ Other Choices

- **Choice A** → This is clearly not abuse. The absence of recent or remote injuries + she being well cared for exclude trauma.
- **Choice C** → Vague

- **Choice D** → Hereditary hemorrhagic telangiectasia (aka Osler-Weber-Rendu)
 - **AD**; Presents as **triad** of **recurrent epistaxis**, **hematuria**, and **GI bleeding**
 - **USMLE can show you a picture of telangiectasia (on lips, tongue, skin, fingernails) + one of the triad above.**
 - They can be super sneaky and **give you a telangiectasia picture + Anemia** (You'd have to connect that the anemia is due to some sort of bleeding)
 - Associated with **AV Fistulas & AVMs**, which can result in:
 - **High-output HF** (HY AFFFF) [asked on NBMEs]
 - Cerebral → **Hemorrhagic Stroke**
 - Lungs → **Pulmonary HTN & Clubbing**

? What are the other HY causes of High-output HF?
▼ **Answer**
AVFs - Thyrotoxicosis - Anemia - Paget disease (of bone) - Sepsis
[They are so HY]



- **Choice E** → **PLT dysfunction** is unlikely due to the distribution of the purpura. They would be seen all over the body not just limited to the arms & hands. Also they say PLT count is normal, which should push you away from blaming the PLTs.

Q4

A newborn is born with a lethal chromosome defect. He is unable to suck sufficiently to maintain life. He has episodes of crying that occur every 2½ hours and are relieved by tube feeding. Which of the following best describes the most appropriate clinical approach?

- A. Feed by mouth only
- B. Feed by whatever means necessary to maintain comfort
- C. Give foods according to normal caloric requirement for age
- D. Withhold feeding because of the severity of the diagnosis

▼ **Explanation**

- **Answer is B (Feed by whatever means necessary to maintain comfort)**
 - Baby will die anyways since this is a lethal chromosomal defect, so **palliative ttt/comfort care**.
 - **Provide care for the baby & whatever he needs to maintain comfort until he passes peacefully & painlessly.**
 - Going all in with intubation, TPN, mechanical ventilation is **not indicated** as they **don't improve outcome** and **prolong suffering**.

Q5

A 48-year-old woman comes to the physician because of a 2-hour history of dizziness and palpitations with a sustained, rapid, irregular heartbeat. An ECG shows atrial fibrillation. If amiodarone is administered, this patient is at greatest risk for which of the following adverse effects?

- A. Aplastic anemia
- B. Bronchoconstriction
- C. Hypothyroidism
- D. Muscle fasciculations
- E. Renal failure

▼ **Explanation**

- **Answer is C (Hypothyroidism)**
 - Q asks for side effects of Amiodarone (Class III antiarrhythmic). Let's go over all the HY Side Effects YOU MUST KNOW:
 1. **Torsades de Pointes** (QT prolongation)
 2. **Drug-Induced Thyroiditis** (Can be hypothyroidism or hyperthyroidism)
 3. **Hepatotoxicity**
 4. **Pulmonary Fibrosis**

? What are HY drugs that cause QT prolongation/Torsades de Pointes on the USMLE?
▼ **Answer**
Class Ia & Class III antiarrhythmics - Macrolides - Metoclopramide - TCA - Antipsychotics

5. Blue-Grey skin discoloration

"Knowing these side effects are so HYYYY. Also knowing what else causes these side effects is equally HY."



What are the HY drugs that cause Pulmonary Fibrosis on the USMLE?

▼ Answer

Methotrexate - Amiodarone - Busulfan - Bleomycin - Nitrofurantoin



What are the HY drugs that cause Drug Induced Thyroiditis on the USMLE?

▼ Answer

Lithium - Amiodarone

Can cause EITHER hypothyroidism or hyperthyroidism.

If hypothyroidism happens, add Levothyroxine + keep drug dose the same.

Q6

A 71-year-old man comes to the physician because of a 6-month history of calf pain and discomfort when he walks more than two blocks; he is unable to walk farther than three blocks. The pain quickly subsides with rest. He also has hypertension and type 2 diabetes mellitus. Physical examination shows weak dorsalis pedis pulses bilaterally and an ankle brachial index of 0.67. The physician knows of a drug that would improve this patient's symptoms and walking distance by altering platelet function and providing direct arterial vasodilation. This drug is most likely which of the following?

- A. Abciximab
- B. Aspirin
- C. Cilostazol
- D. Clopidogrel
- E. Nifedipine

▼ Explanation

• Answer is C (Cilostazol)

◦ IMP Clues

- Calf pain and discomfort when he walks to blocks + unable to walk further than three blocks + pain subsides with rest (sounds like claudication. When the patient moves, blood demand increases which when moving through narrowed vessels cause ischemic pain. When the patient rests, blood demand decreases)
- He also has HTN and T2DM (Major Risk factors for vasculopathy and Claudication)
- Weak Dorsalis Pedis pulses bilaterally + ankle brachial index of 0.67 (This confirms that there is peripheral arterial disease)
- Q asks which drug improves this patient's symptoms by altering PLT function AND providing direct arterial vasodilation?

◦ Dx → Intermittent Claudication

- Pharmacological treatment of claudication on the USMLE is by **Phosphodiesterase inhibitors** (Cilostazol & Dipyridamole)
 - **PDE is an enzyme that breaks down cAMP & cGMP**
 - **MOA → Direct arterial vasodilation & increases cAMP in PLTs, which inhibit PLT aggregation**
 - Side Effects → **Facial Flushing & Abdominal Pain**
- HY Risk Factors → **Smoking, DM, HTN**, Obesity & Dyslipidemia

- Atherosclerosis of arteries cause **decreased blood flow to tissue supplied by these arteries.**

- When the patient **walks** → **increased** blood demand → blood supply DOESN'T match demand → **Ischemia** (Pain & Cramps +/- numbness)
- When patient **rests** → **decreased** blood demand → blood supply matches demand → **no ischemia** (pain improves)

▪ Examination Findings:

- **Absent/Diminished Distal Pulses**
- Trophic Changes ("**shiny smooth skin with no hair**" is HY)

▪ **Ankle-Brachial Index**



What are some other PDE inhibitors assessed on the USMLE?

▼ Answer

- **Theophylline** (*non-selective PDE inhibitor*) used for **asthma** (kinda obsolete rn due to side effects)
 - HY Side effects: **cardiotoxicity & neurotoxicity**
- **Sildenafil** (*PDE-5 inhibitor*) used for **ED**
 - HY Side effects: **blue tint vision, hypotension** (if used with nitrates), headache, and flushing



What is Leriche Syndrome?

▼ Answer

Aortoiliac atherosclerosis, causing classic **triad**:

1. **Bilateral gluteal/thigh/calf claudication**
2. **Weak/absent femoral pulse**
3. **Erectile Dysfunction**

- **if <0.9 → Peripheral Arterial Disease**
- It compares the blood pressure between the ankle (peripheral) with arms (more central) by dividing them:
 - Normal 1.0-1.3
 - If decreased this means that there is decreased peripheral blood flow compared to centrally.

▼ **Other Choices**

- **Choice A** → **Abciximab** is a **glycoprotein IIb/IIIa inhibitor** that **prevents *PLT aggregation***. USMLE refers to them as ***"Fibrinogen Antagonists"***. No effect on Arterial VD + no use in intermittent claudication.
- **Choice B** → **Aspirin** (NSAID) is a **nonselective irreversible COX inhibitor**. Yes, affects PLT function and may ***decrease arterial vasoconstriction*** (via inhibition of **TXA2**). No ***"direct arterial vasodilation"*** though.
- **Choice D** → **Clopidogrel** is an **ADP2Y12 Blocker** that **inhibits PLT aggregation** too. No effect on Arterial VD.
- **Choice E** → **Nifedipine** is **dihydropyridine CCB** that causes **direct arterial vasodilation by inhibiting L-type calcium channels** → **decreased calcium entry** → **decreased intracellular calcium** → **relaxation & vasodilation**. No effects on PLTs though.



What are the HY Side Effects of different types of CCB?

▼ **Answer**

- **Dihydropyridine CCB (*Nifedipine & Amlodipine*)** → **Fluid Retention (Peripheral Edema)**
- **Non-Dihydropyridine CCB (*Verapamil*)** → **Constipation**

Q7

Removal of the thymus at birth results in severely impaired immune responses. However, if the thymus is removed from adults, little if any deficit in immune responsiveness occurs because of which of the following reasons?

- A. Antibody-producing lymphocytes are the most important cells for adult immunity
- B. The bone marrow can take over the role of the thymus
- C. Most antigens that elicit protective immunity in adults are thymus-independent
- D. Thymic lymphocytes produced before thymectomy are long-lived
- E. Thymic nerve cells sequestered in lymph nodes replace the need for thymic lymphocytes

▼ **Explanation**

- **Answer is D (Thymic lymphocytes produced before thymectomy are long-lived)**
 - Let's start with the Role of the Thymus:
 - It is the **site where T-cell precursors mature** (the came from the bone marrow)
 - In the thymus, the undergo
 1. **Positive Selection (In the Thymus *Cortex*)** ***[asked on NBME]***
 2. **Negative Selection (in the Thymus *Medulla*)** ***[asked on NBME]***
 - Once the T-cells mature, they're released into the circulation
 - As we grow, we get **exposed to millions of antigens** → **induce T-cell maturation & produce a large diverse pool of T-cells**
 - **These T-cells are long-lived (up to decades)** (Choice D)
 - If a newborn is born without a thymus (like **DiGeorge Syndrome**) → no site for T-cell maturation → defective T-cell immunity
 - Removal of the thymus:
 - At Birth → No site for T-cell maturation → defective T-cell immunity
 - In Adults → Thymus ***already produced a diverse huge pool of T-cells, which are long lived*** → ***NO*** severely impaired immune response.
 - Note that the **Thymus gland naturally involutes as we grow.**

▼ **Other Choices**

- **Choice A** → Antibody production (by B-cells → plasma cells) is actually mediated by CD4 T-cells' help.
- **Choice B** → Bone marrow produces the T-cells precursors but not involved in maturation.
- **Choice C** → Thymus-dependent antigens are antigens made up of proteins, which stimulate T-cells (hence the name). Thymus-independent antigens produce a weak immune response in comparison.
- **Choice E** → The fuck?

Q8

The frequency of an autosomal recessive disease in a population is 1/1600. A deletion has been identified that accounts for 80% of the mutations at this locus. Twenty percent of the mutations result from point mutations. The frequency of deletion carriers in the population is closest to which of the following?

- A. 1/50
- B. 1/25
- C. 1/5
- D. 1/3
- E. 4/5

▼ Explanation

- Answer is B (1/25)
 - AR disease frequency is **1/1600**
 - Using the **Hardy-Weinberg** equation, let's find the carrier frequency.
 - $p^2 + 2pq + q^2$
 - $p + q = 1$
 - p is frequency of normal people [always calculate it as 1, trust me]
 - q is frequency of affected people
 - 2pq is frequency of carrier people
 - Disease frequency (q^2) = **1/1600**.
 - **q = 1/40**
 - Carrier frequency ($2pq$) = $2 \times p \times q = 2 \times 1 \times 1/40 = 2/40 = \mathbf{1/20}$
 - Q says that 80% of the mutations is caused by deletion.
 - **So, $1/20 \times 80\% \Rightarrow 1/25$ (Choice B)**

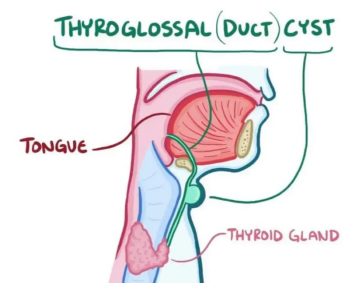
Q9

A 10-year-old boy has a palpable mass in the ventral midline of the neck just inferior to the hyoid bone. This structure most likely developed from which of the following embryonic tissues?

- A. Endoderm of foramen caecum
- B. Endoderm of fourth pouch
- C. Neural crest of second pouch
- D. Neural crest of third pouch

▼ Explanation

- Answer is A (Endoderm of foramen caecum)
 - IMP Clues
 - Palpable Mass in the ventral midline of the neck (location is very important in DD)
 - Just inferior to the hyoid bone (also important)
 - Dx → **Thyroglossal Duct Cyst**
 - The thyroid gland originates from the **endoderm of the foramen caecum (base of tongue)**
 - The thyroid gland then *migrates down* to its location, *whilst still being connected* to **foramen caecum by the thyroglossal duct** (thyro = thyroid; glossal = tongue)
 - This is why thyroglossal duct cysts **move with swallowing or tongue protrusion** (moves with the tongue movement due to duct connecting them)
 - The presence of the duct can be asymptomatic, but sometimes can:
 1. Filled with mucus → **Cyst**
 2. Get infected → **Abscess**
 3. Drain into skin → **Sinus**
 4. Can have **ectopic thyroid gland tissue** (why bother mention it? It *may* be the patient's ONLY thyroid tissue, so removing it may cause hypothyroidism)





What if we have a midline mass that DOESN'T move with swallowing or tongue protrusion?

▼ Answer

Dermoid Cyst - seen several times in answer choices + on the STEP2 differential so just be aware of it.

Q10

A 46-year-old man has dyspnea, orthopnea, and a midsystolic murmur that is best heard over the cardiac apex. An ECG shows a left atrial abnormality. Echocardiography shows an enlarged left atrium and a normally sized left ventricle. Which of the following is the most likely cause of these findings?

- A. Aortic regurgitation
- B. Aortic stenosis
- C. Mitral regurgitation
- D. Mitral stenosis
- E. Ventricular septal defect

▼ Explanation

• Answer is C (Mitral regurgitation)

◦ IMP Clues

- Midsystolic murmur best heard over the cardiac apex (Apex → Mitral; Midsystolic murmur → Regurg)
- ECG shows left atrial abnormality + ECHO shows enlarged left atrium + normal sized left ventricle (features of MR → blood backs up into LA → LA enlarges)
- Dyspnea, Orthopnea (blood backs up LA → lungs)

• Dx → Mitral Regurgitation

- Knowing the murmurs is pass-level. Know the murmurs.
- MR → **Pansystolic blowing murmur best heard at apex, which radiates to axilla.**



Why is acute MR dangerous?

Acute MR → blood backs up into LA → blood backs up into pulmonary vasculature → **acute pulmonary edema**



What are the HY causes of MR on the USMLE?

▼ Answer

1. **MVP** (seen in connective tissue diseases & in young females)
2. **Papillary muscle rupture post-MI** (very HY, hx of MI followed by systolic murmur that radiates to axilla)
3. **IED & RHD**
4. **HOCM** (anterior motion of mitral valve causes MR; just a finding mentioned in Qs)
5. **LV dilation** (dilated cardiomyopathy)

▼ Other Choices

- **Choice A → AR:** Diastolic Decrescendo blowing murmur best heard at left sternal border.
- **Choice B → AS:** Ejection Systolic Crescendo-Decrescendo murmur best heard at right 2nd space, which radiates to neck/carotids
- **Choice D → MS:** Diastolic rumbling murmur best heard at apex +/- opening snap (the more the stenosis, the closer the OS to S2)
- **Choice E → VSD:** Pansystolic murmur best heard at left sternal border.

Q11

A 2-month-old girl is brought to the emergency department by her parents because of a 6-week history of constipation. She has also had poor feeding, sleepiness, and yellow skin during this period. Her parents are migrant workers, and she has not received routine medical care. Physical examination shows lethargy, hypotonia, jaundice, large fontanels, macroglossia, and an umbilical hernia. Which of the following is the most appropriate next step to establish the diagnosis?

- A. Chromosomal analysis
- B. Measurement of serum phenylalanine concentration
- C. Thyroid function tests
- D. MRI of the brain
- E. Muscle biopsy

▼ Explanation

• Answer is C (Thyroid function tests)

◦ IMP Clues

- 2-month-old girl with constipation + hypotonia + large fontanel + macroglossia + umbilical hernia (These 5 here are superrrrr buzzy for congenital hypothyroidism)
- Her parents are migrant workers (this is USA's way of saying it is not our fault, it is the fault of the poor countries) and she has not received routine medical care (NBs are routinely screened for hypothyroidism, she had no care.)

• Dx → Congenital Hypothyroidism

◦ HY Symptoms:

- Hypotonia, lethargy, poor feeding
- Jaundice (as bilirubin metabolism is decreased due to decreased T3/T4)
- Macroglossia, Umbilical Hernia ("pot belly")
- Constipation, dry skin, large fontanelles

◦ Complications (if left untreated) → Intellectual & developmental disability.

◦ Newborns should be routinely screened for TSH levels +/- Free T4

▪ Why TSH?

- T4 levels may be normal due to maternal T4 in babies circulation as they can pass the placental barrier.
- Few weeks after birth, T4 levels drop → Clinical Symptoms.

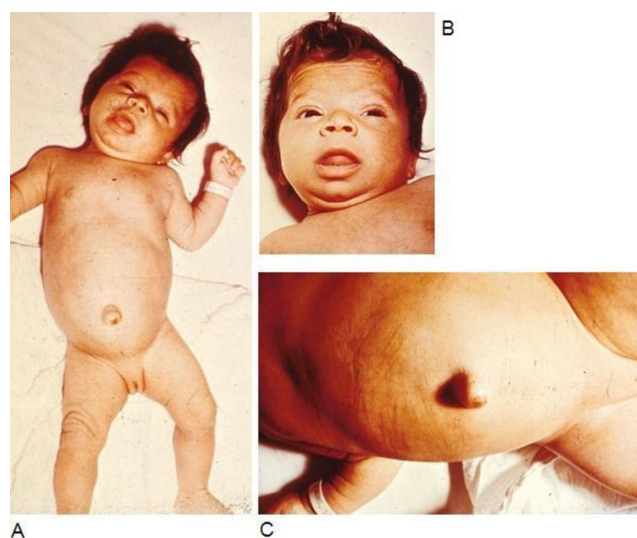


29F with Hashimoto thyroiditis managed with levothyroxine came in for pregnancy follow up. What would be affected if her TSH increases?

▼ Answer

Fetus Brain Maturation

- TSH would *increase* if T3/T4 *decreased*. In other words, Q is asking what would happen to the fetus if the mother develops HYPOTHYROIDISM → Cretinism.



Q12

A 60-year-old woman has prolonged apnea following general anesthesia. Plasma cholinesterase activity is abnormal. Which of the following agents is most likely responsible for the prolonged apnea in this patient?

- A. Bethanechol
- B. Carbachol
- C. Dibucaine
- D. Halothane
- E. Succinylcholine

▼ Explanation

• Answer is E (Succinylcholine)

◦ IMP Clues

- Prolonged apnea following general anesthesia (Usually when this is mentioned, we are talking about succinylcholine & pseudocholinesterase deficiency)
- Plasma cholinesterase activity is abnormal (hinting towards pseudocholinesterase deficiency)

- **Dx → Pseudocholinesterase Deficiency**
 - Basically, Succinylcholine is a **depolarizing neuromuscular blocker** that is used to *relax muscles*.
 - Succinylcholine is **short-acting agent** that is metabolized by **pseudocholinesterase**
 - **If pseudocholinesterase is deficient, the action of succinylcholine is prolonged → prolonged paralyzed respiratory muscles → prolonged apnea**

? What's another HY potential side effect of succinylcholine? What is its treatment?

▼ Answer

Malignant Hyperthermia

- **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**

▼ Other Choices

- **Choice A → Bethanechol** is a muscarinic receptor agonist that is used for neurogenic (flaccid) bladder
- **Choice B → Carbachol** is a muscarinic receptor agonist that is used for open-angle glaucoma
- **Choice C →** Local anesthetic that is NOT assessed on the USMLE. It is however used to measure pseudocholinesterase enzyme activity. Just saying for completeness sake, but really LY/non-existent.
- **Choice D → Halothane** is lipid soluble inhaled anesthetic, which carries a high-risk for malignant hyperthermia.

Q13

A 45-year-old man comes to the emergency department because of a tooth abscess. He has not seen a physician or a dentist in over 10 years. He lives alone, is unemployed, and receives income from an inheritance. When asked what he does with his time, he says that he reads "books on physics." He has no friends, maintains minimal contact with relatives, and says that he is "really quite comfortable." Examination shows no symptoms of a thought disorder. Which of the following is the most likely diagnosis?

- A. Antisocial personality disorder
- B. Avoidant personality disorder
- C. Borderline personality disorder
- D. Dependent personality disorder
- E. Narcissistic personality disorder
- F. Obsessive-compulsive personality disorder
- G. Paranoid personality disorder
- H. Schizoid personality disorder

▼ Explanation

- **Answer is H (Schizoid personality disorder)**
 - **IMP Clues**
 - He lives alone & unemployed + has no friends, maintains minimal contact with relatives (He likes to be alone)
 - Says that he is "really quite comfortable (not annoyed by it)

- **Dx → Schizoid Personality Disorder**
 - **A person who *prefers* to be alone & not annoyed by it.**
 - The distinction between schizoid & avoidant is very HY:
 - **Schizoid personality disorder: is distant/alone & actually *prefers* it**
 - (He is happy / doesn't care that he is single)
 - **Avoidant personality disorder: is distant/alone & *HATES* it.**
 - (He is upset & dreams of having a girlfriend)

▼ Other Choices

- **Choice A → Antisocial personality disorder**

? What is this patient at risk of developing?

▼ Answer

Schizophrenia - Both **Schizoid & Schizotypal** personality disorders are at risk of developing **Schizophrenia**.

- **> 18 years old** person that commits crimes / starts fights / cheats on tests
 - *Must have a history of similar actions before 15 years of age*
- **Choice B → Avoidant personality disorder**
 - Person desires social interactions but can't engage in it. He has this fear of rejection that stops him from meeting / socializing with people. He still wishes he can.
- **Choice C → Borderline personality disorder**
 - Patients have **Unstable relationships, self-image, emotions, and impulsivity**
 - Maybe associated with **suicidal behaviors** that will not actually kill him/her.
- **Choice D → Dependent personality disorder**
 - Pervasive/excessive need to be taken care of; clinging behavior and fear of separation. Patient will often go to great lengths to avoid being alone, constantly seeking to be physically close to intimate partner
- **Choice E → Narcissistic personality disorder**
 - Patient with inflated ego and deep need for excessive attention and admiration. They also lack empathy for others.
- **Choice F → Obsessive-compulsive personality disorder**
 - Same as OCD; however, more generalized **to all aspects of life** (not just towards something)
 - **Patient doesn't feel that there is something wrong with him/her (Ego-Syntonic)**; unlike OCD, where the patient knows that this behavior is not normal (Ego-Dystonic)
- **Choice G → Paranoid personality disorder**
 - A person with **general suspicion and distrust to others**, which affects relationships and work.

Q14

A 59-year-old man develops fatigue and decreased appetite 3 months after receiving a mechanical aortic valve replacement. His pulse is 88/min, respirations are 12/min, and blood pressure is 140/54 mm Hg. He appears tired. Physical examination shows mild scleral icterus. Jugular venous pressure is 8 cm H₂O, and carotid upstrokes are normal. Lung fields are clear. Cardiac examination shows crisp prosthetic valve sounds and a grade 2/6, decrescendo diastolic murmur at the left sternal border. Abdominal examination shows no tenderness, normal liver size, and normal bowel sounds. Laboratory studies of serum show a total bilirubin concentration of 4 mg/dL and a direct bilirubin concentration of 1 mg/dL. Which of the following is the most likely cause of the jaundice in this patient?

- A. Cholelithiasis
- B. Cholestasis
- C. Hemolysis
- D. Hepatocellular disease
- E. Passive congestion

▼ Explanation

- **Answer is C (Hemolysis)**
 - **IMP Clues**
 - After receiving a mechanical aortic valve replacement (This is key to answering this Q)
 - Scleral icterus + total bilirubin of 4mg/dL and a direct concentration of 1mg/dL (Jaundice due to indirect hyperbilirubinemia)
- **Dx → Mechanical Valve hemolytic anemia**
 - Also known as **Cardiac Prosthesis-related hemolytic anemia**
 - Basically, what happened here was the patient got **a new aortic mechanical valve, which caused passing RBCs to rupture due to the shearing forces + the turbulence created by the valves.**
 - RBCs get damaged → **Schistocytes**
 - **Intravascular hemolysis** → Anemia, increased indirect bilirubin, increased LDH, and decreased haptoglobin

"This is basically similar to what happens in conditions like HUS, TTP, DIC where endothelial damage & fibrin accumulation inside small vessels cause rupture of passing by RBCs, causing schistocytes and hemolytic anemia. Hence the name Microangiopathic Hemolytic Anemia (MAHA)"

? What are HY causes of Schistocytes on the USMLE?

▼ Answer
TTP - HUS - DIC - HELLP Syndrome - Mechanical hemolysis by prosthetic heart valves

! Shearing forces caused by **mechanical heart valves** or **aortic stenosis** causes **damage to large vWF multimers**, causing their unfolding & exposure to **ADAMTS13 metalloprotease that cleaves vWF multimers**. This results in **acquired von Willebrand Syndrome**, causing decreased platelet adhesion & bleeding tendencies.

▼ Other Choices

- **Choices A & B** → Would cause a rise in direct bilirubin, as is the site of pathology is “post-hepatic”, then the bilirubin is already conjugated.
- **Choice D** → Hepatocellular disease can cause in increase in both direct and indirect bilirubin; however, the lack of abdominal tenderness and a normal liver size exclude liver pathology.
- **Choice E** → Liver congestion can be seen in Right side HF, especially Tricuspid Regurgitation. However, having a normal JVD + no liver tenderness excludes that condition.

Q15

A 4-week-old infant is brought to the emergency department because he has vomited after every feeding for the past 2 days. The most recent episode of vomiting was very forceful, with regurgitation through the nostrils. Physical examination shows mild abdominal distention with visible peristalsis. Which of the following is the most likely explanation for these findings?

- A. Duodenal atresia
- B. Gastric volvulus
- C. Hypertrophic pyloric stenosis
- D. Intussusception of the small intestine
- E. Meckel diverticulum
- F. Pharyngoesophageal (Zenker) diverticulum
- G. Tracheoesophageal fistula

▼ Explanation

- **Answer is C (Hypertrophic pyloric stenosis)**
 - **IMP Clues**
 - Infant with vomiting after every feeding + vomiting was very forceful with regurgitation through the nostrils (Buzzy description for CHPS, pass-level tbh)
 - Mild abdominal distention with visible peristalsis (confirms our diagnosis)
- **Dx → Hypertrophic Pyloric Stenosis**
 - Pylorus is congenitally thickened, causing an obstruction.
 - Obstruction causes **nonbilious projectile vomiting**, leaving the child *dehydrated & hungry* (“child is eager to eat”).
 - USMLE tests the concept of Pyloric Stenosis by:
 1. **Asking for a diagnosis:**
 - They give you **non-bilious vomiting + olive-like abdominal mass +/- abdominal peristalsis**.
 - **Dx is → CHPS**
 2. **Asking for expected arrows:**
 - They give you an arrows Q asking for **K, Cl, Na, HCO3, PCO2, and pH**
 - Answer is → **low K, low Cl, normal/low Na, high HCO3, high Pco2, high pH**
 - Vomiting causes **hypokalemic hypochloremic metabolic alkalosis**

 **Olive-like abdominal mass:**



 Vomiting vs Diarrhea arrows [K - Cl - Na - HCO3 - PCO2 - pH]

▼ Answer

Vomiting	Diarrhea
<i>low</i> K	<i>low</i> K
<i>low</i> Cl	<i>normal</i> Cl
<i>normal/low</i> Na	<i>normal/low</i> Na
<i>high</i> HCO3	<i>low</i> HCO3,
<i>high</i> PCO2	<i>low</i> Pco2,
<i>high</i> pH	<i>low</i> pH
<i>"Hypokalemic Hypochloremic Metabolic Alkalosis"</i>	<i>"Non-Anion Gap Metabolic Acidosis"</i>

▼ Other Choices

- **Choice A** → **Duodenal atresia** mostly causes bilious vomiting as the atretic level is usually below the **ampulla of Vater** (where bile enters the intestines).
 - **Double Bubble sign** is buzzy. **Associated with Down Syndrome**.

- Embryological cause → **Failure of duodenal recanalization**
- **Choice B → Gastric Volvulus** is not assessed on STEP 1 per my observation. However, if you are an absolute gunner, know the following triad (**Borchardt's triad**): **unproductive retching, epigastric pain with distension, and inability to pass a NGT.**
 - It basically is rotation of the stomach around itself, causing an **obstruction + ischemia (as blood supply also gets compressed)**
- **Choice D → Intussusception**
 - Almost always **under age 2**
 - Idiopathic or 2ry to Viral infection or **Rota vaccination** in which mesenteric adenitis act as a lead point for "telescoping in", and Meckel's Diverticulum
 - Presentation is : **intermittent/colicky abdominal pain + kid draws legs to the chest or squat + blood in the stool +/- bilious vomiting**
 - **Sausage shaped abdominal mass is what differentiates it from Midgut volvulus**
 - CT/AUS shows **Target Sign**
- **Choice E → Meckel Diverticulum**
 - Presents as a healthy **child with bloody stools**
 - One of the omphalomesenteric duct disorders spectrum.
 - Cause of bleeding is → presence of **ectopic (heterotopic) gastric/pancreatic tissue** → inflammation of mucosa → bleeding
 - Site → **Terminal Ileum**
 - Radiology → **Tc99 uptake scan (also called Meckel scan) shows ectopic gastric mucosa in terminal ileum**

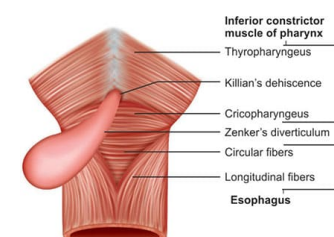
? What type of diverticulum is Meckel's diverticulum?

▼ Answer

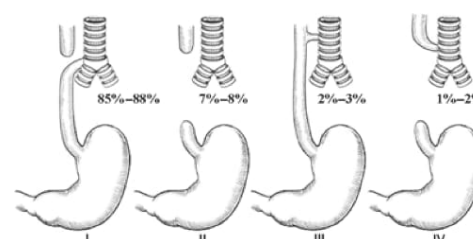
Meckel's → True Diverticulum (contains mucosa, submucosa, and musculosa)

Zenker's → False Diverticulum (contains only mucosa & submucosa)

- **Choice F → Pharyngoesophageal (Zenker) diverticulum**
 - Presents as a **male** (usually) with **regurgitation of undigested food, dysphagia, halitosis**, and a **gurgling sound upon swallowing**. (It's usually a man that presents because his wife complains about his bad breath)
 - Due to **cricopharyngeal muscle dysfunction or impaired relaxation of UES** → **increased intraluminal pressure** → **herniation** due to weakest point (Killian Dehiscence, which is a triangle between thyropharyngeus & cricopharyngeus muscles)
 - HY Complications include **aspiration pneumonia & chronic cough**.
 - Imaging is buzzy so know the picture.
 - USMLE can ask what type of diverticulum Zenker is → **False Diverticulum** (contains only mucosa & submucosa)



- **Choice G → Tracheoesophageal fistula**
 - Has many presentations; **most common Atresia of esophagus + Fistula between lower part of esophagus & trachea.**
 - presents as **non-bilious vomiting immediately after feeding**.
 - They can also show you a scan, where a feeding tube can't go all the way in & stays mid-esophagus:



Q16

A 23-year-old woman, who was diagnosed with Sjogren syndrome 6 years ago, comes to the physician because she has had burning pain in her toes for the past month. She rates the pain as a 3 on a 10-point scale. She uses capsaicin cream as needed for the pain, which has produced partial relief. Medical history is otherwise unremarkable. Vital signs are within normal limits. Neurologic examination shows decreased perception of temperature over the feet bilaterally. Sensation to vibration, proprioception, reflexes, muscle strength, muscle tone, and bulk are normal. Which of the following neurotransmitters is most likely mediating this patient's pain?

- A. γ -Aminobutyric acid
- B. Dopamine
- C. Enkephalin
- D. Serotonin
- E. Substance P

▼ Explanation

- Answer is E (Substance P)

- Pain on NBMEs is assessed like ~10 times, so let's go through what you need to know:
 - Neurotransmitters that regulate pain on the USMLE:
 1. **Excitatory (of pain):**
 - a. **Substance P** (Released from Nociceptors)
 - b. **Glutamate**
 2. **Inhibitory (of pain):**
 - a. **Enkephalins/Endorphins** (inhibit release of Substance P & glutamate)
 - b. **GABA**

**How do nociceptors work?**

Pain is detected by **Nociceptors** (free nerve endings) → **Na & Ca influx into nerve endings** → depolarization & AP fires → **releasing Substance P**

- If we have **overactive/unregulated activation** of nociceptor Na channels → **Allodynia** *[asked on NBME]*

USMLE gives you a Q where there is a patient with allodynia (pain sensation from stimuli that causes no pain, like touch or clothes) and the answer something like → “increased nociceptors activation by unregulated Na influx”

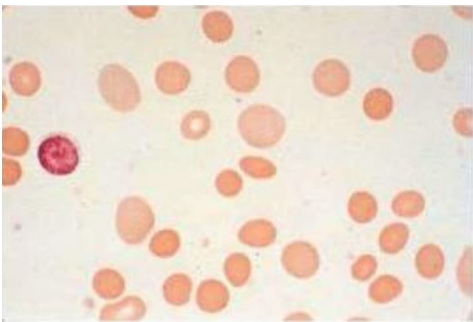
- This is the basis of **local anesthetics (like lidocaine)** which **blocks Na channels** → decreased Na influx → decreased AP firing → **decreased Substance P release**

Q17

A 3-year-old boy is brought to the physician because of a 1-month history of pale skin. His parents are of European descent. He has no personal or family history of major medical illness. Physical examination shows pallor. Laboratory studies show:

Hemoglobin	8 g/dL (N=11-15)
Hematocrit	24% (N=28-45)
Mean corpuscular hemoglobin concentration	34% Hb/cell (N=31-36)
Mean corpuscular volume	90 μm^3 (N=77-98)

A photomicrograph of a peripheral blood smear is shown. Genetic testing is most likely to show which of the following findings in this patient?



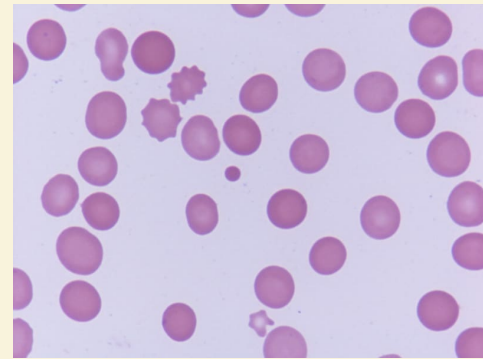
- A. Heterozygous mutation in the ankyrin gene
- B. Heterozygous mutation in the α -globin gene
- C. Heterozygous mutation in the β -globin gene
- D. Homozygous mutation in the ankyrin gene
- E. Homozygous mutation in the α -globin gene
- F. Homozygous mutation in the β -globin gene

▼ Explanation

- **Answer is A (Heterozygous mutation in the ankyrin gene)**
 - **IMP Clues**
 - Pale skin + pallor + hemoglobin 8g/dL + hematocrit 24% + MCV 90 μm^3 (This patient has normocytic anemia)
 - Peripheral smear is shown (Spherocytes are seen with loss of central pallor)
 - MCHC is 34% (In actual practice, MCHC > 35% is buzzy for HS; however, USMLE doesn't really care like in this Q here. However, if MCHC is mentioned think of HS)

- **Dx → Hereditary Spherocytosis**
 - **Autosomal Dominant** disease caused by *“heterozygous mutation in ankyrin, spectrin, or band proteins.”*
 - This mutation causes a **cytoskeletal/cell membrane defect** *[asked on NBME]* ⇒ **Spherocytes** instead of the normal biconcave shape
 - So, smear shows small sphere-shaped (**microspherocytes**) RBCs *lacking central pallor*
 - Anemia → **Normocytic Normochromic Anemia** *[asked on NBME]*
 - **The abnormal cytoskeleton / cell membrane is detected by the spleen** ⇒ **increasing RBC turnover**
 - Increased RBCs turnover can cause **splenomegaly & gallstones** (increased RBC turnover = increased bilirubin, so can cause *jaundice* = increase **pigment stones**)
 - So, vignette may say that kid has *family hx of cholecystectomy +/- splenectomy because of “blood disorder” or “anemia”*.
 - **Diagnosis → Osmotic Fragility test**
 - Due to the abnormal cell membrane of spherocytes, when placed in hypotonic solution → they lysis at a faster rate than normal RBCs.

? What conditions can the patient have according to peripheral smear shown below? How to differentiate?



▼ **Answer**

Spherocytes can be seen in **Hereditary Spherocytosis** AND **Autoimmune Hemolytic Anemia**.

How to differentiate?

- HS → Coomb's negative
- AHA → Coomb's positive

Q18

A 23-year-old woman who is 6 months pregnant develops deep venous thrombosis. Intravenous administration of heparin is started. Seven days later, platelet count is 44,000/mm³. Which of the following is most likely responsible for the decreased platelet count in this patient?

- A. Antimegakaryocyte antibodies
- B. Antiplatelet antibodies
- C. Heparin-induced hemodilution
- D. Hypersplenism
- E. Stem cell antibodies

▼ **Explanation**

- **Answer is B (Antiplatelet antibodies)**
 - **IMP Clues**
 - DVT (patient is hypercoagulable + pregnant, so perfect media for DVTs)
 - IV administration of heparin is started + seven days later, platelet count is 44,000/mm³ (Patient got heparin then develop thrombocytopenia)
- **Dx → Heparin-Induced-Thrombocytopenia (HIT)**
 - Heparin-induced thrombocytopenia is **decreased platelet count that occurs after heparin administration**.
 - MOA → **Autoantibodies against heparin-platelet factor 4 complex (PF4), which bind to the PLTs, causing the spleen to destroy these “tagged” PLTs ⇒ THROMBOCYTOPENIA**
 - USMLE can ask about the MOA as *“anti-platelet production”* or *“destruction of platelets by spleen”*
 - Treatment is to **STOP the heparin + administer Direct-Thrombin inhibitors** (Factor 2 inhibitors) like *Dabigatran, Lepirudin, Bivalirudin, or Argatroban*.
 - **WARFARIN IS INCORRECT.**

? What type of Hypersensitivity is HIT?

▼ **Answer**

Type 2 Hypersensitivity

“USMLE can assess this by asking which of the following has a similar pathophysiology & mention diseases/conditions with different hypersensitivities and expect you to know which of them is also type 2.”

Q19

A 39-year-old man reports bright red spots on the toilet paper after defecating. Rectal examination shows large swollen rectal veins. Which of the following is the primary predisposing cause of these lesions?

- A. Adjacent tubular adenoma

- B. Carcinoma obstructing the venous system
- C. Chronic inflammatory bowel disease
- D. Constipation
- E. Irritable bowel syndrome
- F. Overuse of stool softeners

▼ Explanation

- **Answer is D (Constipation)**

- **IMP Clues**

- Bright red spots on toilet paper after defecating (this is a very buzzy sentence used on USMLE for describing hemorrhoids)
- Rectal examination shows large swollen rectal veins (the hemorrhoids)

- Q asks what is the primary predisposing cause of these hemorrhoids?

- **Primary (and most common) cause is → Constipation**

- Constipation causes increased intraabdominal pressure + contraction on the anorectal body causing compression of venous return of rectal veins → pooling of blood → venous dilation
- Constipation also is usually accompanied by hard, dry stools which injury & irritate the engorged veins as they descend (or try to at least).

? What other condition is super HY and causes rectal bleeding with its major risk factor is constipation?

▼ Answer

Diverticular Bleeding - caused by the **diverticular out pouches** compressing the **vasa vasorum**, causing their ischemia, perforation, and bleeding. *[asked on NBME]*

- It is the most common cause of rectal bleeding in the older population



External vs Internal Hemorrhoids:

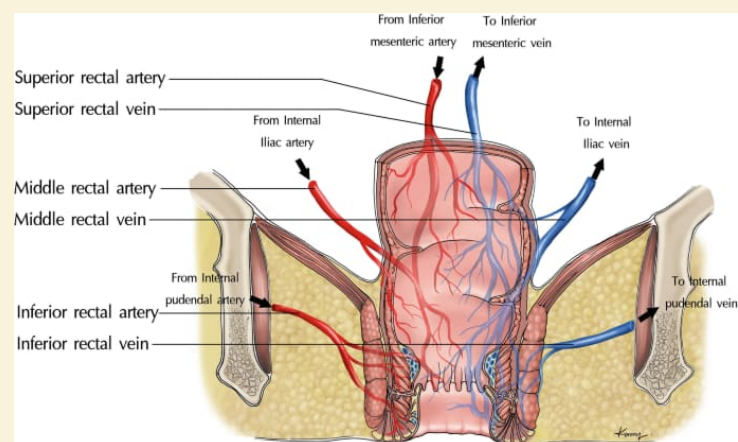
- **External hemorrhoids** → **distal** to dentate line, **ectoderm** in origin, **painful** (somatic innervation via pudendal nerve)
- **Internal hemorrhoids** → **proximal** to dentate line, **endoderm** in origin, **painless** (visceral innervation)



Rectal/Hemorrhoidal Veins:

Superior rectal veins, Middle rectal veins, and Inferior rectal veins form the rectal venous plexus (the source of hemorrhoidal bleeding)

- **Superior Rectal Vein → Portal Circulation** (specifically drains into the **IMV**)
- **Middle Rectal Vein → Systemic Circulation** (specifically drains into **internal iliac vein**)
- **Inferior Rectal Vein → Systemic Circulation** (specifically drains into the **internal pudendal vein**)



Q20

A 45-year-old woman has a thyroidectomy because of asymmetric enlargement of the thyroid gland, first noticed during a physical examination 6 weeks ago. She underwent an adrenalectomy for pheochromocytoma 3 years ago. Microscopically, the bilateral thyroid lesions are composed of spindle cells arranged in small clusters. Deposits of amyloid are present between neoplastic cells. Foci of C-cell hyperplasia are also present. The lesions are confirmed as malignant. Which of the following markers is most appropriate to monitor for the development of recurrence of the thyroid neoplasm?

- A. Calcitonin
- B. α -Fetoprotein
- C. Human chorionic gonadotropin
- D. Norepinephrine
- E. Thyroid-stimulating hormone

▼ Explanation

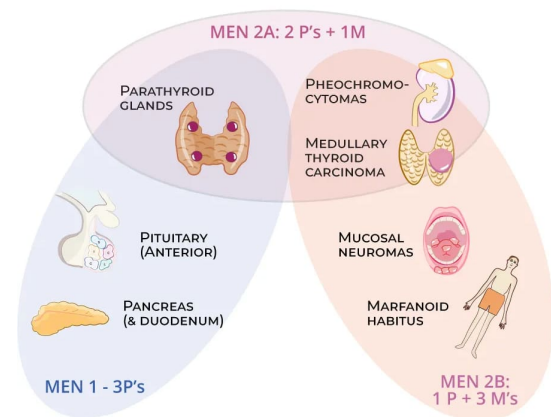
- **Answer is A (Calcitonin)**

- **IMP Clues**

- Thyroidectomy because of asymmetric enlargement of the thyroid gland (so Thyroid Tumor, you must think MEN Syndromes)
- Adrenalectomy for pheochromocytoma (Pheochromocytoma, Okay so MEN2)
- Spindle cells arrange in small clusters + deposits of amyloid are present + foci of C-cell hyperplasia are present (Amyloid & C-cells tells us that this is Medullary Thyroid Carcinoma)

- Dx → MEN 2 Syndrome
 - This could be either MEN2A or MEN2B
 - **MEN 2A → Pheochromocytoma, Medullary Thyroid Carcinoma, and Parathyroid adenoma**
 - **MEN 2B → Pheochromocytoma, Medullary Thyroid Carcinoma, and Mucosal Neuromas**
 - **Medullary Thyroid Carcinoma** is a tumor of the **Parafollicular C-cells, which produce calcitonin**. Q asks us which markers should be monitored for the recurrence, so **Calcitonin** (which is released by the tumor) is the answer.
 - They can refer to it as **“neck mass with cervical lymphadenopathy”**
 - Biopsy findings are buzzy → **spindle-shaped cells/polygonal cells in sheets with amyloid stroma** (Congo red positive)

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



? 19M 6'7 came to the clinic for a neck mass. His mother has history of some abdominal surgery due to intermittent attacks of headache and high blood pressure. The cause of this disease is a mutation in which of the following?

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

▼ **Answer**

Proto-Oncogene - This is **MEN2B Syndrome** which is caused by **RET mutation (which is a proto-oncogene) on chromosome 10**.

How do I know that this is MEN 2B not 2A?

- 6'7 or being tall in general on the USMLE = **Marfanoid Habitus**, which is associated with MEN 2B.
- Intermittent attacks = Pheochromocytoma.

- **MEN 1 Syndrome** is caused by **menin mutation (which is a tumor suppressor gene) on chromosome 11**.

▼ **Other Choices**

- **Choice B → AFP** is used to monitor recurrence of HCC & some germ cell tumors like yolk-sac tumor & embryonal carcinoma
- **Choice C → hCG** is used to monitor GTDs (choriocarcinoma) & some germ cell tumors like choriocarcinoma (in males yes) and embryonal carcinoma
- **Choice D →** It's more common that we monitor **catecholamine metabolites** (rather than catecholamines themselves like norepinephrine) in pheochromocytoma or neuroblastoma
- **Choice E → TSH** is used to monitor recurrence of Thyroid cancers (not medullar though, as they originate from parafollicular C-cells) like papillary or follicular thyroid carcinoma

Q21

A 67-year-old woman comes to the physician for a health maintenance examination. Her brother and mother have a history of colon cancer. The physician recommends colonoscopy, but the patient says that she would prefer only for her stool to be tested for blood. The physician explains that testing the stool for occult blood is not appropriate in this case. The physician is most likely concerned about which of the following regarding this test?

- A. Low sensitivity
- B. Low specificity
- C. Potential for a false-positive result
- D. Uncertain negative predictive value
- E. Uncertain positive predictive value

▼ **Explanation**

- **Answer is A (Low sensitivity)**
 - So basically, the doctor here recommends this patient to get a colonoscopy to rule OUT colon cancer. The patient says she only prefers her stool to be tested for occult blood; however, the physician explains that it is not appropriate in this case. Why?
 - **Occult Blood in Stool CAN detect colon cancer, however, it also misses non-bleeding polyps/cancers.**
 - So, it can have a **LOW** Sensitivity. (Choice A)
 - Colonoscopy, on the other hand, has **HIGH** sensitivity & **HIGH** specificity

Q22

A 50-year-old woman is brought to the emergency department by her husband because he found her in a semicomatose state with an empty bottle next to her. The bottle had contained a sodium salt of a drug with central nervous system effects. Alkalinization of her urine will cause the greatest absolute increase in elimination of the unmetabolized drug if it has which of the following pharmacokinetic profiles?

Choices	pKa	Protein Binding in Plasma (%)	Volume of Distribution at Steady State (L/kg)
A	6.0	20	1
B	6.0	98	1
C	6.0	98	10
D	10.0	20	1
E	10.0	20	10
F	10.0	98	10

▼ Explanation

- Answer is A
 - For a substance to excreted by the kidney, it must have:
 1. **Low Volume of Distribution** (Vd refers to concentration of drug in tissue, the lower the Vd → the less the drug in tissue & the more in plasma)
 2. **Low Protein Binding in Plasma** (the less the bound % of the drug, the more the free % in the plasma, which can be filtered in the kidney unlike the protein-bound portion)
 3. **Weak Acid/Alkali** (weak acids & weak alkali ranges from 4-9 pKa)
 - Think of pKa as pH for simplicity purposes (It is not the same but bear with me).
 - **Weak acids** are cleared in **basic** environments (**4-7 pKa**)
 - Weak **alkali** are cleared in **acidic** environments (**7-9 pKa**)
 - Q here says **alkalinization** of her urine will **increase the elimination** of the drug if ??? **If it were a weak acid.**
 - What is the pKa of a weak acid??? 4-7.
 - **6 is our answer here.**

Q23

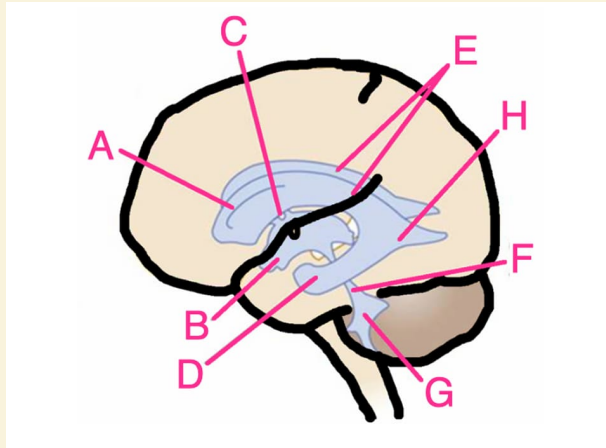
A 22-year-old woman who recently emigrated from rural Mexico is brought to the emergency department 20 minutes after a generalized tonic-clonic seizure. She has a 6-week history of headaches, nausea, vomiting, and decreased visual acuity. Funduscopic examination shows bilateral papilledema. An MRI of the brain shows enlargement of the right ventricle and findings consistent with cysticercosis. Which of the following is the most likely mechanism of the hydrocephalus in this patient?

- A. Obstruction of the cerebral aqueduct
- B. Obstruction of the right aperture of the fourth ventricle (foramen of Luschka)
- C. Obstruction of the right interventricular foramen (foramen of Monro)
- D. Perforated septum pellucidum
- E. Subarachnoid hemorrhage on the right

▼ Explanation

- Answer is C (Obstruction of the right interventricular foramen (foramen of Monro))
 - IMP Clues
 - Bilateral papilledema + hx of headaches, vomiting, and decreased visual acuity (all of these are signs on increased intracranial tension)
 - MRI of the brain shows enlargement of the right ventricle (okay so enlarged right ventricle ONLY tells us the level of obstruction)
 - Dx → Obstructive Hydrocephalus
 - Also known as **non-communicating hydrocephalus** (as not all ventricles are uniformly enlarged)
 - **An obstruction blocks the flow of CSF between the ventricles & the subarachnoid space**
 - What happened here is the *presence of neurocysticercosis* caused lesions, which caused *an obstruction at the level of the right intraventricular foramen* → **CSF accumulates behind the obstruction (Right Ventricle) → Signs on ICP.**
 - MOA → **“Obstruction that impedes CSF free flow” [asked on NBMEs]**
 - HY causes include → Spinal Cord Tumors, **Aqueduct Stenosis**, Colloid Cyst

? Which of the following labeled letters is the Foramen of Monro?



▼ Answer

C → Foramen of Monro

Other Choices

- A → Frontal Horns of Lateral Ventricles
- B → Third Ventricle
- D → Temporal Hons of Lateral Ventricles
- E → Body of Lateral Ventricles
- F → Cerebral Aqueduct of Sylvius
- G → Fourth Ventricle
- H → Occipital Horn of Lateral Ventricles

▼ Other Choices

- **Choice A** → Dilation of lateral ventricles & third ventricle, as the cerebral aqueduct connects the third ventricle to the fourth ventricle, so everything above that level dilates.
- **Choice B** → Will also cause dilation of the lateral ventricles, third ventricle, and disproportionate dilation of the fourth ventricle.
- **Choice D** → Septum Pellucidum is a thin layer that separates the right and left lateral ventricles, usually it is a complication of hydrocephalus.
- **Choice E** → Subarachnoid hemorrhage would cause communicating hydrocephalus as the blood will affect CSF absorption by obstructing arachnoid granulations *[asked on NBMEs]*

Q24

During a clinical study, an investigator tests a new drug for the treatment of breast cancer. A population of 10,000 patients with breast cancer is recruited and randomized into a treatment group and control group. Analysis of the data shows a p-value of 0.1 and no significant difference in the treatment outcomes between the experimental group and the control group. When repeating this study, which of the following is most likely to decrease the likelihood of making a beta error?

- A. Add a second treatment group
- B. Conduct the study for a shorter duration
- C. Decrease the alpha level
- D. Enroll participants with a different type of cancer
- E. Increase the sample size

▼ Explanation

- **Answer is E (Increase the sample size)**
 - Q wants to know how to decrease the likelihood of making a beta error?
 - Let's use the graph on the right to answer this Q.
 - Decreasing beta error essentially means *increasing the power*.
 - How do we increase the power of a study?
 1. **Increase Sample Size**
 2. **Increase precision of measurements**
 3. **Increased α (alpha error)**

		Disease/Reality	
		+	-
Test/Study	+	TP "Power" (1- β)	FP "Type I error" " α "
	-	FN "Type II error" " β "	TN (1- α)

made by: @_ahmadraef

Q25

A 13-year-old girl has an episode of severe cellular rejection necessitating maximal immunosuppression 6 months after a cadaveric renal transplantation. Two weeks later, she develops lymphadenopathy and hepatosplenomegaly. Examination of lymph node tissue obtained on biopsy shows a monomorphous population of B lymphocytes. Which of the following findings is most likely on further evaluation of these cells?

- A. Adenovirus antigen

- B. Cytomegalovirus inclusions
- C. Epstein-Barr virus genome
- D. Herpes simplex inclusions
- E. HIV genome
- F. Parvovirus antigen

▼ Explanation

• Answer is C (Epstein-Barr virus genome)

◦ IMP Clues

- Hx of immunosuppression after cadaveric renal transplantation (Transplant Qs are either about graft rejection or virus reactivation, let's see which one is it here. hint: it is virus reactivation)
- Lymphadenopathy & hepatosplenomegaly + examination of the lymph node tissue shows monomorphous population of B lymphocytes (HSM + lymphadenopathy + increased B-cell population; cmon can it be more obvious? This is EBV)

• Dx → Lymphoproliferative Disorder

- Caused by **Epstein-Barr Virus (EBV)**; which is a **dsDNA virus**
- **EBV binds to CD21 on B-cells → Infects them & causes B-cell proliferation (what is referred to by "monomorphous population of B lymphocytes")**
 - This **B-cell proliferation** is the cause of **hepatosplenomegaly & lymphadenopathy** (*Posterior Cervical Lymphadenopathy* is buzzy & HY for EBV infection)
- So basically, what happened here is patient had a graft rejection for the cadaveric renal she got → doctors gave her maximal immunosuppression drugs → caused **reactivation of EBV** in the host → **EBV enters the B-cells via CD21 [asked on NBMEs]** → causes B-cells to proliferate → HSM & lymphadenopathy. Easy.

? What would be expected to be seen on peripheral smear of this patient?

▼ Answer

Reactive/Downy/Atypical T-cells

- EBV infects B-cells & causes their proliferation in lymph nodes & spleen
- T-cells "react" to EBV by transforming their shape, named Reactive/Atypical T-cells in plasma

? What test is used to diagnose Infectious Mononucleosis?

▼ Answer

Heterophil (or Monospot) test - If Q says these tests are negative, **IT IS NOT EBV**

? 21M with pharyngitis was given ampicillin & developed a maculopapular rash. What is the causative organism?

▼ Answer

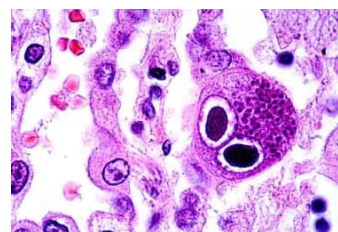
EBV - patients with Infectious Mononucleosis develop a maculopapular rash when given **ampicillin or amoxicillin**.



▼ Other Choices

- **Choice A → Adenovirus** is an important virus to lookout for in renal transplantation, as it causes **hemorrhagic cystitis**. No Red urine here.

- **Choice B → CMV** is buzzy for **CMV pneumonitis**, where they say a patient had an **organ transplant** + show you **XRAY of a lung with a lot of opacities** +/- show you a picture of the **"owl-eye" inclusions of CMV**. Immunosuppression can also cause **CMV retinitis and CMV esophagitis**.



- **Choice D → HSV** reactivation in immunosuppressed patients on the USMLE is HY for 2 things → **Temporal Encephalitis and HSV Esophagitis**. Another LY presentation is wide-spread vesicular lesions (usually reserved for VZV reactivation on the USMLE especially if it presents in a dermatomal distribution).

? Differentiate between Esophageal Ulcers caused by HSV vs CMV?

▼ Answer

HSV Esophagitis → **Punched-out ulcers**
CMV Esophagitis → **Linear or confluent ulcers**

- **Choice E → HIV** can cause HSM & lymphadenopathy; however, they are associated with a low lymphocyte count (CD4 especially) not an increase in their number.

- **Choice F → Parvovirus** is not really that big on renal transplantation Qs. Just HY to know that they cause **arthralgia in adults**, **Slapped Cheeks (lacy) rash in children**, **Aplastic Crisis in sickle cell disease patients**, **Hydrops Fetalis in pregnant women**, and that they **infect progenitor blood cells**.

Q26

A 62-year-old man comes to the physician because of pain in the left hip for 3 weeks. An x-ray of the hip shows a 4.5-cm, destructive, osteoblastic lesion with an associated fracture in the proximal femur and two separate similar smaller lesions in the bony pelvis. A needle core biopsy of the femur shows metastatic carcinoma. Which of the following is the most likely primary site of the cancer?

- A. Colon
- B. Kidney
- C. Lung
- D. Pancreas
- E. Prostate

▼ Explanation

• Answer is E (Prostate)

◦ IMP Clues

- 62-year-old man + osteoblastic lesion with associated fracture in the proximal femur (old man + osteoblastic lesions on the USMLE is prostate cancer)
- Two separate similar lesions in the bony pelvis (Multiple osteoblastic lesions, yep sounds like metastasis)
- Biopsy of the femur shows metastatic carcinoma (Confirmed metastasis)

• Dx → Prostate Cancer

- As I said above, **old male + Osteoblastic lesions is Prostate Cancer** on the USMLE.
- Let's me walk you through the possible presentations of prostate cancer seen all over the NBMEs:
 1. Patient with prostate cancer + develops **acute back pain** (stress fracture of vertebra)
 2. Patient with prostate cancer + develops **pain on palpation of vertebra/pelvis** (metastasis)
 3. Patient with prostate cancer + develops **acute neurological lower limb symptoms** (metastasis + invasion of spinal cord / cauda equina)
- Questions could be tricky (like this one here) and give you an **old man with the above presentations & NO mention of prostate cancer.**
 - If the question is somewhat easy, they will give you "**osteoblastic**" lesions → prostate cancer
 - If the question is hard, they will give you nothing and you will have to infer that the old man most likely has prostate cancer



Why does prostate cancer LOVE to metastasize to the vertebrae & pelvic bones?

▼ Answer

Prostate is drained by the prostatic venous plexus → connected to the vertebral venous plexus, which is valveless & drains the spine, pelvis, and connects to the brain.

Bidirectional Flow allows prostate cancer to flow either to the spine, or down the spine to the pelvis, or up the spine to the brain.



USMLE asks what will increase in a patient with prostate cancer, who underwent orchiectomy; Answer is **Controlled DNA Fragmentation.**

- Removing the testes = less testosterone production = less conversion to DHT = **smaller prostate (apoptosis)**
- So, what will increase? **Apoptosis**. which characterized by **controlled DNA fragmentation** (the answer).



Patient with prostate cancer will undergo orchiectomy as a part of treatment, what change is expected from this step?

▼ Answer

Decreased Dihydrotestosterone - **Testosterone** is converted to **DHT** via *5-alpha reductase*. DHT drives hyperplasia and multiplication of prostate tissue → BPH & Prostate Cancer.

- Orchiectomy is done to **decreased testosterone levels** & hence **decrease DHT levels**, which will **increase apoptosis** (can be referred to on the USMLE as "**controlled DNA Fragmentation**")
- Other steps of ttt include:
 - Surgery → **Risk of injury to pelvic parasympathetic nerves** which lay on the *posterior* aspect of the prostate ⇒ **Urine Retention & Impotence** [asked on NBMEs]
 - GnRH suppression → **Leuprolide** is a **GnRH agonist** given **continuously**, which *increases FSH & LH levels* in first few days then *FSH & LH levels decrease* due to **receptor desensitization (tachyphylaxis)** ⇒ *decreased testosterone production*
 - **Androgen Receptor Blockers** → **Flutamide** administered **BEFORE** **Leuprolide** so that initial increase in FSH & LH doesn't increase testosterone production
 - In actual practice, they are given together, however, for **USMLE purposes** → **flutamide then leuprolide**.

Q27

A 23-year-old woman is brought to the emergency department because of excessive bleeding while brushing her teeth. Physical examination shows multiple ecchymoses. Laboratory studies show:

Hemoglobin	8.8 g/dL
Leukocyte count	106,000/mm ³
Platelet count	15,000/mm ³
Blasts	20%

Intensive multidrug chemotherapy is planned. Before this treatment is initiated to decrease this patient's risk for kidney failure, it is most appropriate to administer a drug that inhibits or binds to which of the following sites?

- A. Bacterial wall transpeptidase
- B. Ergosterol
- C. 30S ribosome
- D. Topoisomerase II (DNA gyrase) and topoisomerase IV
- E. Xanthine oxidase

▼ Explanation

- **Answer is E (Xanthine oxidase)**

- **IMP Clues**

- Excessive bleeding + multiple ecchymoses + anemia + low platelets + high leukocyte count + 20% blasts (So we have a bleeding disorder secondary to TCP caused by an acute leukemia)
- Chemotherapy is planned (so we expect tumor-lysis syndrome) + Q asks what ttt should be given to prevent kidney failure in this patient

- **Dx → Tumor Lysis Syndrome**

- Chemotherapy ttt of Leukemia usually causes **Tumor-Lysis Syndrome**
 - Leukemias are associated with a super high cell count (like here it's in 100,000s) so lysis of these cells due to chemotherapy would cause intracellular ions like **K, PO₄, and uric acid to be released into the circulation**
 - **High levels of uric acid in circulation precipitates in the acidic urine (poor solubility) → Uric acid nephropathy → Renal Failure**
- Prevention of Tumor-Lysis Syndrome is by **alkalinization** of urine, **hydration**, and **Xanthine Oxidase inhibitors** or **Urate Oxidase analogues**

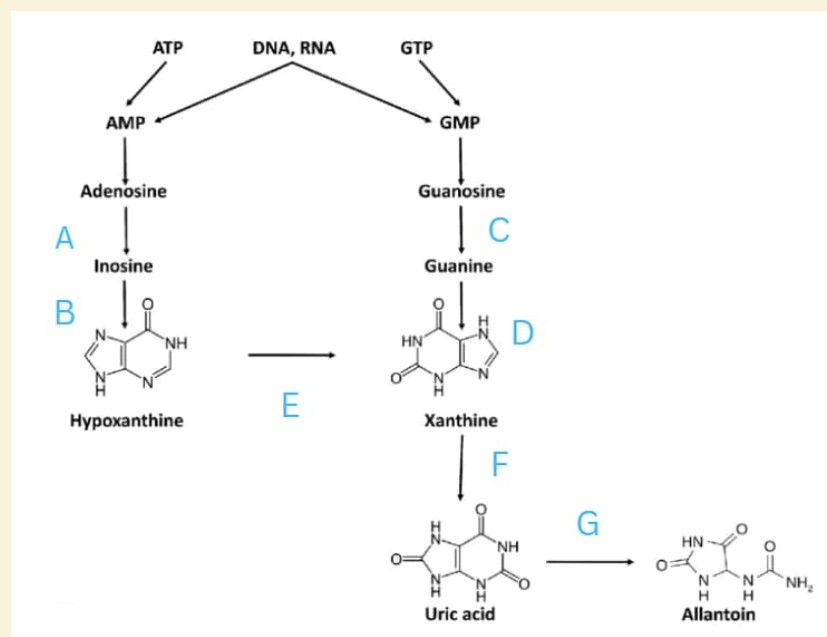
1. **Xanthine Oxidase Inhibitors**

- **Allopurinol & Febuxostat**
- **They inhibit Xanthine Oxidase, which inhibits hypoxanthine/xanthine oxidase (converts Hypoxanthine/Xanthine → Uric acid)**
 - Steps are Purines → Hypoxanthine/Xanthine → Uric acid
 - Purines are liberated from the lysed leukemia cells.

2. **Urate Oxidase analogues**

- a. **Rasburicase & Pegloticase**
- b. **They cleave uric acid into allantoin, which is much more soluble in urine → NO uric acid precipitation in kidney → NO renal failure**

? Label which of the following enzymes are acted upon by Xanthine Oxidase inhibitors and Urate Oxidase analogues.



▼ Answer

- Both **E & F** are **Xanthine Oxidase**.
- **G** is **Urate Oxidase/Uricase**.

“USMLE will do this; they will ask you a Q about Xanthine Oxidase inhibitors (either a case of gout or tumor lysis syndrome) and ask you to point out the enzyme in the metabolic pathway. They WILL NOT label both E & F, so don't worry this is just me being annoying.”

▼ Other Choices

- **Choice A** → Refers to **Penicillin**
- **Choice B** → Can refer to a range of antifungals. **Amphotericin B** and **Nystatin** bind to ergosterol, causing pores formation & cell death. **-azoles** on the other hand inhibit ergosterol formation by inhibiting 14-demethylase enzyme
- **Choice C** → Antibiotics that inhibit 30S ribosome are **Aminoglycosides and Tetracyclines**

- **Choice D** → **Fluoroquinolones** are antibiotics that inhibit prokaryotic topoisomerase II & IV

Q28

A 31-year-old woman receives a prescription for tetracycline and is instructed not to take the tetracycline with milk. If the tetracycline is taken with milk, its absorption is decreased due to which of the following effects?

- A. Alteration of stomach pH
- B. Binding to casein
- C. Formation of complexes with mineral ions
- D. Inhibition of intestinal cytochrome P450 enzymes

▼ Explanation

- **Answer is C (Formation of complexes with mineral ions)**
 - A repeated topic regarding tetracyclines on the NBMEs for some reason is that **“you can’t take tetracyclines with milk, as it chelates to the calcium” causing decreased absorption.**
 - *Another NBME Q says that a man has some sort of infection got prescribed a tetracycline, but is not getting any better + upon hx patient says he takes them with milk to make the pills easier to swallow; Q then asks why is he not getting better?*
 - Answer is something among the lines of **“tetracycline chelates to calcium in milk”.**
- This is also the reason why **giving tetracycline to pregnant women or children < 8 years of age is contraindicated**
 - **Tetracyclines chelates calcium (in bones and teeth) which causes deformities & discoloration.**
 - Qs might assess this by giving an infection, which requires tt by tetracyclines; however, the patient would be pregnant or a child <8 years ⇒ **DO NOT CHOOSE TETRACYCLINES**
 - **Ampicillin** is usually the answer in these Qs.

? What is another HY but underrated side effect of tetracyclines on the USMLE?

▼ Answer

Photosensitivity - Qs can give you **a patient on antibiotics**, which after *“playing soccer”* or *“going to the beach”* got **sunburned**. Q then asks for the antibiotic that caused this or its MOA.

- **Inhibits 30S ribosomal subunit**, which prevents aminoacyl-tRNA from binding to the A site (can be referred to as **“Inhibits protein synthesis”** on the USMLE)

▼ Other Choices

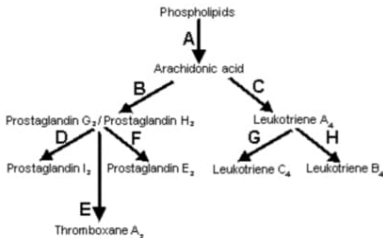
- **Choice A** → Milk does decrease stomach pH, however, it is not really a big deal for tetracyclines. Main problem is formation of insoluble complexes with Calcium.
- **Choice B** → Research actually shows that this is factually correct. Tetracyclines bind to casein. **However, for USMLE know that it is ions (especially Calcium) is what form the insoluble complexes with tetracyclines.**
- **Choice D** → Tetracyclines are not known to cause cytochrome P450 inhibition

Q29

A new drug has the following effects on the activity of the primary arachidonic acid metabolites produced by neutrophils, platelets, mast cells, and endothelium:

Cell Type	Arachidonic Acid Metabolite Activity	Drug Effect
Neutrophil	leukocyte chemotaxis	inhibition
Platelet	platelet aggregation	none
Mast cell	smooth muscle contraction	none
Endothelium	inhibit platelet aggregation	none

Which of the following is the most likely site of drug action?



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

- D. D
- E. E
- F. F
- G. G
- H. H

▼ Explanation

- Answer is H
 - Easy Q here, which assesses the chemotactic molecules.
 - Out of the PGs/LTs, **LTB4 is a chemotactic molecule.**
 - The table shows us that *ONLY* leukocyte chemotaxis is inhibited, while all the other metabolites activities are not ⇒ **ONLY LTB4 synthesis is inhibited (Choice H)**

? What are the chemotactic molecules on the USMLE?
▼ Answer
C5a- **LTB4** - IL-8 - PAF - Kallikrein

Q30

A 55-year-old man with type 2 diabetes mellitus, hypertension, and hyperlipidemia develops severe myalgias with weakness. Serum creatine kinase activity is increased, and urine is positive for myoglobin. Which of the following drugs is most likely responsible for these symptoms?

- A. Acarbose
- B. Captopril
- C. Metformin
- D. Pravastatin
- E. Prazosin
- F. Rosiglitazone
- G. Verapamil

▼ Explanation

- Answer is D (Pravastatin)
 - IMP Clues
 - Patient with hyperlipidemia develops severe myalgia + increased serum creatinine kinase activity + urine is positive for myoglobin (In a patient with hyperlipidemia, you'd expect him to be talking his drugs. 2 HY drugs can cause myopathy → muscle breakdown causing release of myoglobin + high CK)

- Dx → Drug-Induced Rhabdomyolysis
 - 2 HY hyperlipidemia drugs can cause myopathy → **Statins & Fibrates (especially if combined together)**
 - Out of these two drugs, *only statins (Pravastatin)* is in the answer choices.
 - **Statins**
 - *Inhibits HMG CoA reductase* (rate limiting enzyme of cholesterol synthesis) → less cholesterol synthesized by the body.
 - This causes *Up-regulation of LDL receptors* → Cholesterol scattered around the body is picked-up by the LDL-receptors to the liver
 - Side effects: **Hepatotoxicity & Myopathy (especially, if combined with fibrates)**

? Why does combining statins & fibrates increase the risk of rhabdomyolysis?
▼ Answer
CYP450 inhibition

? What are the mRNA levels of HMG CoA reductase in a patient that uses statins?
▼ Answer
mRNA levels of HMG CoA reductase **INCREASED.**

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

▼ Other Choices

| “Let’s review the most HY side effects of these drugs as they ALL were asked somewhere on these NBMEs.”

- Choice A → Diarrhea & GIT disturbance
- Choice B → Dry cough, angioedema, hyperkalemia, teratogenic (renal hypoplasia), and increase in creatinine levels in cases of Renal Artery Stenosis due to atherosclerosis or Fibromuscular Dysplasia
- Choice C → Lactic Acidosis; Contraindicated in patients with renal failure.
- Choice E → Hypotension

- **Choice F** → Weight gain, edema, and heart failure
- **Choice G** → Constipation

Q31

A 23-year-old man with a 3-year history of schizophrenia is brought to the physician for a follow-up examination. He has been taking an antipsychotic medication for auditory hallucinations, paranoia, and disorganized thinking for 2 years. Physical examination shows no abnormalities. During the interview, he does not make eye contact with the physician and occasionally turns his head when no one is talking as if he hears someone. Laboratory studies show a serum sodium concentration of 120 mEq/L, urine sodium concentration of 8 mEq/L, and urine osmolality of 80 mOsmol/kg H2O. Which of the following is the most likely cause of this patient's laboratory findings?

- A. Destruction of the neurohypophysis
- B. Hyperglycemia
- C. Increased degradation of ADH (vasopressin)
- D. Psychogenic polydipsia
- E. Resistance to the antidiuretic action of vasopressin

▼ Explanation

- **Answer is D (Psychogenic polydipsia)**
 - **IMP Clues**
 - Hx of schizophrenia (This is a risk factor for PP)
 - Serum sodium concentration of 120mEq/L (hyponatremia, which signifies that there is decreased serum osmolality → high water: solutes ratio)
 - Urine osmolality of 80 mOsmol/kg (low urine osmolality, which means we have high water:solutes ratio)
 - **Dx → Psychogenic polydipsia**
 - Patient (*usually has some psychiatric disorder*) drinks a shit tone of water → high water: solutes ration in serum & in urine. In other words, **both** the serum & the urine are **diluted**.
 - Labs would be:
 - **Serum → low osmolality & hyponatremia**
 - **Urine → low osmolality & low urine sodium**



Differentiating between Psychogenic Polydipsia, Diabetes Insipidus, and Syndrome of Inappropriate ADH:

- 1. Water Restriction**
 - If serum & urine labs **normalize** → *Psychogenic Polydipsia*
 - If serum & urine labs **DONOT normalize** → either *DI* or *SIADH*
- 2. Measure Serum & Urine labs**
 - If **serum is dilute** (low osmolality/hyponatremia) but **urine is concentrated** (high osmolality/high urine sodium) ⇒ *SIADH*
 - If **serum is concentrated** (high osmolality/hypernatremia) but **urine is dilute** (low osmolality/low urine sodium) ⇒ *DI*
- 3. Differentiating between Central DI vs Nephrogenic DI**
 - Administration of ADH (Vasopressin) causes **massive** change ⇒ *Central DI*
 - Administration of ADH (Vasopressin) causes **no/minimal** change ⇒ *Nephrogenic DI*

Q32

A 51-year-old man has the acute onset of fever and respiratory failure 6 weeks after a cadaveric renal transplant. He currently takes cyclosporine, prednisone, and trimethoprim-sulfamethoxazole. Vital signs are:

Temperature	38.3°C (101°F)
Pulse	120/min
Respirations	40/min
Blood pressure	110/60 mm Hg

He has no rash. Diffuse inspiratory and expiratory crackles are heard; there is no gallop or murmur. Laboratory studies show:

Leukocyte count	4000/mm³
-----------------	----------

Serum	
Urea nitrogen	24 mg/dL
Creatinine	2.1 mg/dL
Urine	
WBC	0-1/hpf
RBC	0-1/hpf

An x-ray of the chest is shown. Which of the following is the most likely cause?



- A. Atypical Mycobacterium infection
- B. Cytomegalovirus infection
- C. Left ventricular failure
- D. Pneumocystis jiroveci (formerly P. carinii) infection
- E. Transplant rejection

▼ Explanation

- **Answer is B (Cytomegalovirus infection)**
 - **IMP Clues**
 - Acute onset of fever and respiratory failure 6 weeks after a cadaveric renal transplant (As mentioned on Q25, transplant Qs are either about viruses reactivation or graft rejection; here we have pneumonitis + hx of transplant, rings any bells?)
 - He currently takes cyclosporine, prednisone (these are immunosuppressants, which predispose to the viral reactivation, but decreases incidence of graft rejection) and trimethoprim-sulfamethoxazole (this here excludes choice D, as PJ ttt/prophylaxis is TMP-SMX)
 - He has no rash (the rash in a patient with hx of organ transplantation usually signifies a graft-vs-host reaction, where the T-cells in the graft attacks the host, causing skin cells apoptosis *[asked on NBME]* which causes the rash)
 - No gallops or murmurs (excludes choice C)
 - Urine EBCs and RBCs 0-1/hpf (this excludes choice E, as renal transplant rejection would yes cause high creatinine/BUN, however, blood & WBCs in urine would be also seen)
 - X-ray is shown (Lung CXR showing diffuse lung opacities)
 - **Dx → CMV pneumonitis**
 - Remember Q25, where in the “Other Choices” section when I mentioned that **USMLE loves CMV reactivation in transplant patients as CMV pneumonitis.**
 - Patient is heavily immunosuppressed by given drugs → **CMV reactivation → CMV pneumonitis → acute respiratory failure, fever, diffuse inspiratory and expiratory crackles, and CXR showing diffuse opacities.**

?

What would be the expected features seen in a child with Congenital CMV infection?

▼ Answer

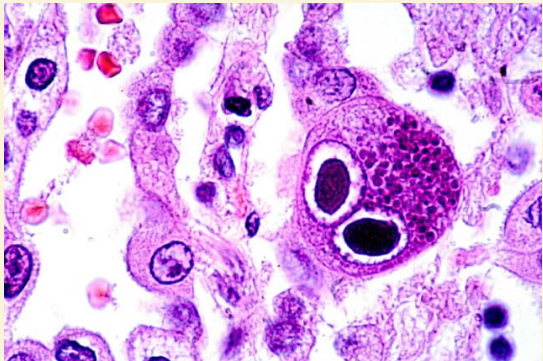
Microcephaly, Ventriculomegaly, SNHL, Periventricular Calcifications, and HSM, jaundice, and blueberry muffin rash.

?

What would be expected to be seen if a biopsy of the lung tissue was taken in this patient?

▼ Answer

Owl-Eye inclusions



▼ Other Choices

- **Choice A** → This garbage answer choice refers to Mycobacterium avium complex, which yes can cause pneumonia. However, you will not see this shit as a correct answer choice on the USMLE. If you want the real reason why this answer choice is incorrect then this is due to the CXR NOT showing calcified/fibrotic cavities, which are very specific for MAC.
- **Choice C** → LVF would present with **pulmonary edema (crackles)** which are seen here yes; however, **no gallops or murmurs** + the **presence of a fever makes LVF unlikely.**

- **Choice D** → **Pneumocystis jiroveci (formerly P. carinii) infection is a common cause of pneumonia** in immunosuppressed patients, however, the fact that **this patient is taking *TMP-SMX*** excludes the possibility of this infection being caused by Pneumocystis jiroveci (formerly P. carinii)
- **Choice E** → Renal Transplant rejection would cause hematuria & WBCs seen in urine.

Q33

A 2-year-old child undergoes resection of the right kidney because of chronic infections secondary to reflux. The left kidney is grossly normal. Which of the following structural adaptations will eventually occur in the left kidney?

- A. Atrophy of tubules and glomeruli
- B. Hyperplasia of parietal epithelium
- C. Increase in glomerular size
- D. Increase in number of glomeruli
- E. Metaplasia of tubular epithelium

▼ **Explanation**

- **Answer is C (Increase in glomerular size)**
 - If you remove a kidney, the other kidney will have to adapt by **compensatory hypertrophy** to balance the increased workload.
 - What we care about to increase in the functional part of the kidney → **The Nephron**
 - *Can the nephron increase in **number** (hyperplasia)?* → **NO**. We are born with ~million nephrons in each kidney; **this number is fixed and can't increase.**
 - *So, the other option is that the nephrons need on increase in **SIZE** (hypertrophy):*
 - **A nephron is made up of Glomeruli + Renal Tubules**
 - Increase in the **glomerular size** would *increase the surface area* available for **filtration**
 - Increase in **tubular size** would *increase the surface area* for **reabsorption and secretion**
 - Overall, these 2 major changes compensate for the other missing kidney.

▼ **Other Choices**

- **Choice A** → Atrophy of tubules and glomeruli would cause a smaller kidney. This can be seen in some Qs when they say the patient has a smaller kidney + angio shows a renal artery stenosis.
- **Choice B** → Hyperplasia of parietal epithelium is seen in RPGN.
- **Choice D** → Number of glomeruli CAN'T INCREASE. Only the size.
- **Choice E** → Metaplasia is change from one type of epithelium from another due to some sort of chronic stressor/irritant. Not really a big thing in kidneys.

Q34

A 3-month-old boy is brought to the physician because of facial abnormalities and weakness since birth. Physical examination shows coarse facial features and hypotonia. Urinary excretion of mucopolysaccharides is within the reference range. The concentrations of lysosomal enzymes are increased in serum and decreased in cultured skin fibroblasts. Which of the following molecular markers is most likely decreased in this patient's lysosomal enzymes?

- A. N-Acetylglucosamine
- B. Fucose
- C. Galactosamine
- D. Mannose 6-phosphate
- E. Sialic acid

▼ **Explanation**

- **Answer is D (Mannose 6-phosphate)**
 - **IMP Clues**
 - Facial abnormalities and weakness since birth (okay so not an acquired cause, but a congenital one)
 - Coarse facial features and hypotonia (nonspecific really but as you read on you'd start to understand that this is a lysosomal storage disease)
 - Concentration of lysosomal enzymes are increased in serum & decreased in cultured skin fibroblasts (The enzymes should be in the cells "the skin fibroblasts" and not in serum)
 - Q asks for most likely decreased in this patient lysosomal enzymes

- **Dx → I-cell Disease**
 - *Enzyme deficiency* = **acetylglucosamine-1-phosphotransferase**
 - Buildup = Many lysosomal enzymes
 - Pathophysiology
 - **Cannot synthesize mannose-6-phosphate at the Golgi**
 - **Mannose 6-Phosphate** needed to *target lysosomal enzymes to the lysosomes* (What the Q asks for, the “molecular markers”, which is missing/decreased here)
 - **Missing M6P = lysosomal enzymes are secreted into cytosol + serum**
 - Clinical Features
 - **Course facial features**
 - **Joint contractures**
 - Hepatomegaly
 - Recurrent ear infections



I-CELL DISEASE HACKS:

- If USMLE asks for the location of the error/problem → **Golgi**
- If USMLE asks for where the enzymes can't go → **lysosome**
- If USMLE asks for where the enzymes do go → **cytosol/plasma/serum**

Q35

An 83-year-old man is brought to the emergency department after being found at home bedridden and confused. He takes no medications. Temperature is 35.6°C (96°F), pulse is 100/min, and blood pressure is 85/50 mm Hg. Blood pressure is unchanged after intravenous infusion of 1 liter of isotonic saline. A pulmonary artery catheter is inserted and the following findings are obtained:

Cardiac output	high
Pulmonary capillary wedge pressure	low
Systemic vascular resistance	low

Which of the following is the most likely cause of the hypotension?

- A. Early septic shock
- B. Gastrointestinal bleeding
- C. Hypothyroidism
- D. Massive pulmonary embolism
- E. Silent myocardial infarction

▼ **Explanation**

- **Answer is A (Early septic shock)**
 - **IMP Clues**
 - 83-year-old man is brought to the ED after being found at home bedridden and confused (an old male + delirium, YOU MUST THINK UTIs, which can cause sepsis. This is not related to the Q, but I'm saying it because it is important clinically & is mentioned on the USMLE)
 - Temperature is 35.6C (patient is hypothermic, which is a bad sign because we think this sepsis, which should have a high fever; however, if the sepsis progresses & the immune system collapses → Hypothermia)
 - Blood pressure is 85/50 mmHg (Hypotensive) + blood pressure is unchanged after IV infusion (this means it is not a blood volume issue)
 - CO (high, so not a cardiac problem) + PCWP (low, so NOT cardiogenic shock) + SVR (low, this seals the deal; low SVR is either septic shock, neurogenic shock, or anaphylactic shock)
 - **Dx → Septic Shock**
 - This patient most likely has an occult infection (my bet is that it is a UTI, the BPH is the most likely cause in my opinion), which caused sepsis → **Release of inflammatory cytokines (TNF-alpha & IL-1)**
 - **TNF-alpha** ⇒ **Increases Nitric Oxide synthase** → **Increases NO release** → **HYPOTENSION [asked on NBME]**
 - **IL-1** ⇒ **alters hypothalamic thermostat temperature point** → **FEVER**
 - Hypotension causes **decreased SVR (patient is warm & flushed)**, which cause a compensatory **increase in CO**.
 - PCWP is Left Atrial pressure. PCWP is **increased ONLY** in **CARDIOGENIC SHOCK** on the USMLE.

▼ **Other Choices**

- **Choice B** → GI bleeding would cause a decreased preload & decreased CO, which would cause increased heart rate & increased SVR.
- **Choice C** → No relation to hypothyroidism here

- **Choice D** → Massive PE would present as severe chest pain + dyspnea +/- hemoptysis. An embolism in the PA would decrease LA blood flow → decreased LV blood flow → decreased CO & increase compensatory SVR.
- **Choice E** → Silent MI usually causes a cardiogenic shock, which causes a low CO, high PCWP, and a high SVR.

Q36

In patients with breast cancer, metabolically stable agonists of gonadotropin-releasing hormone are effective because they inhibit release of which of the following?

- A. Activin from the gonads
- B. Gonadotropin by the pituitary gland
- C. Inhibin from the gonads
- D. Prolactin by the pituitary gland

▼ Explanation

- **Answer is B (Gonadotropin by the pituitary gland)**
 - You must know that GnRH PULSES causes secretion of FSH & LH. Yes, it is the pulses that stimulate the secretion of FSH & LH from the pituitary gland.
 - If a metabolically stable GnRH agonist is given → initial increase in FSH & LH, then after a couple of days → Receptor desensitization → decreased FSH & LH release.
 - This is referred to as **tachyphylaxis**, and I have mentioned it in Q26
 - **Leuprolide** is a **GnRH agonist** used in ttt of prostate cancer. It is given *continuously* causing initial increase in FSH & LH production (as a result increases testosterone production), however, after a couple of days → **Receptor desensitization (Tachyphylaxis)** → decreased FSH & LH → testosterone production decreases.
- The same concept is applied here. In patients with breast cancer, GnRH agonists are given so that FSH & LH levels decrease, so that Estrogen & Progesterone levels also decrease.



What drug is given with Leuprolide in prostate cancer to avoid side effects?

▼ Answer

Flutamide - Androgen Receptor antagonist used BEFORE leuprolide is given to inhibit effects of initial increase in FSH & LH levels.



What type of cells are FSH & LH released from?

▼ Answer

Basophils of Anterior Pituitary



What is the 2nd messenger of FSH & LH?

▼ Answer

cAMP

Q37

A 62-year-old man comes to the physician because of a 1-week history of muscle cramps accompanied by painful spasms in his arms and legs. He tells the physician that, for the past 4 months, he has had trouble opening jars and using silverware. Examination shows muscle weakness and exaggerated deep tendon reflexes. An appropriate treatment of the muscle cramps and spasms in this patient includes systemic administration of a drug with which of the following mechanisms of action?

- A. Agonist at γ-aminobutyric acid B (GABA B) receptors
- B. Antagonist at glycine receptors
- C. Blockade of acetylcholine release from nerve terminals
- D. Inhibition of the norepinephrine transporter
- E. Inverse agonist at benzodiazepine receptors

▼ Explanation

- **Answer is A (Agonist at γ-aminobutyric acid B (GABA B) receptors)**
 - Patient has UMNL of some sort (I know that it is an UMNL due to the exaggerated deep tendon reflexes) + has muscle weakness, cramps, and painful spasms.
 - Q asks us for what drug he should take?
 - **Muscle Relaxant** → **Baclofen (GABA B Receptor Agonist)**
 - **GABA** is an **inhibitory neurotransmitter**, so agonism causes **inhibition of excitatory signals** (like that of *glycine* & *glutamate*) → **hyperpolarization of neurons** → **muscle relaxation**
 - Used in ttt of **multiple sclerosis** & **muscle spasticity**



KNOW THE DIFFERENCE:

GABA A agonist → Benzodiazepines & barbiturates

GABA B agonist → Baclofen

Q38

A 62-year-old woman comes to the physician because of progressive bilateral lower abdominal pain and distention during the past month. Pelvic examination shows an adnexal mass on the right. Pelvic ultrasonography shows a 6 × 6-cm mass in the right ovary with an internal echo pattern highly suggestive of ovarian cancer. Microscopic examination of peritoneal fluid obtained by paracentesis shows malignant cells. Paclitaxel therapy is initiated. This treatment will target which of the following in this patient's tumor?

- A. Dihydrofolate reductase
- B. Dihydroorotate dehydrogenase
- C. DNA polymerase α
- D. DNA polymerase β
- E. DNA topoisomerase I
- F. DNA topoisomerase II
- G. Ribonucleotide reductase
- H. RNA polymerase
- I. β -Tubulin

▼ Explanation

- Answer is I (β -Tubulin)

- Q asks what will Paclitaxel target in this patient's tumor.

- Taxanes (Paclitaxel & Docetaxel) are microtubule stabilizers.

- They bind to **β -Tubulin in microtubules & hyper-stabilizes** them → Microtubules CAN'T breakdown (this is needed for cell division) → Cells are "**stuck**" & CAN'T undergo cell division/mitosis.
- This "paralysis" causes → **apoptosis of cells.**

? What are the other HY microtubules related drugs on the USMLE? How does their mechanisms differ?

▼ Answer

Microtubules **stabilizers**

- Binds β -Tubulin causing **hyper-stabilization** → halting cell division → apoptosis
- Examples → Taxanes (Paclitaxel & Docetaxel)

Microtubules **inhibitors**

- Bind β -Tubulin causing **inhibition of assembly** → halting cell division → apoptosis
- Examples are:
 1. Colchicine
 2. Albendazole & Mebendazole (-bendzoles)
 3. Vincristine
 4. Vinblastine
 5. Griseofulvin

| "Yes, you have to know **ALL OF THEM.**"

Q39

A 19-year-old woman has severe refractory pustular acne that has been unresponsive to several topical and systemic therapies. Treatment with daily oral isotretinoin is begun. Which of the following pharmacologic effects of this drug is dependent on its binding to the RXR receptor?

- A. Decreased Propionibacterium acnes proliferation
- B. Decreased wax formation
- C. Maturation of oocyte follicles
- D. Teratogenic effects in the embryo
- E. Trafficking of neutrophils through endothelial tight junctions

▼ Explanation

- Answer is D (Teratogenic effects in the embryo)

- Q asks what effect is dependent on isotretinoin's effect on its binding to the RXR receptor

- Isotretinoin is a vitamin A derived drug that is used in treatment of severe acne (pustular cystic type), however, you must know that the use of isotretinoin is contraindicated in pregnancy + need concurrent use of contraceptive in females due to its teratogenic effect.
- Why is it teratogenic?
 - Isotretinoin binds to RXR Receptors (Retinoid X Receptors), which is nuclear receptor that regulates transcription factors of HOX gene, which plays a role in organization of the embryo in the craniocaudal direction.
 - Excessive isotretinoin intake → excessive RXR stimulation → abnormal signaling to HOX gene (and other regulators) → abnormal embryogenesis (Teratogenic effect)

?

HOX gene plays a role in embryogenesis through which of the following processes?

A) Allele exclusion
B) Alternate mRNA splicing
C) Regulation of transcription
D) Regulation of translation
E) Signal transduction

▼ Answer

Regulation of transcription

“This is an actual NBME Q.”

Q40

A 54-year-old woman with terminal metastatic pancreatic cancer comes to the physician for a follow-up examination. She asks the physician to prescribe her a sufficient quantity of medication to allow her to commit suicide if the pain becomes unbearable. The physician refuses to do so, but he informs the patient that he will do everything he can to manage her pain. The physician's decision in this situation is most consistent with which of the following ethical principles?

- A. Autonomy
- B. Beneficence
- C. Dignity
- D. Justice
- E. Nonmaleficence

▼ Explanation

- Answer is E (Nonmaleficence)
 - Differentiating between Nonmaleficence & Beneficence is HY for the USMLE:
 - Nonmaleficence is NOT doing something that can hurt the patient (essentially, “do no harm”)
 - This Q is an example of that. You REFUSE to help allow the patient to commit suicide. Another example is NOT doing a surgery that patient want because the patient is not indicated for this surgery. You are NOT doing something.
 - Beneficence is DOING something for the benefit of the patient.
 - An example of that is giving a Jehovah's Witness child a blood transfusion after RTA. JWs on the USMLE are not given blood transfusions due to their religious beliefs, however, JWs children MUST be given blood transfusion even if the parents don't consent. You are DOING something for the benefit of the patient.

?

34M + 9F came to the ED after RTA. They are in critical condition and in need of blood transfusion. You found a note saying that they are Jehovah's Witnesses and not to give him or his child blood. What should you do?

▼ Answer

Give the child blood and do not give the father blood.

Q41

A 22-year-old woman comes to the emergency department because of a 2-hour history of fever, chills, and muscle aches. Six hours ago, she received an injection of penicillin G benzathine for syphilis. Her temperature is 38.9°C (102°F). Physical examination shows no other abnormalities. Which of the following best explains this patient's symptoms?

- A. Antibiotic resistance
- B. Drug allergy
- C. Drug-induced disseminated intravascular coagulation
- D. Release of bacterial products
- E. Serum sickness

▼ Explanation

- Answer is D (Release of bacterial products)
 - IMP Clues
 - 2hr hx of fever, chills, and muscle aches + 6hr hx of penicillin G injection for syphilis (Syphilis is the giveaway here. Timing is also important)
 - Dx → Jarisch-Herxheimer reaction

“We talked about this when we discussed Syphilis on this NBME.”

- Rapid release of cell wall components/organism products ⇒ LPS-like reaction ⇒ Fever, chills, hypotension
- This happens with all spirochetes infections, most commonly syphilis on the USMLE, however, some Qs ask about this with *Lyme Disease [asked on NBME]*

▼ Other Choices

- **Choice A** → Antibiotic resistance would present as persistence of the infection, in this case here syphilis.
- **Choice B** → Drug allergy would cause an immediate reaction, not a few hours after. **Type 1 HS.**
- **Choice C** → DIC? Nope.
- **Choice E** → Serum sickness is HY. **Type 3 HS** due to antigen-antibody complexes depositing in tissue.
 - Presents as arthritis and/or erythema nodosum (panniculitis) 3-7 DAYS after injection of drug
 - If it was localized rash/muscle pain at site of injection 3-7 DAYS after, then this is **Arthus reaction** (a type of serum sickness)

Q42

An 18-year-old woman comes to the physician because of fever, a severe sore throat, and fatigue for 1 week. Her temperature is 38.1°C (100.6°F). Physical examination shows pharyngeal erythema, generalized tender lymphadenopathy, and splenomegaly. Laboratory studies show a leukocyte count of 4400/mm³ with 20% atypical lymphocytes. Which of the following cell types most likely accounts for the atypical lymphocytes in this patient's peripheral blood?

- A. Gamma delta T lymphocytes
- B. Reactive B lymphocytes
- C. Reactive T lymphocytes
- D. Virus-infected B lymphocytes
- E. Virus-infected T lymphocytes

▼ Explanation

- **Answer is C (Reactive T lymphocytes)**
 - **IMP Clues**
 - Fever, severe sore throat, and fatigue for 1 week (Sounds like an infection)
 - Pharyngeal erythema, generalized tender lymphadenopathy, and splenomegaly (This triad is buzzy for? We just talked about this a few Qs back... It is EBV)
 - 20% atypical lymphocytes + Q asks what cell types account for these cells?
 - **Dx → Infectious Mononucleosis**
 - The concepts keep repeating guys. Master them.
 - We know that **EBV infects B-cells**, however, the **reactive/atypical cells on smear are the T-cells**. It told you it is HY.

? What test is used to diagnose Infectious Mononucleosis?
▼ Answer
Heterophil (or Monospot) test - If Q says these tests are negative, **IT IS NOT EBV**

? What is the receptor that EBV uses to enter B-cells
▼ Answer
CD21

? What would a lymph node biopsy of this patient show?
▼ Answer
Monomorphous population of B lymphocytes

? If this patient received ampicillin, what would be expected to happen?
▼ Answer
Maculopapular Rash

Q43

Two days after admission to the hospital because of drug-induced thrombocytopenia, a 37-year-old woman develops a severe headache and becomes comatose. On admission, examination showed a few petechiae over the lower extremities, and her platelet count was 5000/mm³. A CT scan of the head shows an intracranial hemorrhage. A platelet transfusion is recommended, but the patient is a Jehovah's Witness and had stated on admission that she did not want to receive transfusion of any blood products. Her husband is not a Jehovah's Witness and wants her to have the transfusion. Which of the following is the most appropriate management regarding transfusion?

- A. Do not proceed with the transfusion

- B. Obtain consent from the hospital ethics committee
- C. Obtain consent from the patient's husband
- D. Obtain consent from the patient's minister
- E. Proceed with the transfusion without consent

▼ Explanation

- Answer is A (Do not proceed with the transfusion)

“We just talked about this, and I promise you I didn’t know this Q was here.”

- JWs patients are not given blood under any circumstances **EXCEPT** → **Children** (< 18 years) EVEN IF parents refuse.
- This is an example of **Autonomy**.

Q44

An 18-year-old woman comes to the physician to request screening for colon cancer. Her father and grandfather died of colon cancer at the ages of 36 and 45 years, respectively. Physical examination shows no abnormalities. Colonoscopy shows approximately 200 lesions throughout the colon. A colectomy is done, and a section of the colon removed is shown in the photograph. Which of the following is the chance that this patient's offspring will eventually develop adenocarcinoma of the colon?



- A. 0%
- B. 25%
- C. 50%
- D. 75%
- E. 100%

▼ Explanation

- Answer is C (50%)

- IMP Clues

- Her father and grandfather died of colon cancer at age of 36 and 45 years (sounds like aggressive hereditary colon cancer, so we’re thinking Lynch or FAP)
- Colonoscopy shows ~200 lesions (hundreds of lesions is FAP. Lynch is some/couple)
- Q asks for chances that this patient's offsprings will develop adenocarcinoma

- Dx → Familial Adenomatous Polyposis (FAP)

- It is an **Autosomal Dominant** disease.
- Patients with FAP usually develop colon cancer 100% of the time, so colectomy is done in teens.
- There is a **50% chance** (because it is AD) that this patient's offsprings get the disease.



What are the genetic basis of FAP?

▼ Answer

Mutation in **APC** (tumor suppressor gene) on **chromosome 5**

Q45

A 41-year-old woman with systemic lupus erythematosus is scheduled to undergo surgical placement of a peritoneal dialysis catheter. The surgeon asks the resident physician to get the consent form signed the evening before the procedure. The resident has never seen this procedure performed and has read little about it. He will not be assisting with the procedure. Which of the following actions by the resident physician is most appropriate?

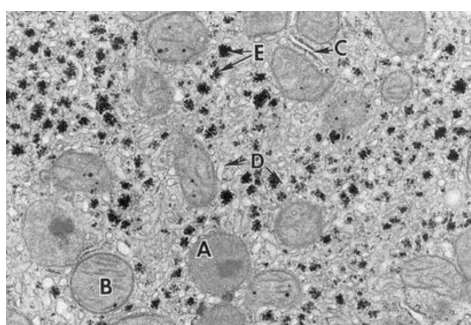
- A. Ask a nurse to get a signature on the form
- B. Ask the attending physician to obtain informed consent
- C. Ask the patient to sign the form and tell her that the surgeon will answer questions the next morning
- D. Obtain an informed consent by explaining what he believes is the major risk
- E. Try to answer any of the patient's questions concerning the procedure

▼ Explanation

- **Answer is B (Ask the attending physician to obtain informed consent)**
 - **Informed consent** must be obtained by the **person performing the surgery (or will be involved/assisting with it)**.
 - The physician should also be able to **explain the nature of the surgery/procedure**, the **risks and benefits**, any **alternative options**, the **expected outcome/complications**, and **answer any Qs the patient might have**.
 - The resident in this Q has never seen the procedure performed and has read little about it + he will not be assisting with the procedure ⇒ He can't do any of the above requirements.

Q46

A 23-year-old man comes to the physician because of a 1-month history of weakness and muscle pain after vigorous exercise. His mother, sister, and grandmother have a similar condition; however, his father's sister and her children are unaffected. A muscle biopsy specimen shows ragged red fibers. This condition most likely results from a mutation in a gene located in which of the following labeled structures in the photomicrograph?



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

▼ **Explanation**

- **Answer is B**
 - **IMP Clues**
 - Weakness and muscle pain after vigorous exercise (Some kind of myopathy which causes pain & weakness on exertion)
 - His mother, sister, and grandmother have a similar condition (mother → all her children; this is mitochondrial transmission)
 - Muscle biopsy shows ragged red fibers (seals the deal, this is a mitochondrial disease)
- **Dx → Mitochondrial Disease**
 - We can't for sure point out which mitochondrial disease this is (can be MELAS, MERRF...) like we did on Q1 of this NBME.
 - What we know that the **ragged red fibers + maternal (mitochondrial) transmission ⇒ Mitochondrial disease**
 - **Defective mitochondria → defective oxidative phosphorylation → decreased ATP → muscle weakness and pain**
 - Q was asking about the location of mutated gene (the mitochondria), which as I said on Block 1 Q1, it is the **double membraned organelle with cristae inside (the wavy lines)**

? If this was MELAS, what gene would be mutated?
 ▼ **Answer**
 MT-TL1, "mitochondrial-tRNA Leu"

Q47

A 45-year-old woman develops proteinuria and hematuria. She has taken 3 g of ibuprofen for headaches almost daily for the past 2 years. Which of the following findings is most likely in tissue obtained on renal biopsy?

- A. Crescentic glomerulonephritis
- B. Focal segmental glomerulonephritis
- C. IgA nephropathy
- D. Membranoproliferative glomerulonephritis
- E. Tubulointerstitial nephritis

▼ **Explanation**

- **Answer is E (Tubulointerstitial nephritis)**
 - **IMP Clues**

- Proteinuria and hematuria following 2-year hx of daily 3g ibuprofen (high dose NSAIDs causing renal damage → proteinuria & hematuria)

- **Dx → Tubulointerstitial Nephritis**

- Inflammation of the **renal tubules + interstitial tissue** [*asked on NBME*] around it, so can also be referred to as **"Interstitial Nephritis"**
- Caused by intake of **NSAIDs, Antibiotics (Beta-lactams & cephalosporins), or Sulfa drugs (Allopurinol is HY)**
- 2 Presentations on the USMLE
 1. **Proteinuria +/- Hematuria (rarer) after intake of the above drugs** (Remember that on your exam they might be sneaky and refer to the proteinuria as *"peripheral edema,"* as proteinuria causes peripheral edema. Hematuria = Red urine)
 2. **WBCs in urine (classically Eosinophils) +/- Rash (classically maculopapular) +/- Fever after intake of above drugs**



What would be seen on biopsy?

▼ Answer

Lymphocytes, Eosinophils, and Plasma cell infiltrates in the interstitium

▼ Other Choices

- **Choice A → Refers to RPGN**, presents as **rapid deterioration of renal functions** in patients with **Goodpasture Syndrome, Wegner Granulomatosis, Microscopic Polyangiitis**, and **Eosinophilic granulomatosis with Polyangiitis**.
 - Biopsy shows **Fibrin Crescents**.
- **Choice B → FSGS** presents as **proteinuria** in a patient with **sickle cell disease, Heroin use, or HIV**
- **Choice C → IgA nephropathy** presents as **hematuria** ~2 days after onset of **URTI** (usually viral)
- **Choice D → MPGN** presents as **hematuria** in a patient with hx of **Heroin use, HCV, or Malignancies**
 - EM shows → **Splitting of GBM** *"Tram-Track appearance"*

Q48

A 4-year-old boy has had fever, abdominal cramping, and repeated bloody mucoid stools with tenesmus over the past 3 days. Several other children at his day-care center have a similar illness. Direct microscopic examination of a methylene blue-stained fecal smear shows numerous neutrophils. Which of the following is the most likely causal organism?

- A. Clostridium difficile
- B. Clostridium perfringens
- C. Enterococcus faecalis
- D. Escherichia coli
- E. Listeria monocytogenes
- F. Proteus vulgaris
- G. Shigella sonnei
- H. Vibrio parahaemolyticus

▼ Explanation

- **Answer is G (Shigella sonnei)**
 - **IMP Clues**
 - Fever, abdominal cramping, and repeated bloody mucoid stools with tenesmus (Inflammatory diarrhea, tenesmus is buzzy for shigella)
 - Fecal smear shows numerous neutrophils (Presence of neutrophils means that this bacteria is invasive, invasion of GI wall → strong immune response, the leukocytes)
 - Let's go through the answer choices:
 - **Choice A → Clostridium difficile** causes **pseudomembranous colitis** in patients **after antibiotics use** (especially **clindamycin**)
 - Diarrhea is **watery** (can be blood sometimes) + **Fever** + **Abdominal Pain**. Not really associated with day-care center transmission.
 - ttt → **oral vancomycin**
 - **Choice B → Clostridium perfringens** causes **watery diarrhea** (**NOT** bloody) + associated with **food poisoning** due to ingestion of **spores**, so **no** leukocytes on fecal smear.
 - **Choice C → Enterococcus faecalis** causes **UTIs, Endocarditis, and Biliary Tree Infections** (remember the "U heart Trees" sign in sketchy?). **NO** diarrhea.
 - **Choice D →** The use of "E.coli" is vague. Which Type?
 - **ETEC** causes **watery diarrhea**.

- EHEC causes bloody diarrhea with **NO** fever & **NO** fecal leukocytes as it is caused by a toxin, not direct invasion.
 - EIEC causes bloody diarrhea + **Fever** + **Fecal leukocytes**, so can be an answer; however, it being transmitted at a “day-care center” is unlikely.
- **Choice E** → **Listeria monocytogenes** on the USMLE is associated with **neonatal / elderly meningitis**.
 - **Choice F** → **Proteus vulgaris** causes **UTIs + Struvite stones** as it is *urease* **positive**.
 - **Choice G** → **Shigella sonnei** causes **inflammatory diarrhea + Fever + Tenesmus + Fecal leukocytes** (as it is invasive) + has **high infectivity** (as it is acid stable, so perfect for feco-oral transmission, especially day-care centers)
 - **Choice H** → **Vibrio parahaemolyticus** causes watery diarrhea following **seafood ingestion**.

Q49

A 35-year-old man comes to the physician because of a 2-month history of inflamed thickened skin covered with silvery scales on the scalp, trunk, elbows, and knees. This condition has been poorly responsive to coal tar preparations, calcipotriene, and triamcinolone cream. Which of the following drugs is the most appropriate next step in treatment?

- A. Azathioprine
- B. Cyclophosphamide
- C. Methotrexate
- D. Tetracycline
- E. Tretinoin cream

▼ **Explanation**

- **Answer is C (Methotrexate)**
 - **IMP Clues**
 - Inflamed thickened skin covered with silvery scales (This description is buzzy for psoriasis)
 - Condition has been poorly responsive to coal tar preparations, calcipotriene, and triamcinolone
 - Q asks for next step in treatment?
- Treatment of Psoriasis goes like this:
 1. Topical Therapy
 - a. **Topical Corticosteroids (Triamcinolone)**
 - b. **Vitamin D analogs (calcipotriene)** → inhibits keratinocyte differentiation
 - c. Adjuvants (**Coal Tar preparation, Salicylic acid**)
 2. Systemic Therapy
 - a. **Methotrexate** (Dihydrofolate Reductase Inhibitor) **[1st-Line]**
 - b. **Cyclosporine** (Inhibits Cyclophilin)
 - c. **TNF-alpha inhibitors (Etanercept, Adalimumab, infliximab, certolizumab pegol, golimumab)**
 - d. **IL-12/23 inhibitors (ustekinumab)**
 - e. **IL-17 inhibitors (Ixekizumab + secukinumab)**



Psoriasis Rapid Review!

- Site: classically on **extensors** (**most commonly on knee/elbows**)
 - Vignettes will say a patient with **bloody diarrhea** (associated UC) + **Scales** → **think psoriasis**
 - May also ask about psoriatic arthritis → **Pencil-in-cup deformity**
- Associations: **HLA-B27** (**"PAIR"** → **P**soriasis - **A**nkylosing Spondylitis - **I**BD - **R**eactive Arthritis)
- **Auspitz sign**: Bleeding of scales on removal
- **Munro micro-abscesses**: collection of neutrophils in stratum corneum of epidermis



What are other HY drugs that share the same MOA with MTX?

- ▼ **Answer**
Trimethoprim & Pyrimethamine

Q50

A 62-year-old man with alcohol-induced liver disease develops massive ascites. Infection is ruled out. The most appropriate diuretic treatment, in addition to loop diuretics, includes which of the following drugs?

- A. Acetazolamide
- B. Hydrochlorothiazide
- C. Indapamide
- D. Metolazone
- E. Spironolactone

▼ Explanation

• Answer is E (Spironolactone)

◦ IMP Clues

- Man with alcohol-induced liver disease develops ascites (expected complication, pretty standard)
- Infection is ruled out (So no need for antibiotics therapy, we use ceftraxione by the way)

◦ In addition to loop diuretics, what is another diuretic drug that should be used?

- Patients with liver failure & ascites usually have **decreased oncotic pressure** (due to decrease albumin production from the cirrhotic liver) and **increased hydrostatic pressure** (due to fibrosis of hepatic sinusoids)
 - This cause **extravasation of the intravascular volume into extravascular spaces** (third space, like peritoneal cavity → ascites)
 - The **decreased intravascular volume (Effective Plasma Volume)** causes **increased** secretion of **renin** → **increased aldosterone** production → **hypokalemia**
- How to treat the ascites?
 - Most effective diuretic → **Loop Diuretic** (but major side effect is **hypokalemia**; this side effect + the already pre-existing hypokalemia can cause cardiac arrest)
 - To deal with hypokalemia, **we add another diuretic** → **Spironolactone (increases diuresis + potassium sparing)**

? What is a super HY side effect of Spironolactone (other than hyperkalemia)?

▼ Answer

Gynecomastia (due to anti-androgen effects of the drug)

▼ Other Choices

- **Choice A** → **Acetazolamide** is a *Carbonic Anhydrase inhibitor* diuretic used mainly in people going on trips to high altitude places.
 - High altitude = decreased FiO_2 → hypoxia → increased RR → Respiratory Alkalosis
 - **Acetazolamide causes loss of HCO_3 in urine** → **Metabolic Acidosis**
 - Now the pH is **normalized**.
 - Why take CA inhibitors in the first place? *Well, the kidneys take about 24hr to start adapting, so people with respiratory/cardiac diseases need to take CA inhibitors until the kidneys can do their work.*
- **Choices B, C, D** → **Thiazide diuretics** are used as **HTN medication** in those with **NO DM** or **cardiovascular/cerebrovascular diseases**.
 - It is also used in those with **renal stones as they cause decreased urine calcium secretion**.

? What is the site of action of Acetazolamide?

▼ Answer

Proximal Convoluted Tubules - inhibits CA enzyme

? What is the site of action of Thiazide Diuretics?

▼ Answer

Distal Convolute Tubules - Blocks Na/Cl channels

? What are the HY side effects of Thiazides assessed on the USMLE?

▼ Answer

[] mnemonic: "**hyperGLUC** + other"

1. Hyper**G**lycemia
2. Hyper**L**ipidemia
3. Hyper**U**ricemia
4. Hyper**C**alcemia
5. Others → **Hyperprolactinemia**, **Hyponatremia**, **Hypokalemia**, **Metabolic alkalosis**, **Lithium toxicity**



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