



NBME EXPLANATIONS

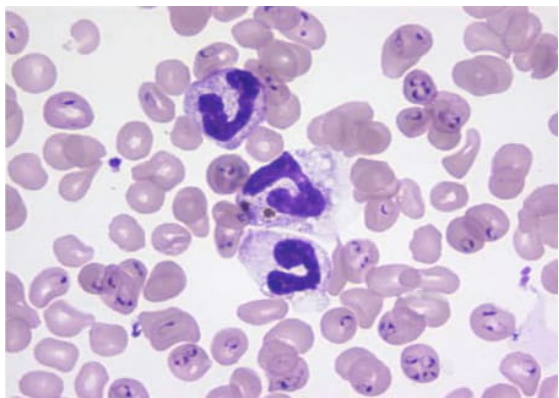
NBME 23 Block 3

from CrackNBME

23-Block 3

Q1

A 31-year-old primigravid woman at 32 weeks' gestation comes to the physician because of a 3-day history of fever and chills. She recently immigrated to the USA from Ghana. She appears drowsy. Her temperature is 39.4°C (103°F), pulse is 136/min, respirations are 24/min, and blood pressure is 95/62 mm Hg. Physical examination shows a uterus consistent in size with a 32-week gestation. A photomicrograph of a peripheral blood smear is shown. This patient is at greatest risk for which of the following complications?



- A. Adrenal insufficiency
- B. Diabetes insipidus
- C. Hypoglycemia
- D. Hypoparathyroidism
- E. Thyrotoxicosis

▼ Explanation

• Answer is C (Hypoglycemia)

◦ IMP Clues

- 3-day history of fever and chills + appears drowsy
- She immigrated to the USA from Ghana
- Temperature is 39.4C + pulse is 136/min + blood pressure is 95/62
- Peripheral Smear shows Ringed-Shaped Inclusions

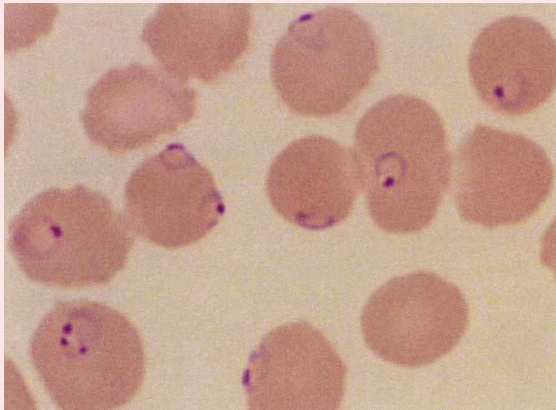
• Dx → Malaria Infection

- Most questions will mention **history to travel to an African or South American country**
- Caused by **Plasmodia**, which has multiple species:
 - **Plasmodium falciparum:**
 - **Most virulent** and causes the **most severe disease** [*Dominant in Africa so most likely the one in this patient*]
 - Causes **Irregular** Fever Spikes
 - **Plasmodium vivax & Plasmodium ovale:**
 - **Less virulent** species and causes **milder disease** (Dominant in areas outside Sub-Saharan Africa)
 - Causes Fever spikes every **48 hours**
 - **Plasmodium malariae:**
 - Less common and cause milder disease
 - Causes fever spikes every **74 hours**
- Vector: the **female Anopheles mosquito** [*asked on NBME*]
- Presentation:
 - General symptoms
 - **Flu-like symptoms, headache**
 - Diaphoresis
 - **High fever with periodic fever spikes depending on infective species**
 - Organ-specific symptoms
 - **Blood** ⇒ **Thrombocytopenia, Hemolytic anemia**

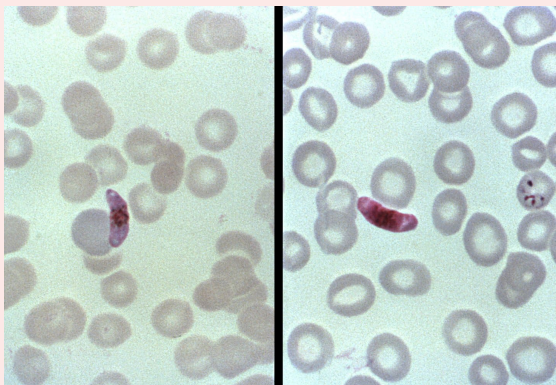
⚠ If **NO** history of travel, think Babesiosis

Pictures below are for Plasmodium Falciparum specifically:

Ring-Shaped Inclusions (Trophozoites):

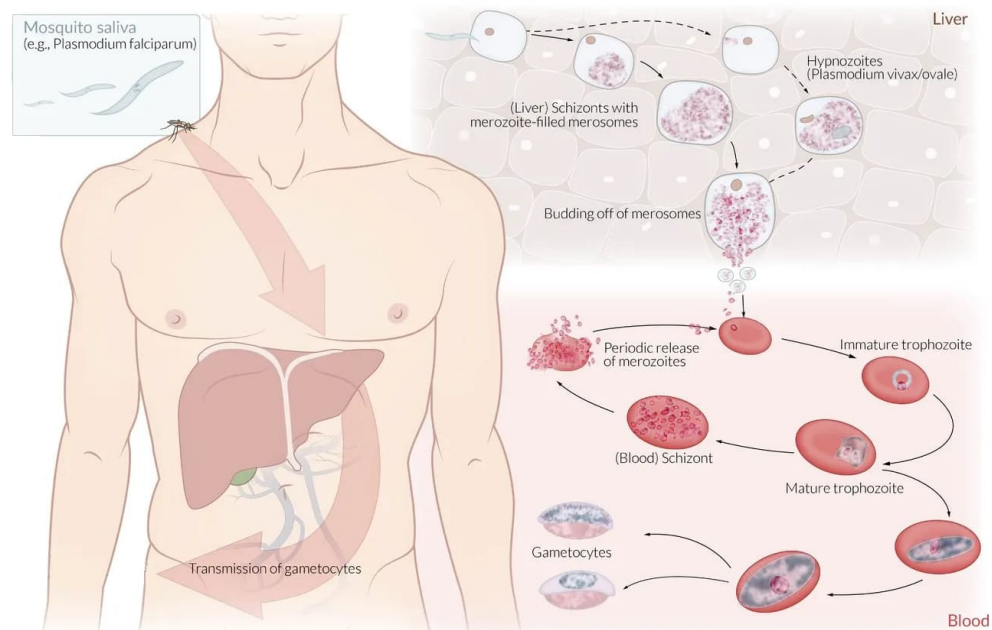


Crescent-Shaped Gametocytes:



- Gastrointestinal ⇒ Nausea, Vomiting, Diarrhea, Abdominal pain
- Liver ⇒ Hepatosplenomegaly, Jaundice, and Hypoglycemia
- Renal ⇒ Flank pain, Oliguria, Hemoglobinuria
- Cardiac ⇒ Heart failure
- CNS ⇒ Hallucinations, Confusion, Impaired consciousness, Seizures, Coma

◦ Life Cycle:



? Why does Malaria cause Hypoglycemia?

▼ Answer

1. Increased Consumption

- Malaria relies heavily on glucose for energy, raising the cells glucose consumption.
- Inflammatory State & Increased Metabolic demands also contribute to the hypoglycemia.

2. Decreased Production

- Hepatic Dysfunction impairs gluconeogenesis

Rapid Fire Malaria Treatment Questions:

- MOA of chloroquine & mefloquine?
 - Answer ⇒ Inhibits *Plasmodium* heme polymerase
- 16F + went to Africa + was taking chloroquine prophylactically + still got malaria anyway; why?
 - Answer ⇒ "Resistance to chloroquine"
- 20F + went to Africa + got malaria + took chloroquine for Tx and it was effective + weeks later now has resurgence; why?
 - Answer ⇒ "Presence of extra-erythrocytic form of organism" (Refers to hypnozoites)
- 23F + went to Africa + came back with hemolytic disease; Dx?
 - Answer ⇒ Malaria
- What is the combo of atovaquone + azithromycin a Tx for?
 - Answer ⇒ Babesiosis
- What is the combo of atovaquone + proguanil a Tx for?
 - Answer ⇒ Malaria

Q2

Genetic analyses of cells obtained on amniocentesis confirm that a fetus has a familial loss-of-function genetic mutation that leads to impairment of G-protein-coupled receptor-mediated signal transduction. This defect would most directly impair transcription of genes whose expression is regulated by which of the following hormones?

- Epinephrine
- Estradiol
- Hydrocortisone
- Insulin
- Progesterone
- Testosterone
- Thyroid hormone

▼ Explanation

- Answer is A (Epinephrine)
 - This Q just assesses the 2nd messengers, so let's go through them together as they are all very HY:

1. Intracellular/nuclear Receptors ⇒ **Steroid/Cholesterol-derived Hormones AND Thyroid Hormones**
 - Examples are **Estrogen, Progesterone, Testosterone, Vitamin D, Cortisol, Aldosterone, AND T3/T4.**
2. Receptor Tyrosine Kinase ⇒ **Insulin AND Growth Factors**
 - Examples are **Insulin, IGF-1, FGF, PDGF, and EGF**
3. Non-Receptor Tyrosine Kinase ⇒ **Acidophils, Cytokines, AND Colony Stimulating Factors**
 - Examples are **GH, Prolactin, Interleukins & Interferons, EPO, TPO, and G-CSF**
4. cGMP (CYTOSOLIC ACTION) ⇒ **NO, ANP, BNP**
5. IP3 (G-Coupled Protein Membrane Receptor Action) ⇒ **Oxytocin, ADH (V1), AT-II, Gastrin, GnRH, TRH, H-1**
6. cAMP (G-Coupled Protein Membrane Receptor Action) ⇒ Remaining
 - Examples are **FSH, LH, ACTH, TSH, CRH, hCG, ADH(V2), MSH, PTH, Calcitonin, GHRH, Glucagon, H-2, PGs, LTs**



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



Distinction between **GHRH, GH, and IGF-1** is very HY:

- GHRH → **cAMP**
- GH → **Non-Receptor Tyrosine Kinase**
- IGF-1 → **Receptor Tyrosine Kinase**



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



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



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

Q3

The parents of a 1-year-old boy with a bilateral cleft palate come to the physician for counseling prior to conception. Both parents have a family history of cleft palate. They ask about the risk of recurrence in future offspring. Which of the following best describes the pattern of inheritance of this disorder?

- Autosomal dominant
- Autosomal recessive
- Multifactorial
- Sporadic mutation
- X-linked

▼ Explanation

- **Answer is C (Multifactorial)**
 - **Isolated non-syndromic cleft lip/palate**
 - Basically, cleft lip/palate most commonly presents alone (non-syndromic).
 - It does run in families and is thought to be due to a mixture of environmental + genetic causes.
 - Skip the garbage talk, what you need to know is: **Most cleft lips/palates are multifactorial & not associated with syndromes. [Q repeats on future NBMEs]**



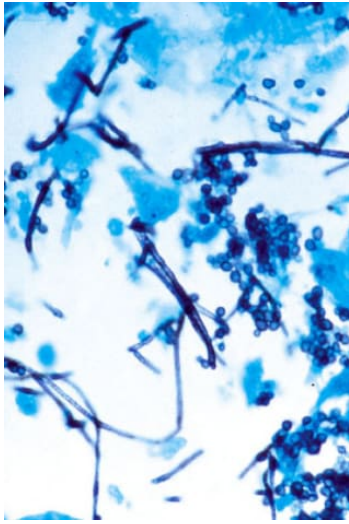
USMLE asks a similar Q regarding isolated VSD.

Patient had an isolated VSD & no other findings + family history of some sort of a similar isolated VSD. Patient came in for genetic counseling & asks what are the chances that my baby has a similar condition?

- Isolated VSD in newborns is estimated to be found in **2-3%** of the population
- Yes, USMLE asks for the %. Crazy I know.

Q4

A 20-year-old woman comes to the physician because of a 10-day history of vaginal discharge and vaginal itching and soreness. Current medications include a multivitamin and an antibiotic for acne. Pelvic examination shows vulvar erythema and edema and a thick, white vaginal discharge. Her vaginal pH is 4.2. A photomicrograph of the vaginal discharge is shown. The most appropriate pharmacotherapy for this patient is an oral agent with which of the following mechanisms of action?



- A. Inhibition of the cytochrome P450-dependent demethylation reaction
- B. Inhibition of DNA and RNA synthesis
- C. Pore formation in the fungal cell membrane
- D. Prevention of cross-linking of p-glucans in the cell wall
- E. Prevention of tetrahydrofolic acid synthesis

▼ Explanation

- Answer is A (Inhibition of the cytochrome P450-dependent demethylation reaction)

- IMP Clues

- Vaginal discharge and vaginal itching and soreness
- Current medications include an antibiotics for acne (Risk factor of candidiasis is antibiotic intake, as they kill normal vaginal commensals)
- Vulvar erythema and edema and a thick, white vaginal discharge (buzzy for candidiasis. Pass level)
- Vaginal pH is 4.2 (acidic pH)
- Photomicrograph of the vaginal discharge is shown (Shows budding yeast and pseudohyphae, which are also characteristic of candida)
- Q asks for **ORAL** agent.

- Dx → Vulvovaginal Candidiasis

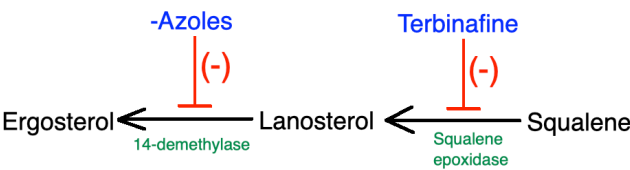
- Vaginal Candidiasis has 2 treatment options:

- Topical Nystatin

- MOA: **Ionophore** - Binds to ergosterol (fungal plasma membrane) and causes holes

- Oral fluconazole

- Used if topical nystatin is ineffective.
- MOA: **Inhibits 14-demethylase**, which inhibits ergosterol synthesis (fungal plasma membrane)



? What diabetes drug causes vulvovaginitis?

▼ Answer

SGLT-2 Inhibitors

- **Glucosuria** promotes vaginal fungal growth

? What drugs on the USMLE are ionophores?

▼ Answer

Nystatin - Amphotericin B - Natamycin

Differentiating the 3 main causes of vaginal discharge on the USMLE:

Features	Vaginal Candidiasis	Bacterial Vaginosis	Trichomoniasis
CA	Candida Albicans	Gardnerella Vaginalis	Trichomonas Vaginalis
Discharge	"Thick white discharge", "clumpy white", "cottage cheese-like"	"Thin Gray-White discharge", "Fishy"	"Frothy", "Yellow-Greenish discharge", 'malodorous'
Vaginal pH	Acidic (<4.5)	> 4.5	> 4.5
Microscopy	Budding yeast & pseudohyphae	Clue Cells	Flagellated Motile Trophozoite
Vaginal Mucosa	Erythematous & Inflamed	Normal	Strawberry Cervix
STD?	No	No	Yes

Q5

A 25-year-old man is brought to the emergency department 30 minutes after he sustained blunt trauma to the abdomen in a motor vehicle collision. Abdominal examination shows mild tenderness but no distention. During the next 3 hours, he develops progressive abdominal tenderness and swelling. His blood pressure decreases to 90/60 mm Hg. Appropriate fluid therapy is initiated, and operative repair of a ruptured spleen is scheduled. During the operation, several episodes of hypotension occur, but the bleeding is controlled. During the next 24 hours, he develops azotemia. He is fully volume-restored, but his urine volume remains less than 20 mL/h. Urine studies are most likely to show which of the following findings in this patient at this time?

- A. Fractional excretion of sodium greater than 2%
- B. Hemoglobinuria
- C. Numerous RBC casts
- D. Numerous WBC casts
- E. Urine osmolality greater than 1000 mOsmol/kg H₂O

▼ Explanation

- **Answer is A (Fractional excretion of sodium greater than 2%)**

◦ IMP Clues

- Blunt trauma to the abdomen + His blood pressure decreases to 90/60 mmHg + operative repair of ruptured spleen is scheduled (Patient has BAT, which caused splenic rupture → hypotension)
- During the operation, severe episodes of hypotension occur, but the bleeding is controlled (again, they're trying to spam you with sudden onset hypotension here)
- During the next 24 hours, he develops azotemia (increased blood urea levels) + urine volume remains less than 20mL/h (Oliguria)
- Q asks what is expected to be seen on urine studies of this patient?

• Dx → Renal Tubular Necrosis

- This patient has **Acute Tubular Necrosis** caused by **acute renal ischemia**, caused by sudden hypotension.
 - Other HY causes are **Acute CHF, MI, acute Arrhythmias, trauma, or blood loss in surgery** (USMLE favorite is "Aortic grafting")
- Pathophysiology: **Sudden Hypotension → Acute Renal Ischemia → Acute Tubular Necrosis**
 - **Why the tubules?**
 - Tubules have lots of **Na/K ATPases**, especially the **Proximal Tubules** [asked on NBME]
 - Tubular epithelial injury → sloughing and necrosis, which then causes **obstruction** of the tubules → **Increases tubular hydrostatic pressure → decreased GFR**
 - The necrotic/sloughed off epithelium is mixed with the *Tamm-Horsfall protein*, which then precipitate to form "**Muddy Brown**" or "**Granular**" casts and "**Epithelial casts**".
 - This **acute kidney injury** causes failure of renal functions → **high creatinine & low urine output**
 - Causes **High-gap metabolic acidosis** [asked on NBME]
- ATN is a type of intra-renal azotemia, which is characterized by **FENa >1% and BUN/Cr < 20** [VS PRERENAL AZOTEMIA]
 - FENa > 1% is because the failure of Na/K ATPases causes decreased Na and Water reabsorption → Increased Na excretion in diluted urine (**high urinary sodium & low urine osmolality**)
 - BUN is normally reabsorbed with water, however, as the Na/K ATPases are defective and water is NOT being reabsorbed → Less BUN is reabsorbed (**hence BUN/Cr <20**)



Remember that **pre-renal azotemia**, which is caused by **subacute/chronic** ischemia causes **FENa <1%** and **BUN/Cr >20**.

- Causes of pre-renal azotemia are **NSAIDs, diuretics, Chronic HF, dehydration, vomiting, or diarrhea** (for days).



HY to know that ATN is a type of **coagulative necrosis**.



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

▼ Answer

1. **ACUTE Ischemia** → **Acute Hypotension - Acute HF - MI - Acute Arrhythmia - Trauma - Blood Loss during Surgery**
2. **Drugs** → **Aminoglycosides - Cisplatin - Contrast**
3. **Rhabdomyolysis**
4. **Tumor Lysis Syndrome**



Na/K ATPases:

- Na/K ATPases are one of the most energy (ATP) demanding channels in our bodies, this makes them very liable to hypoxia.
 - **Hypoxia = decreased Oxygen = decrease aerobic respiration = decreased Oxidative phosphorylation = decreased ATP production**
- **Na/K ATPases use ATP** because they move molecules **against** their concentration gradient
 - Normally, Na is more outside the cell so naturally Na moves passively to the inside, while K is more on the inside so moves passively to the outside.
 - **So, normally Na in & K out**
 - **Na/K ATPases though moves them in the opposite direction, against the concentration gradient → Na out & K in**
- **If hypoxia occurs, Na/K ATPases dysfunction occurs → Can't do their job → Na move in & K moves out.**
 - This causes **Water to follow Na in → Cellular Swelling** (can be referred to as "hydropic changes") [asked on NBME]



What would be seen on biopsy of this patient after 8 weeks?

▼ Answer

Normal Tubular Epithelium - It regenerates and everything returns to normal.

Q6

A 20-year-old woman comes to the physician because of a 1-year history of intermittent low-grade fever fatigue; and joint pains. One week ago, she had a severe exacerbation of these symptoms after a trip to the beach; she also developed a red rash; even on areas that were not exposed to sun. Her temperature is 38.3°C (101aF) Physical examination shows an erythematous rash over the malar areas, trunk, and upper extremities; oral ulcerations; 1-cm axillary lymph nodes bilaterally; and mild swelling and tenderness of the joints of the hands. Serologic studies show an antinuclear antibody titer of 1:2GG. Further studies are most likely to show a mutation of a gene encoding which of the following proteins?

- A. C1q
- B. C-reactive protein
- C. Interferon gamma
- D. Mannose-binding lectin
- E. Serum amyloid A

▼ Explanation

• Answer is A (C1q)

◦ IMP Clues

- 20-year-old woman (classic epidemiology)
- Intermittent low-grade fever, fatigue, joint pains (Young woman + these symptoms ⇒ You must be thinking SLE)
- Severe exacerbation of these symptoms after a trip to the beach (Photosensitivity in SLE patients cause exacerbation of SLE flares)
- Erythematous rash over the malar areas (Classic butterfly rash)
- Oral ulcerations (usually painless)
- 1-cm axillary lymph nodes bilaterally (lymphadenopathy)
- Mild swelling and tenderness of the joints of the hands (again, the arthritis)
- Serology shows ANA titer (Sensitive)
- Q asks for mutation of gene encoding which of the protein below

• Dx → Systemic Lupus Erythematosus (SLE)

◦ C1q deficiency is one of the strongest genetic risk factors for SLE.

- C1q is part of the first component of the *classical complement pathway*.
- It helps in clearing immune complexes from circulation, so if deficient/mutated ⇒ **Complexes deposition Everywhere!**
 - This is exactly SLE's main *pathophysiology*:
 - **Type 3 Hypersensitivity Reaction = Antigen-Antibody Complexes deposition → T-cell reaction [asked on NBME]**

◦ Associated by **complement deficiencies (C1q, C2, C4) [asked on NBMEs]**

◦ Features (plenty of them):

▪ HY Ones Include:

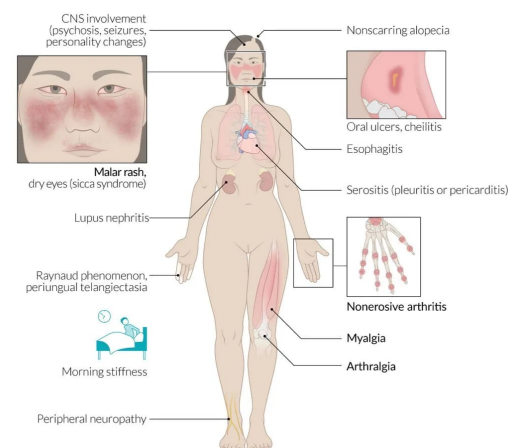
- **Rash** (usually malar)
- **Arthritis** (non-erosive)
- **Serositis** (Pericarditis, Pleuritis)
- **Hematological Disorders** (especially anemia & **Thrombocytopenia**)
- **Nephritis** (specific for **Anti-dsDNA** complexes deposition on glomerulus) → **Diffuse Proliferative Glomerulonephritis (DPGN) [asked on NBMEs]**
 - Biopsy of DPGN would show **"wire-loop" thickening of capillaries [asked on NBME]**

▪ Others: Uveitis, cerebritis, seizures, psychosis, **ulcers, photosensitivity**, LSE

◦ **Most Common Cause of Death → renal disease**

◦ **Pregnant female with SLE, newborn is at risk of → Congenital Heart Block**

- **Anti-SS-A(Ro) & Anti-SS-B(La) positive.**



Remember these Key Points:

- **ANA → Sensitive** for SLE
- **Anti-Smith → Specific** for SLE
- **Anti-dsDNA → Specific** for **Lupus Nephritis**
- **Complements → LOW C3 and C4**
- **Anti-phospholipid Syndrome** → Female patient with **recurrent 2nd trimester miscarriages + False Positive VDRL + thromboses with prolonged aPTT.**

? If a patient were to take a drug and develop similar symptoms, which drugs could she have taken?

▼ Answer

Sulfasalazine - Hydralazine - Isoniazid - Phenytoin - Procainamide - Minocycline - Methyldopa

- This is **Drug-induced Lupus**, which is associated with **anti-histone antibodies positive**.
 - **anti-dsDNA negative**

Q7

A 44-year-old woman comes to the physician because of a 3-week history of severe headache. She is 157 cm (5 ft 2 in) tall and weighs 86 kg (190 lb); BMI is 35 kg/m². Funduscopic examination shows papilledema. An MRI of the brain shows no abnormalities. A lumbar puncture is done. Cerebrospinal fluid (CSF) analysis shows an opening pressure of 32 mm H₂O. In addition to recommendations regarding dietary changes and weight loss, treatment with acetazolamide is begun. This drug will most likely improve the patient's symptoms by which of the following mechanisms?

- A. Decreased CSF production by the choroid plexus
- B. Decreased venous pressure around the arachnoid granulations
- C. Increased permeability of tight junctions (zonulae occludentes) between endothelial cells
- D. Increased sodium permeability of the ependyma
- E. Increased water transport by astrocyte end-foot processes

▼ Explanation

- Answer is A (Decreased CSF production by the choroid plexus)

- IMP Clues

- Severe headache + papilledema + CSF analysis shows an opening pressure of 32 mm H₂O (Signs of Increased Intracranial Pressure)
- BMI is 35 (She's obese, so this is probably Idiopathic Intracranial HTN, or previously referred to as "pseudotumor cerebri")
- Treatment with Acetazolamide is begun, and Q asks via what mechanism will this drug improve these patient's symptoms

- Acetazolamide

- What USMLE wants you to know is that **Carbonic Anhydrase is the driving enzyme for CSF secretion**
 - So, giving a **CA inhibitor (like acetazolamide)** will cause **decreased CSF secretion** → **decreases intracranial pressure**.

? What CNS cell is responsible for CSF secretion?

▼ Answer

Ependymal Cells

? What are the HY uses of Acetazolamide on the USMLE?

▼ Answer

1. **Diuretic**
2. **Altitude Sickness** (Induced metabolic acidosis to offset the respiratory alkalosis)
3. **Glaucoma** (decreases aqueous humor production)
4. **Pseudotumor Cerebri** (decreases CSF production)

Q8

A 30-year-old man reports increasing fatigue and dyspnea on exertion. There is a right ventricular lift, fixed wide splitting of S₂, and a grade 2/6 early systolic murmur that is heard best at the left upper sternal border. Which of the following is the most likely diagnosis?

- A. Aortic insufficiency
- B. Atrial septal defect
- C. Innocent murmur

- D. Mitral stenosis
- E. Mitral valve prolapse

▼ Explanation

- **Answer is B (Atrial septal defect)**
 - **Fixed Wide Splitting of S2 is Atrial Septal Defect.** It is that simple.
 - On the USMLE, they give you a 12-lead with tons of physical findings & an ECG; then they sneak in "Wide Fixed Splitting of S2" ⇒ **choose ASD.**

? If this patient were to develop a DVT for some reason, what is our biggest concern?

▼ Answer

Paradoxical Embolism, causing a stroke.

- DVT → Femoral Vein → Iliac Vein → IVC → RA → LA → LV → Aorta → Carotids → Cerebral Stroke

Normally, it would be **RA → RV → Pulmonary artery → Pulmonary Embolism**

! When going in for an **ASD repair**, the **AV Bundle** is at greatest risk for intraoperative injury.

? What are the different splitting of S2 on the USMLE?

▼ Answer

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

📌 USMLE can give you a cardiac catheterization Q with O2 saturation pattern and ask for the diagnosis:

- The answer will be ASD if O2 sat increases from 70 in SVC → 70 in RA → 80 in RV.
 - The 70/80 are just for demonstration.
 - Increased of O2 sat before reaching the Lungs means there is a connection between the right and left side of the heart.

Q9

A 62-year-old man with a blood pressure of 220/160 mm Hg requires treatment with a drug that decreases heart rate and systemic vascular resistance. Which of the following drugs would acutely decrease his heart rate and systemic vascular resistance?

- A. Albuterol
- B. Labetalol
- C. Phentolamine
- D. Prazosin
- E. Propranolol

▼ Explanation

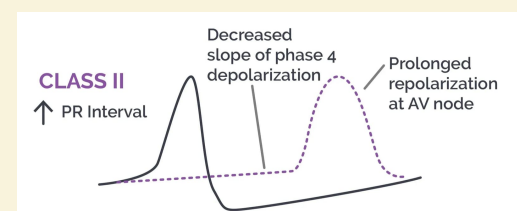
- **Answer is B (Labetalol)**
 - Q wants a drug that decreases heart rate and systemic vascular resistance.
 - **Decreases HR** means that we're **blocking Beta 1 Receptors**
 - **Decreased SVR** means that we're **blocking Alpha 1 Receptors**
 - This means the drug we need is **non-selective alpha & beta blocker** ⇒ **Labetalol**

? How does beta blockers affect cardiac action potential?

▼ Answer

Decreases Slope of Diastolic Depolarization

- **BB** → decreased cAMP → decreases calcium influx → decreases slope of phase 4 depolarization → hearts fill slower and pumps slower.



**Beta Blockers Cheat Sheet:**For beta blockers ending with “**-olol**”:

- Starts with **A → M**: **SELECTIVE** BETA BLOCKER (B1 selective)
- Starts with **N → Z**: **NON-SELECTIVE** BETA BLOCKER

For beta blockers **NOT** ending with “**-olol**”:

- **Labetalol** & **Carvedilol** → **NON-SELECTIVE ALPHA AND BETA BLOCKERS**

Q10

A 65-year-old man with a history of gout comes to the physician because of a 3-day history of pain and swelling of his left knee related to his condition. The physician prescribes appropriate medication and recommends that the patient stay as active as possible. At the follow-up visit 2 days later, the patient states that he continues to have episodes of limited activity because of pain. Between episodes he is able to walk up to a half mile, but he has noted that the pain in his knee causes him to walk more slowly. He says, "I think it would really help me if you could authorize a disabled parking permit for me." Which of the following is the most appropriate response by the physician?

- A. "I cannot authorize the permit because it is intended only for individuals who are wheelchair-dependent."
- B. "I will authorize the permit, but I recommend that you continue with regular exercise and only use the permit when you are having severe pain."
- C. "I will refer you to a physical medicine and rehabilitation specialist for a full assessment before I decide to authorize this permit."
- D. "I would be glad to authorize the permit, but not until you become more disabled."
- E. "I would be glad to authorize the permit, but you first need the motor vehicle agency to determine your eligibility."

▼ Explanation

- **Answer is B ("I will authorize the permit, but I recommend that you continue with regular exercise and only use the permit when you are having severe pain.")**
 - The patient has **gout with intermittent severe pain limiting ambulation**.
 - During flares, **mobility is significantly impaired, which qualifies for a disabled parking permit**. The physician already has enough clinical information to authorize it.
 - **Choice B is the best answer as it:**
 - **Authorizes use of disabled parking** (to help with patient's life quality)
 - **But encourage exercise/limited use** (because it provides support without discouraging activity)

Q11

A 19-year-old woman is severely burned over 35% of her total body surface area in a fire. Which of the following is most likely to occur in this patient over the next 7 days?

- A. Increased extracellular volume
- B. Increased metabolic rate
- C. Increased serum cholesterol concentration
- D. Loss of B vitamins through denuded skin
- E. Loss of insulin-dependent glucose transporters

▼ Explanation

- **Answer is B (Increased metabolic rate)**
 - Burns are super HY (especially for STEP 2), so let's go through its complications and how do they happen:
 1. **Hypovolemia [Greatest Complication within 24 hours of burn]**
 - Widespread thermal injury causes *diffuse capillary endothelial damage*, causing **increased** capillary permeability, which allows **escape of albumin into extracellular space**
 - This causes **shifting of intravascular fluid (low oncotic pressure) into extravascular space (higher oncotic pressure)**
 - The **decreased** intravascular volume → **decreased** preload → **decreased** CO & **hypovolemic shock**
 - Additionally, the **absence of skin** (outer protective layer) causes **increased water evaporation** → **increases** volume loss

2. **Hypermetabolic Syndrome** [Greatest risk **24hr → few weeks** from burn]
- Burns, especially those with **≥40% TBSA**, are usually associated with a **massive increase in metabolic rate**. This puts risk of lethal electrolyte derangements that may cause *cardiac arrest* or *seizures*.
 - Massive surge of stress hormones (catecholamines, glucagon, cortisol), sympathetic system, and inflammatory cytokines (IL-6, TNF-α, IL-1) cause increase in catabolic activity:**
 - Increased** protein catabolism, lipolysis, glycogenolysis, and gluconeogenesis.
 - Additionally, the elevated HR, O2 consumption, and need for wound healing requires energy.
3. **Infection & Burn Sepsis**
- < 5 days** post burn, most common is ⇒ **Staph aureus**
 - > 5 days** post burn, most common is ⇒ **Pseudomonas or Candida (Fungal)**
4. **Curling Ulcer**
- Duodenal Ulcer a few days after burns, caused by **decreased blood volume → ischemia → mucosal ulceration**.

Q12

A 3-day-old male infant with Down syndrome has had repeated episodes of vomiting bile-stained fluid and has passed only small amounts of meconium-stained stool since birth. His stomach is distended. Pregnancy was complicated by polyhydramnios. Which of the following is the most likely diagnosis?

- A. Duodenal atresia
- B. Extrahepatic biliary atresia
- C. Omphalocele
- D. Pyloric stenosis
- E. Tracheoesophageal fistula

▼ Explanation

- Answer is A (Duodenal atresia)**
 - IMP Clues**
 - Down Syndrome (2 HY GI associations with DS; Annular Pancreas & Duodenal Atresia)
 - Repeated episode of vomiting bule-stained fluid (level of obstruction is duodenum)
 - Small amounts of meconium-stained stool since birth (due to decreased intake)
 - His stomach is distended + Pregnancy was complicated by polyhydramnios (due to obstruction, so infant couldn't swallow amniotic fluid)
- Dx → Duodenal Atresia**
 - Atresia of duodenum caused by **failure of duodenal recanalization [asked on NBME]**
 - Causes duodenal obstruction, which causes:
 - Bilious vomiting** (as the atretic level is below the *ampulla of Vater*)
 - Abdominal Distention & decreased stool formation**
 - Polyhydramnios** (infant can't swallow amniotic fluid)
 - Associated with **Down Syndrome & Double-bubble Sign** on AXR.



Jejunal/Ileal Atresia also presents with **bilious vomiting**; however, CXR shows "**triple-bubble sign**", abdominal distention is **more marked**, and the embryological cause is **vascular infarction of jejunal/ileal blood supply**.



Neonate + greenish vomiting + AXR shows below imaging. Differentiate between the possible causes.



▼ Answer

	Annular Pancreas	Duodenal Atresia
Presentation	bile-tinged vomiting/regurgitation	bile-tinged vomiting/regurgitation
AXR	Double Bubble Sign	Double Bubble Sign
Embryological causes	Failure of ventral pancreatic bud rotation	Failure of duodenal recanalization
HY Syndromic Association	Down Syndrome	Down Syndrome

The X-Ray provided shows the "**double-bubble sign**"

- The bubble on the right (small one) → **Duodenum**
- The bubble on the left (big one) → **Stomach**

Q13

A 70-year-old man comes to the physician because of decreased urinary output and fatigue during the past 2 days. At his last visit 2 weeks ago, he had a 6-month history of bilateral pain in the joints of his fingers. His pulse was 72/min, and blood pressure was 130/82 mm Hg. Physical examination showed tenderness with full flexion of the proximal and distal interphalangeal joints; there was no synovial thickening. There were bony prominences on the distal interphalangeal joints. Laboratory studies were ordered. Treatment with ibuprofen (600 mg three times daily) was started 2 weeks ago. Laboratory studies show:

	2 Weeks Ago	Today
Serum		
Urea nitrogen (mg/dL)	15	70
Creatinine (mg/dL)	1.1	4.8
Urine		
pH	–	5.0
Specific gravity	–	1.015
Blood	–	negative
Glucose	–	negative
Protein	–	negative
Eosinophils	–	negative

Which of the following most likely caused the change in this patient's serum urea nitrogen and creatinine concentrations?

- A. Increase in blood viscosity
- B. Induction of distal tubular acidosis
- C. Inhibition of prostaglandin synthesis
- D. Postobstructive uropathy
- E. Precipitation of myoglobin in the tubule

▼ Explanation

- Answer is C (Inhibition of prostaglandin synthesis)
 - IMP Clues
 - Decreased urinary output and fatigue during the past 2 days
 - Treatment with ibuprofen 600 mg three times daily was started 2 weeks ago
 - Lab studies today show increase in Urea and Creatinine
- Q asks for most likely cause of these lab changes?
 - Patient has **history of NSAIDs use followed by nephropathy**. This is pass-level and classic USMLE concept.
 - NSAIDs decreased PG synthesis → Reduction of PGs cause decreased dilation of afferent renal arterioles → decreased GFR
 - Normally, PGs cause vasodilation of afferent renal arterioles, maintaining GFR.
 - Decreased GFR causes the kidney to think that there is intravascular volume depletion, causing:
 - Less Urine Output (Increased reabsorption of water in descending Loop)
 - High Urea (Increased reabsorption in ascending loop to increase medullary osmolality, causing water absorption in descending loop)
 - High Creatinine

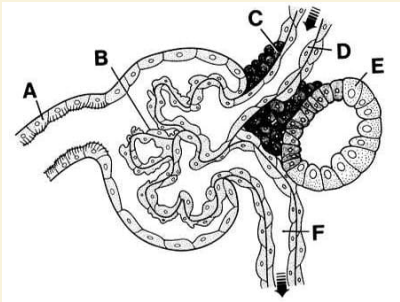
? What is the expected FENa % and BUN/Cr in this patient?

- ▼ Answer
- FENa < 1% and BUN/Cr > 20%
- This is because NSAIDs cause **pre-renal azotemia (subacute/chronic renal ischemia)**
 - In contrast to ATN, which is caused by acute ischemia (FENa > 1% and BUN/Cr < 20)

? How does NSAIDs affect Filtration Fraction?

- ▼ Answer
- NO CHANGE
- PGs causes dilation of afferent renal arterioles → increase RPF → increase GFR
 - FF = GFR/RPF; so net effect is NO CHANGE
 - NSAIDs decrease dilation of afferent renal arterioles → decrease RPF → decrease GFR
 - FF = NO CHANGE

"USMLE will give you a picture like the above pic & asks you to where NSAIDs/PGs and ACEi/AT-II act on the nephron. So, get comfortable with it."



- ▼ NSAIDs/PGs act on afferent arterioles (D)
- ▼ AT-II act on efferent arterioles (F)

Where does ACE inhibitors act?

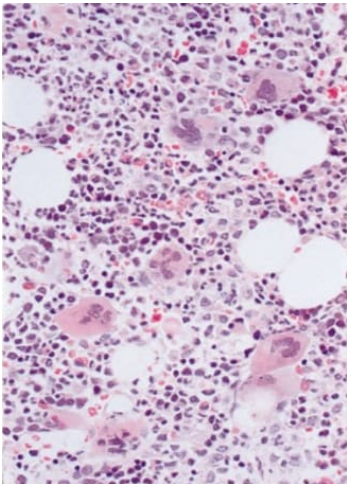
- IN THE LUNGS
 - ACE is produced in the lungs

Q14

A 5-year-old boy who has recently recovered from an upper respiratory tract infection develops easy bruising. Examination shows petechiae on the lower extremities. Laboratory studies include:

Hemoglobin	12 g/dL
Hematocrit	36%
Leukocyte count	8000/mm ³
Platelet count	18,000/mm ³

The erythrocytes are normochromic and normocytic. A photomicrograph of tissue obtained on bone marrow biopsy is shown. Which of the following is the most likely mechanism of the thrombocytopenia?



- A. Consumption of platelets by intravascular thrombosis
- B. Disseminated mycobacterial infection
- C. Immune destruction of platelets
- D. Replacement of bone marrow by fibrosis
- E. Replacement of bone marrow by leukemic cells

▼ Explanation

• Answer is C (Immune destruction of platelets)

◦ IMP Clues

- Recently recovered from an upper respiratory tract infection develops easy bruising (Viral infection is a common precipitating factor of ITP)
- Petechiae on the lower extremities (Tells us that there is TCP)
- Platelet count 18,000 (TCP confirmed)
- A photomicrograph of tissue obtained on bone marrow biopsy is shown (Megakaryocytes are seen, which tells us that there is compensatory increased PLT formation)

• Dx → Immune Thrombocytopenic Purpura (ITP)

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

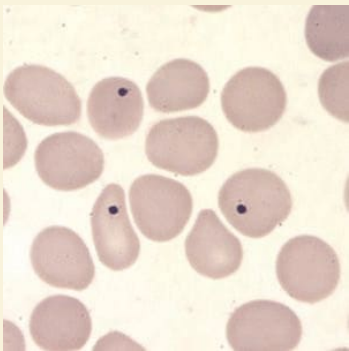


As a result of antibody-coated platelets clearance by splenic macrophages, the decreased platelet count is compensated by an **increase in megakaryocytes in bone marrow.**



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

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



Q15

A pregnant 28-year-old woman is found to have symmetrical enlargement of the pituitary gland on an MRI performed for head trauma. Which of the following cell types accounts for the pituitary enlargement?

- A. Corticotrope
- B. Gonadotrope
- C. Lactotrope
- D. Somatotrope
- E. Tanycyte

▼ Explanation

• Answer is C (Lactotrope)

◦ IMP Clues

- Pregnant
- Symmetrical Enlargement of the pituitary gland
- Q asks for cell types accounting for pituitary enlargement?

• Dx → Physiological Lactotroph Hyperplasia

- Normally seen in pregnancy, as the **estrogen rise stimulates an increase in prolactin levels by stimulating hyperplasia in lactotrophs of the anterior pituitary.**
 - **As it is physiological, the growth is symmetrical** (VS pituitary adenomas, which is asymmetrical)
- This prepares the gland for prolactin secretion for lactation after delivery
 - So, after cessation of breastfeeding, the pituitary gland involutes

⚠ Remember that **estrogen stimulates prolactin secretion**; however, **progesterone inhibits the production of milk.**

- This is why during **pregnancy**, the **high levels** of estrogen & progesterone **increase PRL levels with no milk production.**
- After **delivery**, the levels of estrogen & progesterone **crash**, causing **milk production.**

? What are the 2 types of hormone-producing cells in the anterior pituitary?

▼ Answer

1. Acidophils

- Lactotrophs (Mammotrophs) → **Prolactin**
- Somatotrophs → **Growth Hormone**

2. Basophils

- Thyrotrophs → **TSH**
- Gonadotrophs → **FSH & LH**
- Corticotrophs → **ACTH & MSH**

Q16

A 48-year-old woman has severe gastroesophageal reflux. Antacids do not provide symptomatic relief. Which of the following is the mechanism of action of the most effective suppressor of acid production?

- A. Blockade of gastrin/cholecystokinin receptors
- B. Blockade of gastric motility receptors
- C. Inhibition of gastric H⁺-K⁺-ATPase
- D. Inhibition of gastric muscarinic (M₃) receptors
- E. Inhibition of gastric secretion of prostaglandins

▼ Explanation

• Answer is C (Inhibition of gastric H⁺-K⁺-ATPase)

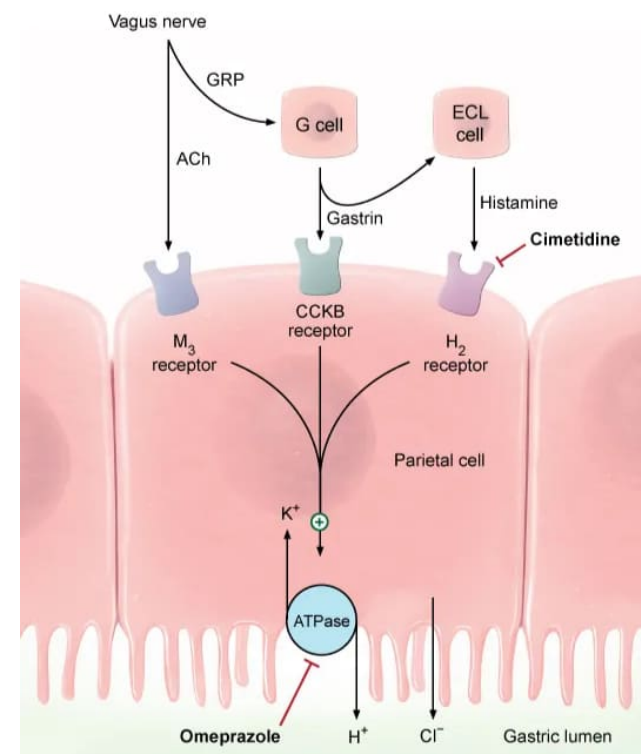
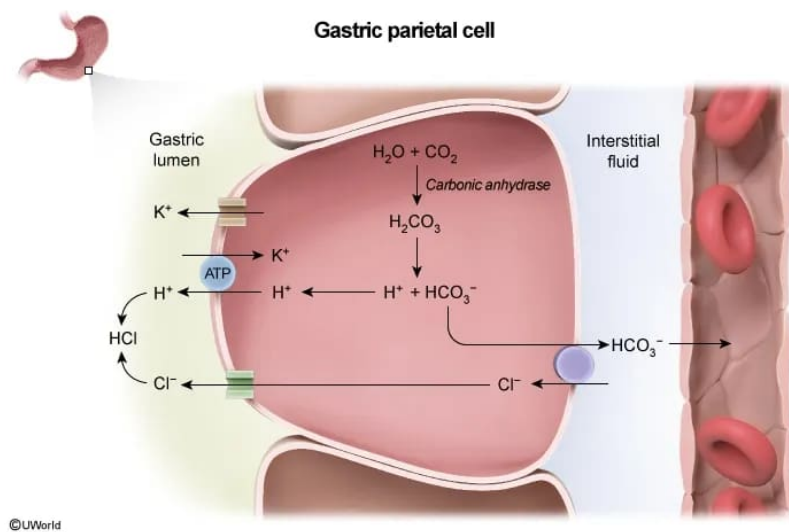
- Q asks for the mechanism of action of the most effective suppressor of acid production.
 - We know that **Proton Pump Inhibitors** are hands down **the most effective suppressors of acid production**
 - PPIs end with **"-prazole"**
 - **Omeprazole, Esomeprazole, Pantoprazole, Lansoprazole....** you get the idea.

• **PPIs irreversibly inhibit H⁺/K⁺ ATPase (the proton pumps) of the parietal cells of the stomach**

- Due to its **irreversible inhibition**, acid secretion is inhibited until new pumps are synthesized, hence the effectiveness/potency and long duration of action

📌 H2 Blockers are **inferior** to PPIs in suppression of gastric acid, as H2 blockers **reversibly** block histamine (H₂) receptors on gastric **parietal** cells.

- Used in all conditions associated with **acid hypersecretion like GERD, PUD, ZE Syndrome, and H.pylori infection**



? What are the HY side effects of PPIs on the USMLE?

▼ Answer

- Increased **Cl.difficile infection**
- Decreased** absorption of **Iron, Vitamin B12, calcium, and magnesium**
- Increased risk of **Osteoporosis**
- Rebound Hypersecretion**
- Increases risk of **acid labile** infections



USMLE asks about a patient with NSAIDs intake that causes a stomach ulcer. USMLE then asks you what drug is most effective at blocking acid production and hence promoting mucosal healing; answer is Omeprazole (PPIs).

- PGs analogue (Misoprostol) is incorrect.

Q17

An 82-year-old woman is brought to the physician by her daughter because of fecal incontinence for 2 months. Physical examination shows no abnormalities. Which of the following is the most likely underlying mechanism of this patient's condition?

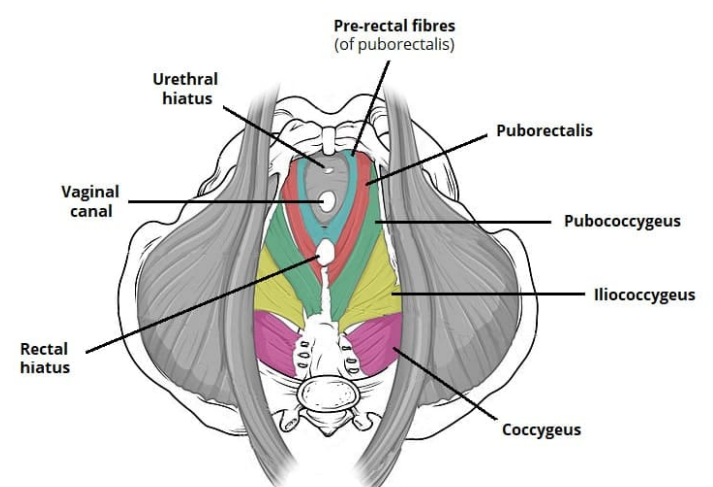
- Aganglionosis in the rectosigmoid region of the large intestine
- Decreased function of the puborectalis muscle
- Enhanced sensitivity of the anal canal below the dentate line
- Hypertonicity of the internal anal sphincter
- Painful hemorrhoids

▼ Explanation

- Answer is B (Decreased function of the puborectalis muscle)**

◦ IMP Clues

- 82-year-old woman with fecal incontinence and the Q asks for the most likely cause of the underlying mechanism of this patient's condition.
 - Puborectalis muscle is part of the Levator Ani muscle, which acts as a "pelvic diaphragm" that supports the pelvic organs & controls their sphincters by forming "slings" around them.**
 - In cases of levator ani weakness or insufficiency, sphincteric incompetence occurs, which presents as either:
 - Fecal Incontinence** (the puborectalis muscle forms a muscular sling around the anorectal junction, pulling it forward to create the "anorectal angle", which helps maintain continence)
 - Urinary Incontinence** (loss of bladder neck and urethra support)
 - Vaginal Prolapse** (loss of vaginal walls & uterine support)



? What are common causes of Levator Ani muscle injury?

▼ Answer

- **Obstetric Injuries** (Vaginal delivery, Forceps use, Episiotomy (posterior ones especially))
- **Pudendal or Sacral Nerve injuries**
- **Pelvic floor trauma or surgery**
- **Aging & Straining**

Q18

A 45-year-old woman comes to the physician for a follow-up examination. She has mild renal failure, cholelithiasis, and eczema. She is 163 cm (5 ft 4 in) tall and weighs 95 kg (209 lb); BMI is 36 kg/m². Physical examination shows hoarseness and coarse hair. Serum studies show hyperglycemia, increased thyroid-stimulating hormone concentration, hypercholesterolemia, and hypercalcemia. In addition to treatment for hypothyroidism, pravastatin is prescribed. This patient is at increased risk for which of the following conditions as a result of this treatment?

- A. Myopathy
- B. Nephrolithiasis
- C. Pancreatitis
- D. Toxic hepatitis
- E. Type 2 diabetes mellitus

▼ Explanation

- **Answer is A (Myopathy)**
 - **IMP Clues**
 - Patient is prescribed pravastatin
 - Q asks what is this patient at increased risk of as a result of this treatment
- **Statins**
 - **Inhibits HMG CoA reductase** (rate limiting enzyme of cholesterol synthesis) → less cholesterol synthesized by the body
 - This causes **Up-regulation of LDL receptors** → Cholesterol scattered around the body is **picked-up by the LDL-receptors to the liver. So, it is the drug of choice in patients with high LDL-cholesterol.**
 - Side Effects: **Hepatotoxicity & Myopathy** (especially, if combined with fibrates)

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

▼ Answer

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

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

! Hypothyroidism and Hyperthyroidism **BOTH** are HY causes of **muscle weakness**.

- **Hypothyroid myopathy** → proximal muscle weakness + **HIGH CK**
- **Thyrotoxic myopathy** → proximal muscle weakness + **NORMAL CK**

📌 **Statins + Fibrates = Myopathy** (muscle pain & soreness) + **high CK levels** (muscles are breaking down)

- **Fibrates + Statins ⇒ Rhabdomyolysis ⇒ Acute Tubular Necrosis**
- Caused by **CYP450 Inhibition**

Q19

A patient with a 20-year history of type 1 diabetes mellitus has episodes of prolonged hypoglycemia following injections of insulin. Which of the following is the most likely cause of the prolonged hypoglycemia?

- A. Decreased hepatic glycogen concentrations
- B. Decreased number of hepatic catecholamine receptors
- C. Decreased number of insulin receptors in muscle
- D. Impaired release of glucagon

E. Increased rate of inactivation of insulin

▼ Explanation

- **Answer is D (Impaired release of glucagon)**
 - **IMP Clues**
 - 20-year history of type 1 diabetes mellitus (Late T1DM)
 - Episodes of prolonged hypoglycemia following insulin injections (cause be due to increased insulin dose OR dysfunction counter-regulation)
 - This topic is HY and very underratedly mentioned/explained in our medical schools
 - **Late Type 1 DM is characterized by hypoglucagonemia, which predisposes the patient to severe hypoglycemia**
 - This is caused by 2 main mechanisms:
 1. **Loss of intra-islet paracrine regulations**
 - When stimulated, **B-cells produce insulin** which also **suppresses glucagon release** from **α-cells**.
 - If the patient is fasted, the drop of insulin secretion of **B-cells** allows for glucagon release by **α-cells**
 - In long standing DM, these **paracrine regulations are lost** causing **dysfunction of glucagon release in response to hypoglycemia**
 2. **α-cell destruction**
 - The autoimmune destruction of **B-cells** in DM can also **directly damage α-cells**, which further **reduce glucagon release**
 - As a result, **BOTH insulin and glucagon** secretion are **dysfunctional**.
 - When a patient takes exogenous insulin, hypoglycemia occurs. **Glucagon, however, is intrinsically dysfunctional & can't contribute to needed counter-regulatory hyperglycemia.**
 - **Result is Prolonged hypoglycemia following injections of insulin.**

Q20

A 60-year-old woman comes to the physician 1 week after she discovered a lump in her right breast. Examination of the right breast shows a 2-cm, palpable mass in the upper medial aspect. Examination of a core needle biopsy specimen shows an invasive ductal carcinoma. Immunohistochemistry shows overexpression of estrogen and progesterone receptors; fluorescent in situ hybridization shows that the HER2/neu receptor is overexpressed with greater than 10 receptors per cell. Which of the following mechanisms is the most likely cause of the overexpression in this patient's tumor cells?

- A. Amplification
- B. Anticipation
- C. Chromosomal rearrangement
- D. Imprinting
- E. Loss of heterozygosity

▼ Explanation

- **Answer is A (Amplification)**
 - **IMP Clues**
 - Invasive ductal carcinoma that shows overexpression of estrogen and progesterone receptors
 - FISH shows that the HER2/neu receptors is overexpressed with > 10 receptors per cell
 - Q asks what is the most likely cause of overexpression on receptors in these cells?
 - Let's exclude to get there:
 - **Choice A → Amplification makes sense, which means increased gene expression causing increased receptor production.**
 - **Choice B → Anticipation** is repeat expansion seen in *TNR associated diseases* like **Huntington Disease, Myotonic Dystrophy, Fragile X Syndrome**, and **Friedreich Ataxia**.
 - **Choice C → Chromosomal Rearrangement** is seen in translocation mutations, like **t(9;22) of CML**.
 - **Choice D → Imprinting** is seen in **Prader-Willi Syndrome (Paternal deletion) & Angelman Syndrome (Maternal deletion)**.

? If this patient is started on Herceptin, what is expected complication?

▼ Answer
Dilated Cardiomyopathy - Trastuzumab (Herceptin) is **HER2/neu receptor monoclonal antibody** used in **HER2/neu positive breast cancer**

- Choice E → Loss of heterozygosity is what is seen in **tumor suppressor gene mutations** like those seen in **TP53 mutations causing Li-Fraumeni syndrome or Rb mutation in Retinoblastoma**.



Remember the HY TNR Repeats:

- Huntington Disease → **CAG**
- Myotonic Dystrophy → **CTG**
- Fragile X Syndrome → **CGG**
- Friedreich Ataxia → **GAA**

Q21

A 34-year-old woman with a long-standing history of alcoholism comes to the physician because of frequent foul-smelling stools for 2 weeks. She has been admitted to the hospital for treatment of alcohol-induced pancreatitis eight times within the past 10 years. Vital signs are normal. Abdominal examination shows mild distention and tympany. The remainder of the physical examination shows no abnormalities. Treatment with a pancreatic enzyme replacement preparation is begun. For dosage adjustments, it is most appropriate to monitor which of the following in this patient's stool?

- A. Amylase
- B. Bacteria
- C. Fat
- D. Hydrochloric acid
- E. Soluble fibers
- F. Water

▼ **Explanation**

- **Answer is C (Fat)**
 - **IMP Clues**
 - Foul-smelling stools + alcohol-induced pancreatitis
 - Treatment with a pancreatic enzyme replacement is begun
 - Q asks for dosage adjustment, what must be monitored in stool?
- **Dx → Pancreatic Insufficiency**
 - Patient has chronic pancreatitis secondary to alcohol abuse.
 - **Chronic pancreatitis causes fibrosis & destruction of pancreatic ducts, in addition, of destruction of pancreatic cells themselves.**
 - Cellular destruction is classically exocrine initially, then endocrine:
 - **Exocrine Pancreatic Insufficiency:**
 - **Decreased** secretion of pancreatic digestive enzymes (Lipase, Amylase, Protease, Elastase, ...) ⇒ **Malabsorption**
 - **Steatorrhea & Fat-Soluble Vitamins Deficiencies**
 - **Weight Loss & Increased Catabolism**
 - **Endocrine Pancreatic Insufficiency:**
 - **Destruction of Islet cells (α-cells of glucagon and β-cells of Insulin)**
 - Loss of β-cells → **Diabetes Mellitus**
 - Loss of α-cells → **Prolonged Hypoglycemia**
 - So, if the patient has pancreatic insufficiency, **fats will NOT be absorbed → Steatorrhea**
 - If the patient is started on pancreatic enzymes replacement, **fats will be absorbed → resolution of steatorrhea**
 - **You can monitor fat levels in stool to control the dosage, by increasing dosage until fecal fat levels are normalized.**



How can USMLE assess this?

1. They can give you a case of **Cystic Fibrosis** and asks what would be **expected to be seen in stool**.
 - Answer is **Increased fecal fat OR Increased fecal elastase**
2. They can give you a case of **Chronic Pancreatitis** or **Cystic Fibrosis + Steatorrhea** and ask **what should this patient receive**.
 - a. Answer is **Pancrelipase**, which is basically a mixture of pancreatic digestive enzymes (lipases, amylases, proteases)
3. They can give you a patient with **Cystic Fibrosis + one of fat-soluble vitamin deficiencies** (most HY is vitamin E) and **ask you for the reason**.
 - a. Answer is **Pancreatic Insufficiency due to inspissated pancreatic secretions**.



USMLE loves to monitor **fecal elastase** and **fecal fats** for chronic pancreatic insufficiency.

Q22

A 70-year-old woman comes to the physician because of a 3-month history of increasingly severe pain of her joints. She says that her fingers have become so stiff that she can no longer play the piano. Physical examination shows rheumatoid nodules underneath the skin close to the joints of the elbows and hands. The immunologic mechanism of this patient's inflammation is most similar to which of the following?

- A. Apoptosis of macrophages
- B. Mast cell degranulation
- C. Natural killer cell killing
- D. Serum sickness
- E. Wheal and flare reaction

▼ Explanation

• Answer is D (Serum Sickness)

◦ IMP Clues

- They basically handed us the diagnosis by mentioning "rheumatoid nodules underneath the skin", so we know this is Rheumatoid Arthritis.
- The Q assess if you'd know the type of immunological reaction seen in RA

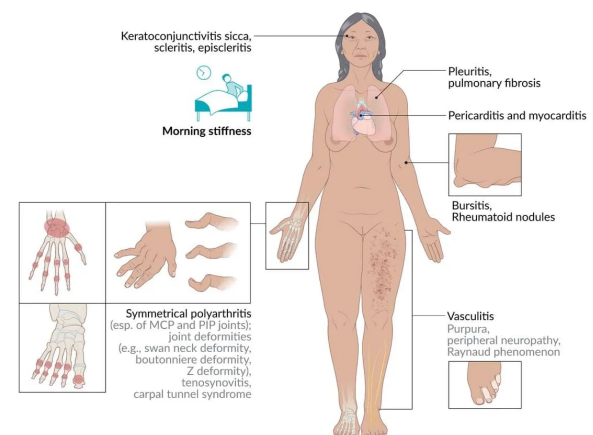
• Dx → Rheumatoid Arthritis

- Autoimmune disease characterized by **CD4 T-cell activation** in response to **antigen-antibody complex deposition**, causing release of cytokines that induce **pannus formation** (synovial hyperplasia by proliferative granulation tissue)
 - This results in **erosion of articular cartilage and bone**
 - The autoantibodies are **Rheumatoid Factor** and **anti-cyclic citrullinated peptide** (anti-CCP, specific)
- As the main immunological mechanism is antigen-antibody complexes deposition, causing T-cell activation; This is **Type 3 Hypersensitivity Reaction**.
 - **Serum Sickness (Choice D)** is also a **Type 3 Hypersensitivity Reaction**, due to **antigen-antibody complexes deposition** 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)

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

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



Treatment of RA has 2 arms

1. Relief of Pain

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

2. Slowing Disease Progression (DMARDs)

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

? HY Related Qs:

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

▼ Answer

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

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

▼ Answer

Etanercept - TNF-alpha recombinant receptor

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

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

▼ Answer

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

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

Q23

A 32-year-old woman, gravida 2, para 1, at 39 weeks' gestation is admitted to the hospital in labor. Her membranes ruptured spontaneously with clear fluid. Epidural analgesia is initiated. The cervix is 5 cm dilated and 80% effaced, and the vertex is at -1 station. External electronic fetal monitoring shows a normal fetal heart rate of 150/min with variable spontaneous decelerations to 110/min. Umbilical cord compression is suspected. Which of the following best explains the decrease in the fetal heart rate because of this compression?

- A. Decreased fetal systemic vascular resistance
- B. Decreased maternal systemic vascular resistance
- C. Increased fetal systemic vascular resistance
- D. Increased maternal systemic vascular resistance
- E. Negative inotropic effect on the fetal heart muscle
- F. Positive inotropic effect on the fetal heart muscle

▼ Explanation

- Answer is C (Increased fetal systemic vascular resistance)

- IMP Clues

- External Electronic fetal monitoring shows a normal fetal heart rate of 150/min with variable spontaneous decelerations to 110/min
- Umbilical cord compression is suspected
- Q asks what best explains the decrease in the fetal heart rate because of this compression?

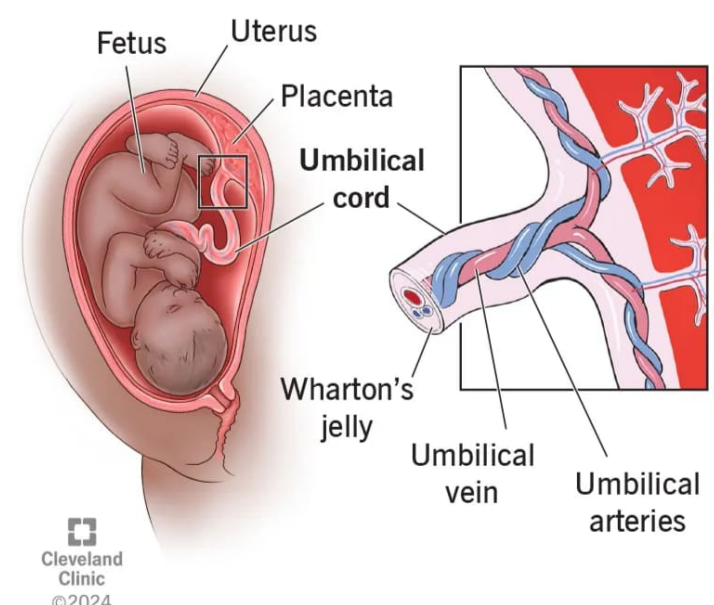
- Dx → Variable Decelerations

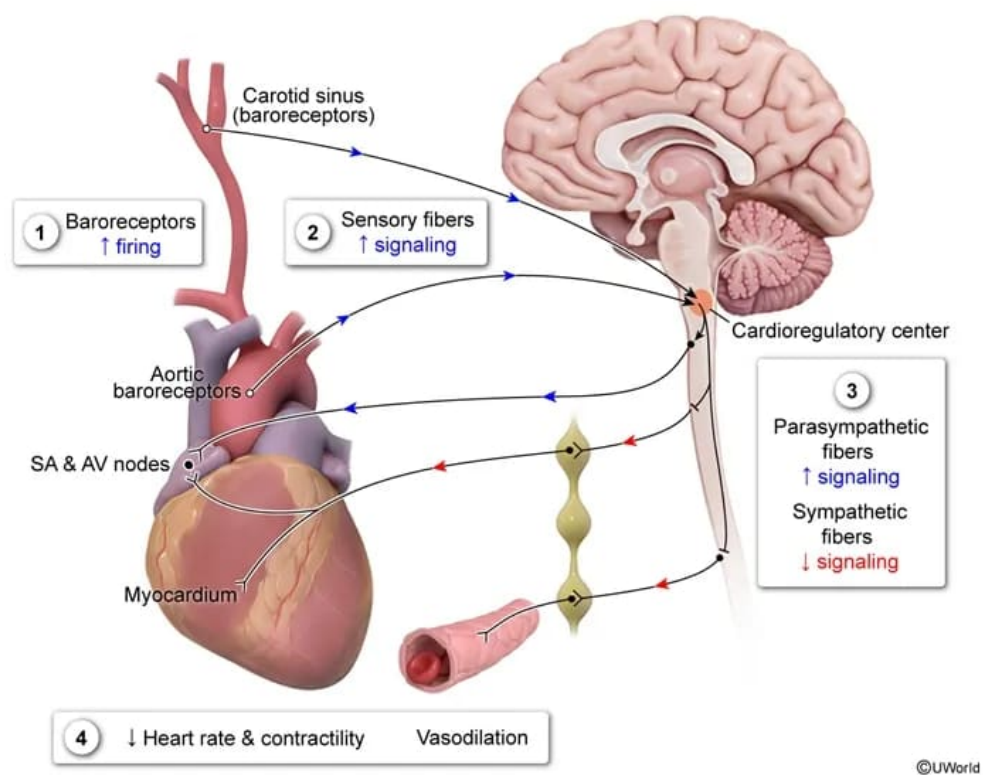
- Decreased fetal heart rate caused by **umbilical cord compression**.

- How does it happen?

- The Umbilical cord contains **2 umbilical arteries** and **1 umbilical vein**.
- The compression of the umbilical cord → compression of umbilical arteries → **increases fetal systemic vascular resistance** (Choice C) → **increases** fetal cardiac afterload → **increases** fetal blood pressure
 - The increase in fetal blood pressure is detected by the **carotid baroreceptors**, which (as we know previously) **increases parasympathetic** signaling.
 - **Increased vagal stimulation causes depression in SA Node activity → decrease in fetal HR**

- Benign in nature & usually **resolves by maternal reposition**.





[For Nerds/STEP 2]

Main Types of Fetal Decelerations:

1. Early Decelerations

- Benign
- Caused by **Fetal Head Compression**
 - Increases vagal stimulation → decrease in HR

2. Late Decelerations

- Pathological
- Caused by **Uteroplacental Insufficiency**
 - Fetal Hypoxia → Chemoreceptors activation → Vagal stimulation → decrease in HR

3. Variable Decelerations

- Benign
- Caused by **Umbilical Cord compression**
 - Fetal HTN → Baroreceptors activation → Vagal stimulation → decrease in HR

Q24

A 39-year-old man comes to the physician for a routine health maintenance examination. He has no history of major medical illness. His pulse is 62/min, and blood pressure is 124/80 mm Hg. A grade 3/6, systolic ejection murmur is heard at the apex and does not radiate. The murmur is louder when the patient is standing. An ECG shows left ventricular hypertrophy. This patient most likely has a mutation in which of the following?

- Collagen, type IV
- Cytochrome P450
- Endothelin structure
- Lysosomal enzymes
- β -Myosin

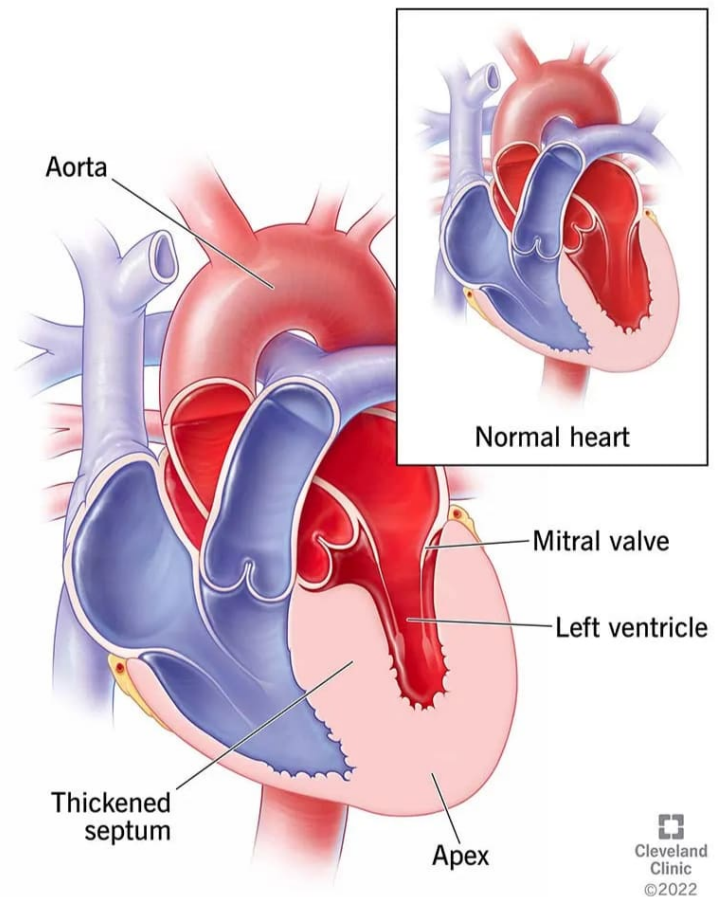
▼ Explanation

• Answer is E (β -Myosin)

◦ IMP Clues

- A grade 3/6 systolic ejection murmur is heard at the apex (The site of the murmur here is not what you would classically find it. Normally it is LSB)
- Does not radiate (Differentiates it from AS)
- Murmur is louder when the patient is standing (This is the keyword we needed)
- ECG shows left ventricular hypertrophy (Increased LV pressure causes hypertrophy)
- Q asks for most likely mutation in?

- Dx → Hypertrophic Cardiomyopathy (HCM)
 - It is an **asymmetrical hypertrophy of the interventricular septum** diagnosed by ECHO as septum being ≥ 15 mm (you don't need to know the number, just saying)
 - In cases where the hypertrophied septum **obstructs the LV outflow tract**, it is called **Hypertrophic Obstructive Cardiomyopathy (HOCM)**
 - Presents as kids or young adults that get **syncope/dyspnea/chest pain on exertion** OR sudden death.
 - Murmur: **Ejection Systolic murmur** (similar to that of AS, however, **DOESN'T** radiate) which:
 - **INCREASES** in intensity with **Valsalva & Standing**
 - **Why?**
 - Valsalva & standing **decrease** VR to heart → **less** blood going to LV → **less** LV pressure → **septum bulges** into the cavity → turbulence ⇒ **louder murmur**
 - **DECREASES** in intensity with **Squatting & Handgrip**
 - **Why?**
 - Squatting & Handgrip **increase** VR + **increase** Afterload.
 - **Increased** VR → **increased** blood to LV → **more** LV pressure → septum **bulges less** into cavity → **less** turbulence ⇒ **softer murmur**
 - **Increased** afterload = **more** LV pressure → septum **bulges less** into cavity → **less** turbulence ⇒ **softer murmur**
 - Pathophysiology: **AD** disease characterized by **mutation in Beta-myosin heavy chain & Myosin binding protein C**
 - Muscle fibers added in **parallel** (with septal favoring),
 - Which essentially means: **LV concentric hypertrophy + septum enlarged more (so Asymmetric hypertrophy) = Myofibrillar disarray & Fibrosis [asked on NBME]**



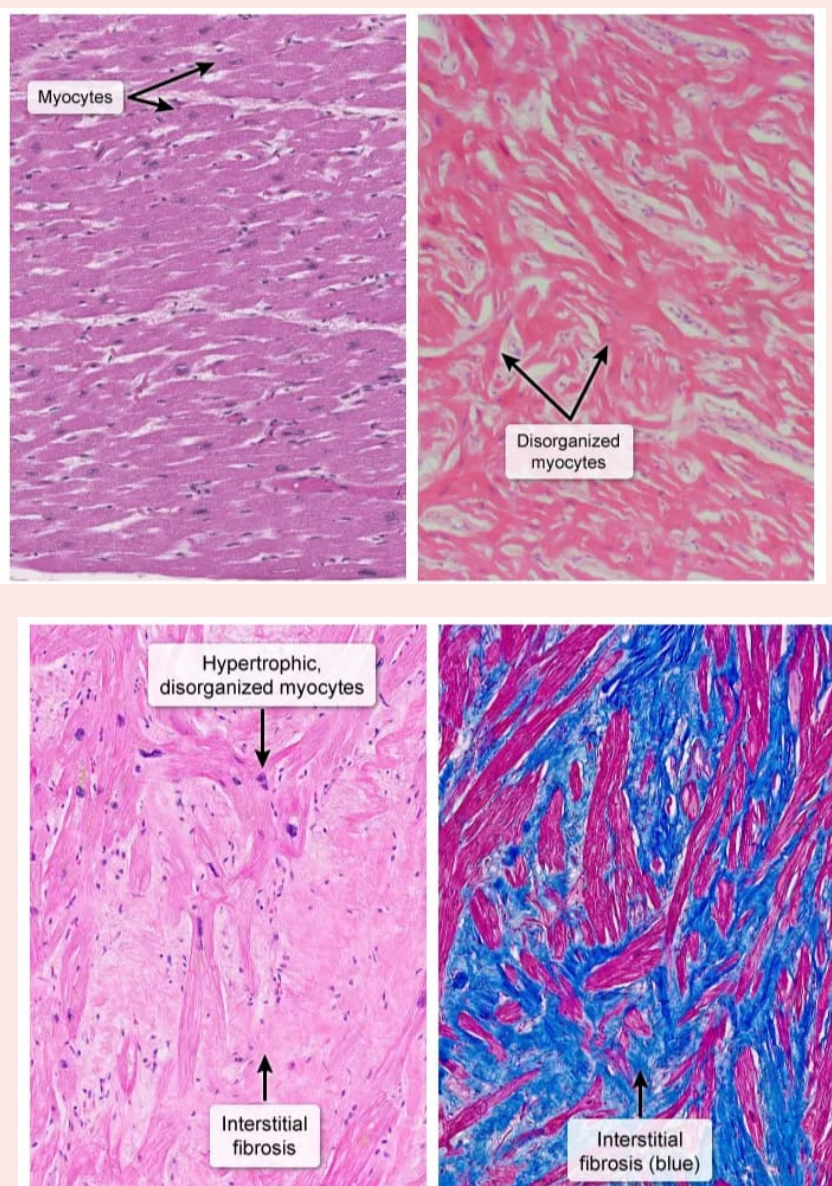
? What is the treatment for patients with HOCM?

▼ Answer

Beta Blockers

- **Longer diastole** → more filling of RV → more blood to LV → more pressure → **less septal bulge** ⇒ **LESS outflow obstruction**

Pictures below show Myofibrillar disarray & Fibrosis of HOCM:



! On the USMLE, LVH can be described as "Left Axis deviation on ECG" or "Left Bundle Branch Block" or "Paradoxical Splitting of S2"

HCM vs DCM Rapid Review:

Features	Hypertrophic Cardiomyopathy	Dilated Cardiomyopathy
Causes	Familial	Idiopathic or Familial, Alcohol, Doxorubicin, Coxsackie B Virus, Chagas Disease, Peripartum Cardiomyopathy, Wet Beri Beri, Stress Cardiomyopathy
Mutation	AD mutation in genes encoding sarcomere proteins B-myosin heavy chain & myosin binding protein C)	Mutation in gene encoding sarcomere protein titin (TTN gene)
Dysfunction	Diastolic Dysfunction (small cavity)	Systolic Dysfunction (thin-ish walls)
Findings	S4, Septal hypertrophy + SAM	S3, Diffuse enlargement
	Concentric Hypertrophy (sarcomeres added in parallel)	Eccentric Hypertrophy (sarcomeres added in series)

Q25

A 23-year-old woman comes to the physician for advice regarding diet. She has a family history of breast cancer. Last week, she read a magazine article that stated that gamma radiation is used as a sterilization method for many food items, such as meat and raw poultry. She says, "I'm concerned that exposing myself to ionizing radiation by consuming irradiated food could lead to cancer." Which of the following initial responses by the physician is most appropriate?

- A. "Although there is a small increased risk for adverse health effects from consuming irradiated food, it is small compared with the risk for foodborne illness from improper sterilization."
- B. "Because irradiated food is not radioactive, you will not be exposed to ionizing radiation by consuming it."
- C. "Because of your young age, you should avoid consumption of irradiated food to minimize your lifetime exposure to ionizing radiation."
- D. "You should be sure to heat irradiated food thoroughly so that the hazardous by-products of irradiation break down during the cooking process."
- E. "You should limit your consumption of irradiated foods to one serving weekly."

▼ Explanation

- Answer is B ("Because irradiated food is not radioactive, you will not be exposed to ionizing radiation by consuming it.")
 - This response (Choice B) directly and accurately addresses the patient's specific concern.
 - Food irradiation uses ionizing radiation (like gamma rays or X-rays) to sterilize food, but the process does not make the food itself radioactive.
 - The radiation passes through the food, killing bacteria and other pathogens, but does not remain in the food.
 - Therefore, consuming irradiated food does not expose a person to ionizing radiation.

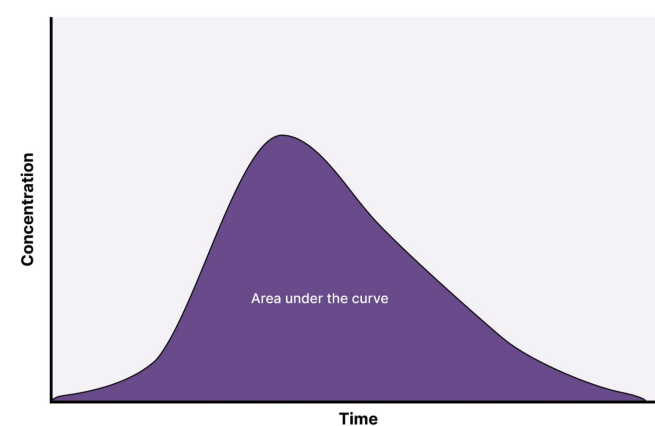
Q26

An investigator is studying two drugs, Drugs X and Y, to determine which has the greater bioavailability in a healthy human volunteer. The drugs have similar mechanisms of action. If Drug X has the greater bioavailability compared with Drug Y, which of the following parameters is most likely to be greater for Drug X than for Drug Y if both are administered at the same dose?

- A. Area under the curve
- B. Beta half-life
- C. Clearance
- D. $E_{\max}$ (peak effect)
- E. Volume of distribution

▼ Explanation

- Answer is A (Area under the curve)
 - Bioavailability
 - Describes the rate and concentration at which a drug reaches systemic circulation
 - Expressed as a percentage of the dose that was initially administered:
 - Drugs administered intravenously have a bioavailability of 100%.
 - Drugs administered orally undergo First Pass Metabolism, which decreases their bioavailability as they pass by the liver.
 - Drugs administered rectally or sublingually bypass the first pass metabolism, and are absorbed into blood stream directly
 - Bioavailability is calculated by using the area under curve (AUC)
 - Y-Axis $\Rightarrow$ Drug Concentration
 - X-Axis $\Rightarrow$ Time



Bioequivalence: Two proprietary preparations of a drug are said to be bioequivalent if they exhibit the same bioavailability when administered in equal doses.

Q27

A 65-year-old man has had increasing shortness of breath over the last 3 months and slowly increasing low back and hip pain for the last 5 years. High output cardiac failure is diagnosed. Radiologic studies show extensive, intermixed osteosclerotic and osteolytic areas in his pelvic bones. Serum calcium concentration is within the

reference range, and serum alkaline phosphatase activity is markedly increased. Which of the following is the most likely diagnosis?

- A. Aneurysmal bone cyst
- B. Angiosarcoma
- C. Niacin deficiency
- D. Osteitis deformans (Paget disease)
- E. Osteosarcoma
- F. Prostatic carcinoma

▼ **Explanation**

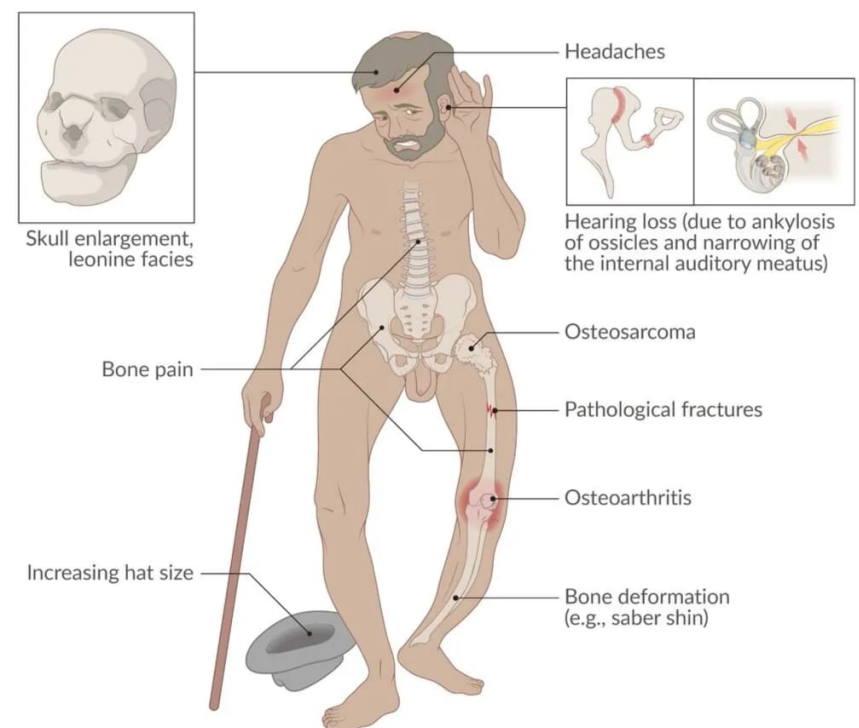
• **Answer is D (Osteitis deformans (Paget disease))**

◦ **IMP Clues**

- Shortness of breath + High-Output cardiac failure
- Low back and hip pain
- Radiological studies show extensive, intermixed osteosclerotic and osteolytic areas
- Serum calcium is within the reference range
- Serum ALP activity is markedly increased

• **Dx → Paget's Disease (Osteitis deformans)**

- **Abnormal bone remodeling disorder** characterized by following 3 phases:
 1. **Lytic Phase** (Increased number & activity of **osteoclasts** = increased bone resorption)
 2. **Mixed Phase** (Increased activity of **osteoblast & osteoclasts** = **Woven hypervascularity bone** → **Mosaic pattern** "woven + lamellar bone")
 3. **Sclerotic Phase** (**Decreased** Osteoclast & Osteoblast activity)
- As a result of the disorganized bone remodeling, patients experience **bone pain**, **skull enlargement**, and the USMLE favorite **tinnitus** (due to involvement of the ossicles)
- Characterized by **HIGH ALP activity with all remaining labs found to be NORMAL**
- USMLE loves to give you the XRAY descriptions of **"Picture-Frame Vertebra"**, **"Mixed osteosclerotic and osteolytic areas"**, or **"Cortical thickening of vertebral endplates"**.
- HY Complications on the USMLE are **High-Output Heart Failure** (due to AV-Shunting in bone) & **Osteosarcoma**.



📌 Paget Disease Presentations on the USMLE:

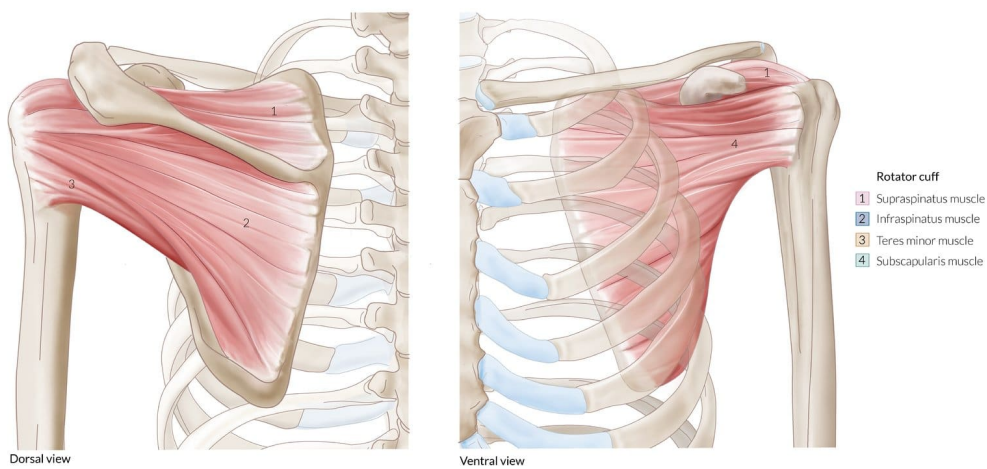
1. They give you a 55M + bone pain + high ALP+ normal calcium & phosphate.
 - a. Ask for Dx ⇒ **"Paget Disease"** or **"Osteitis Deformans"**
 - b. Ask for cause of shortness of breath ⇒ **"High Cardiac Output"** or **"high-output HF"** or **"AV Fistula"**
2. They give you an elderly patient with a hat that doesn't fit him anymore + tinnitus
 - a. Ask for Expected Labs ⇒ **HIGH ALP** + normal Calcium + normal Phosphate
 - b. Ask for Diagnosis ⇒ **"Paget Disease"** or **"Osteitis Deformans"**
 - c. Ask for expected bone complication ⇒ **Osteosarcoma**

A previously healthy 45-year-old man comes to the physician because of a 3-day history of left arm pain and weakness. Use of ibuprofen has provided no relief. He does not smoke or drink alcohol. His vital signs are within normal limits. Examination of the left upper extremity shows weakness with external rotation of the shoulder but full strength with the elbow in extension. There is no weakness on shoulder mid-arc abduction or internal rotation. There is no pain or weakness on flexion of the shoulder at 30 degrees against resistance with the elbow fully extended and the arm fully supinated. The most likely cause of this patient's condition is injury to which of the following tendons?

- A. Biceps
- B. Infraspinatus
- C. Subscapularis
- D. Supraspinatus
- E. Triceps

▼ Explanation

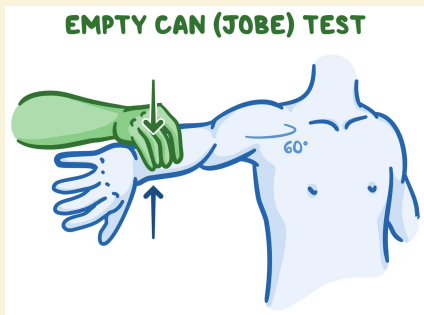
- Answer is B (Infraspinatus)
 - IMP Clues
 - Weakness with external rotation of the shoulder (External rotators are either infraspinatus or teres minor)
 - Remaining findings are normal
- Dx → Infraspinatus Injury
 - **Infraspinatus** is one of the *rotator cuff muscles* that stabilize the shoulder.
 - **Most commonly injured in athletes performing repetitive overhead/throwing movements**
 - Function is **external rotation**, so **pain & weakness are produced on resisting external rotation**.



? What is the most common rotator cuff injury?

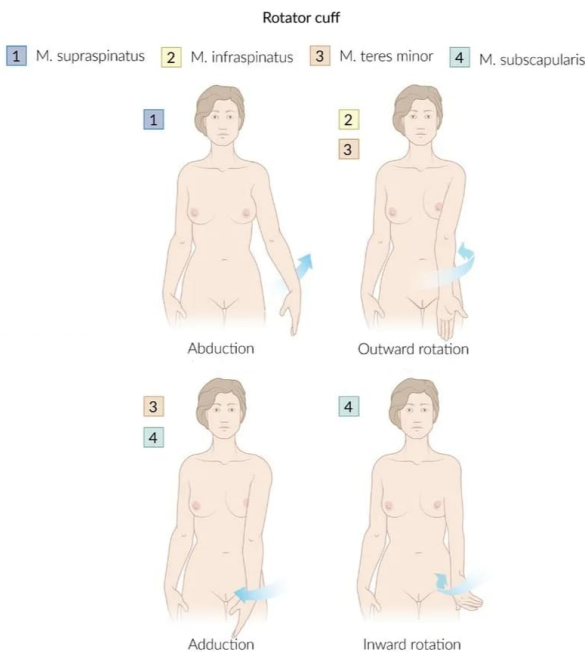
▼ Answer
Supraspinatus tear - presents as **pain and weakness/loss of shoulder abduction of FIRST 15 DEGREES**

- Tested for by **"Empty Can Test"**
 1. Patient raises arms 90 degrees in the scapular plan
 2. Patient fully rotates his arms internally, so that his thumb is pointing to the floor "as if emptying a can"
 3. Doctors pushed down on arm while patient resists ⇒ **Patient feels pain = positive test**



Rotator Cuff Muscles are HY and are 4 muscles:

1. **Supraspinatus**
 - Action → **Abduction (0 → 15 degrees)**
 - Nerve Supply → **Suprascapular nerve**
2. **Infraspinatus**
 - Action → **External Rotation**
 - Nerve Supply → **Suprascapular nerve**
3. **Teres Minor**
 - Action → **External Rotation** (and weak adduction)
 - Nerve Supply → **Axillary Nerve**
4. **Subscapularis**
 - Action → **Internal Rotation** (and weak adduction)
 - Nerve Supply → **Subscapular nerve** (upper & lower)



Q29

A 54-year-old woman with rheumatic heart disease is brought to the emergency department 45 minutes after the onset of severe shortness of breath. Her pulse is 115/min and irregular, respirations are 24/min, and blood pressure is 110/80 mm Hg. Crackles are heard over the lower lung fields bilaterally. Cardiac examination

shows a grade 2/6 systolic ejection murmur radiating to the right side of the neck that is heard best at the second right intercostal space; a diastolic murmur heard best at the apex also is present. An ECG shows atrial fibrillation and left atrial enlargement; there is no ischemia. Which of the following pulmonary mechanisms best explains this patient's dyspnea?

- A. Arterial hypertension
- B. Atelectasis
- C. Hemorrhage
- D. Intra-alveolar transudates
- E. Vascular constriction

▼ Explanation

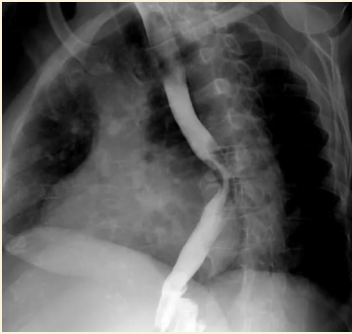
- Answer is D (Intra-alveolar transudates)
 - IMP Clues
 - Woman with RHD (RHD causes MR early & MS late)
 - Crackles are heard over the lower lung fields bilaterally (Probably pulmonary edema)
 - Pulse is 115/min and irregular (AFib)
 - Systolic Ejection murmur radiating to the right side of the neck (AS)
 - Diastolic murmur heard best at the apex is also present (MS)
 - ECG shows atrial fibrillation and left atrial enlargement (Consistent with MS)

- Dx → Mitral Stenosis
 - Mitral Stenosis causes *less* blood flow from LA to LV → pressure of left atrium *increases* → overtime causes the left atrium to *enlarge*.
 - LA enlargement is the most important risk factor to AFib.
 - If a patient gets an *AFib* attack, the *left atrium CAN'T pump blood across the already stenotic mitral valve*, causing *blood to acutely regurgitate into the pulmonary vasculature*:
 - This causes *increased* pulmonary capillary hydrostatic pressure, which ends up causing *extravasation* of fluid into pulmonary interstitial space ⇒ *Pulmonary Edema/Transudate* (Choice D)

? What esophageal complication can this patient have?

▼ Answer
Dysphagia

- Patients with LA enlargement (usually due to MS) experience dysphagia as LA compresses the anterior aspect of the esophagus



Another HY Complication of LA enlargement is:

- Ortner's Syndrome
 - Hoarseness due to left recurrent laryngeal nerve compression by enlarged LA

Q30

A 44-year-old woman comes to the physician because of a 2-week history of episodes of shortness of breath, perioral tingling, and vague chest tightness. These episodes, which last 20 to 30 minutes, are unrelated to physical exertion and are relieved by alcohol or lorazepam. She appears mildly anxious. Her temperature is 37°C (98.6°F), pulse is 108/min, respirations are 28/min, and blood pressure is 128/82 mm Hg. Physical examination shows no other abnormalities. An ECG shows sinus tachycardia. Laboratory studies are most likely to show which of the following at this time?

- A. Decreased arterial Pco₂
- B. Decreased arterial Po₂
- C. Decreased pH
- D. Increased serum bicarbonate concentration
- E. Increased serum thyroid-stimulating hormone concentration
- F. Presence of an anion gap

▼ Explanation

- Answer is A (Decreased arterial Pco₂)
 - IMP Clues
 - Episodes of SOB, perioral tingling, and vague chest pain
 - Episodes last 20-30 mins and are unrelated to exertion + relieved by alcohol or lorazepam

- Respirations are 28/min

• Dx → Panic Attack Disorder

- Panic Attacks cause **hyperventilation**
 - Hyperventilation causes **increased washing-out of CO₂ = hypocapnia: (Choice A)**
 - **Brain Flow to decrease (vasoconstriction)** → *Blurring of vision & dizziness*
 - Less CO₂ causes **Respiratory Alkalosis** → less protons (H) bound to albumin → Calcium binds to albumin → less ionized (free) Calcium → **Hypocalcemia**
 - Hypocalcemia causes the **peri-oral numbness** in the vignette.
 - [🧠] Hypocalcemia can also cause **Trousseau's sign & Chvostek's sign**
 - **Trousseau's sign** → Carpopedal spasm when BP is measured
 - **Chvostek's sign** → Facial twitching on percussion of facial nerve

? How can anesthesiologists play with the settings of mechanical ventilators in patients with brain trauma?

▼ Answer

Increase RR to decreased Intracranial Pressure - Higher RR causes increased CO₂ washing, this causes cerebral vessels to constrict → less intracranial pressure.

- The increased ICP can cause the brain to herniate, because of the edema caused by the head trauma.



Q31

A 40-year-old woman comes to the physician because of a 1-year history of progressive facial puffiness and weight gain. She also has had several upper respiratory tract infections during the past 6 months. Her temperature is 37.2°C (99°F), pulse is 82/min, respirations are 18/min, and blood pressure is 160/95 mm Hg. Physical examination shows increased fat around the neck, facial plethora, moon facies, red striae over the breasts, abdomen, and buttocks, and proximal muscle weakness. Serum studies show a mildly increased adrenocorticotrophic hormone concentration that is suppressed after an oral administration of dexamethasone for several days. The most likely cause of the findings in this patient is hypersecretion of a hormone from a tumor located in which of the following organs?

- A. Adrenal cortex
- B. Hypothalamus
- C. Lung
- D. Pancreas
- E. Pituitary gland

▼ Explanation

- Answer is E (Pituitary gland)
 - IMP Clues
 - Facial puffiness and weight gain
 - Several upper respiratory tract infections
 - Blood pressure is 160/95 mmHg
 - Fat around the neck + facial plethora + moon facies + red striae over breasts, abdomen, and buttocks + proximal muscle weakness
 - Increased ACTH hormone concentration that is suppressed after an oral administration of dexamethasone for several days
 - Q asks for site of hormone hypersecretion
 - Dx → Cushing Disease
 - **ACTH hypersecretion by a pituitary gland adenoma** (Choice E) resulting in **increased** serum levels of cortisol
 - **Increased** ACTH production → **Increased** stimulation to adrenals → **bilateral adrenal hyperplasia** → **increased cortisol production from Zona Fasciculata [asked on NBME]**

- Features:
 - **Central Obesity, Moon Facies, Buffalo Hump, and Thin Extremities** (Cortisol *increases lipolysis* and causes *fat redistribution* that favors trunk, face, and upper back with thin limbs)
 - **Proximal Muscle Weakness** (due to *increased protein catabolism*, which is then used in *hepatic gluconeogenesis*)
 - **Glucose Intolerance, Diabetes Miletus, and Weight Gain** (Caused by *increased hepatic gluconeogenesis*, *lipolysis*, and *hyperinsulinemia*)
 - **Red/Purple Striae & Ecchymoses** (due to cortisol *inhibition of fibroblast proliferation & collagen synthesis*, causing *thinning of the dermis & capillary fragility*)
 - **Hypertension** (due to *permissiveness*, causing potentiation of catecholamines effects on alpha-1 receptors **[asked on NBME]** & due to *mineralocorticoid receptor activity*, acting like aldosterone causing salt and water retention → increased blood volume)
 - **Osteoporosis** (due to *inhibition of osteoblastic activity*, causing less bone mineralization and more bone resorption) **[asked on NBME]**
 - **Increased Infection Risk** (due to *inhibition of PLA2 activity* decreasing LTs/PGs + *inhibition of neutrophils migration* + *inhibition of IL-2 production*, causing reduced T-cells activation and proliferation → Lymphopenia)
 - **Darker skin, Facial Plethora, and Posterior Subcapsular Cataract** **[asked on NBME]**

- How to Find Source of hypercortisolism? (Super HY and all over NBMEs, so concentrate pleaseeee)

- High cortisol levels (urinary/salivary)?

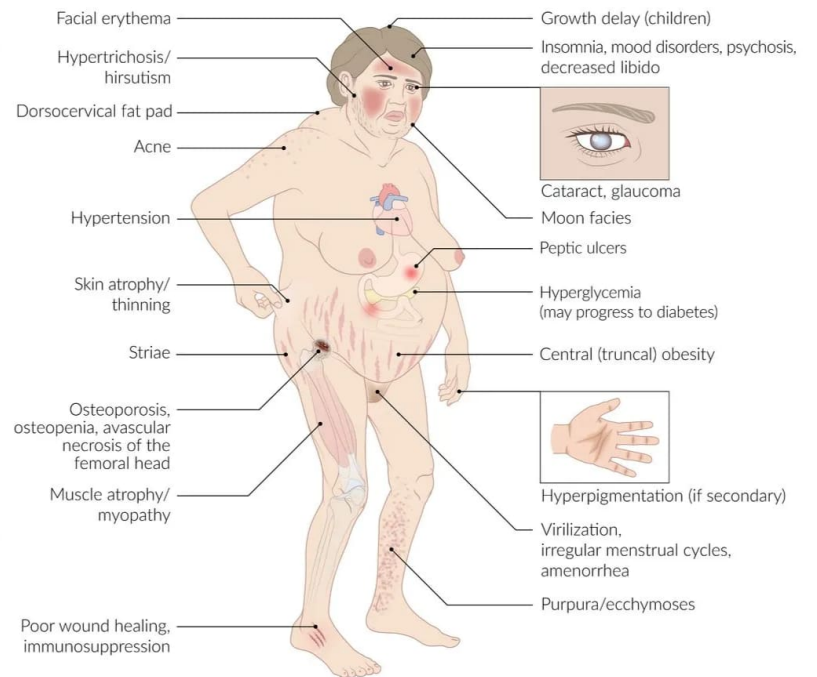
1. **Measure serum ACTH:**

a)Low?

- Exogenous glucocorticoids intake OR Adrenal Tumor
 - Do Abdominal CT:
 - **Bilateral Atrophied** ⇒ *Exogenous glucocorticoids intake*
 - **Unilateral enlargement + contralateral atrophy** ⇒ *Adrenal Tumor (Adenoma/Hyperplasia/Carcinoma)*

b)High?

- Do High-dose dexamethasone suppression test:
 - **Suppressed ACTH & Cortisol** ⇒ *Cushing Disease (ACTH-secreting Pituitary Adenoma)*
 - Do MRI to confirm pituitary mass
 - **NO CHANGE/Suppression of ACTH & Cortisol** ⇒ *Ectopic ACTH Secretion*
 - Do Chest/Abdomen/Pelvis CT to find source
 - Both adrenals will be enlarged
- Most commonly will be *small cell lung cancer* (vignette will mention hx of smoking +/- cough and hemoptysis)



? Patient on HIV therapy for few months and now presents with central obesity, moon face, buffalo hump, and thin extremities + labs show hyperglycemia. What is the cause of these side effects?

▼ **Answer**

Protease Inhibitors ("navir") cause *lipodystrophy*, which is at redistribution with Cushing syndrome-like presentation & *hyperglycemia* (may present as insulin resistance or DM)

! USMLE gives you a patient that has eczema and *uses local steroids for a long period of time* & presents now with *purpura, skin atrophy*, and *telangiectasia*. They ask you for the reason; Choose *Dermal Thinning*.

? Patient with SLE presents to ED after MVA. During surgery the patient gets hypotensive despite fluid resuscitation, however, blood pressure normalizes after IV steroids and Norepinephrine. Why?

▼ **Answer**

Patients with SLE are usually on long-term systemic steroids, which cause *bilateral adrenal atrophy*. When patients undergo massive stress (in this case MVA & hypotension), the *cortisol production is insufficient*, hence causing *decreased effects of the circulating catecholamines on their respective receptors*, the alpha-1 in this case → *Hypotension*. Giving IV steroids + Norepinephrine improves patient's blood pressure as *cortisol is permissive to the effects of catecholamines*, causing *upregulation of alpha-1 receptors* → *more pronounced effects of norepinephrine* → *increase* in blood pressure

Q32

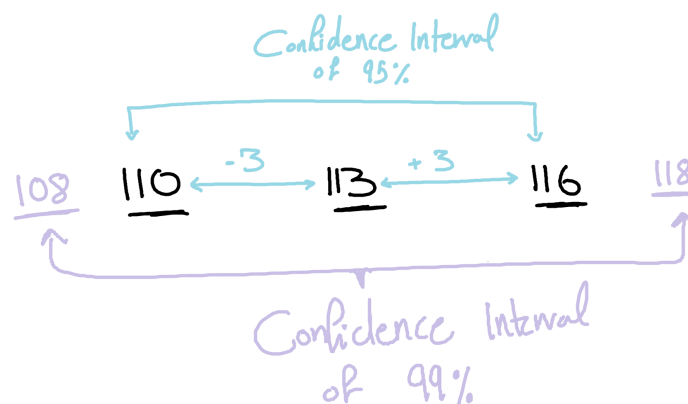
A 48-year-old man is referred for evaluation of possible hypertension. On the basis of four measurements, the patient's average diastolic blood pressure is 113 mm Hg, with a 95% confidence interval of 110 to 116 mm Hg. Which of the following (in mm Hg) most likely represents the 99% confidence interval for these data?

A. 108 to 114

- B. 108 to 118
- C. 110 to 116
- D. 112 to 114
- E. 112 to 120
- F. 112.5 to 113.5

▼ Explanation

- Answer is B (108 to 118)
 - Mean = Average = 113
 - 95% confidence interval is 110 → 116, which is a space interval of "6"
 - If we wanted to measure the 99% confidence interval, we'd assume that it is wide than the 95% space interval of "6".
 - This means that it would be an interval that is less than 110 but greater than 116 with 113 in the middle
 - The only answer choice with this criterion is Choice B (108 → 118)



Q33

A 78-year-old man has had progressive loss of hearing in his right ear over the past year. Bone conduction is better than air conduction in both ears. Which of the following is the most likely cause of the hearing loss?

- A. Acoustic neuroma (vestibular schwannoma)
- B. Lesion of the cochlear nuclei
- C. Loss of hair cells
- D. Ménière disease
- E. Otosclerosis

▼ Explanation

- Answer is E (Otosclerosis)
 - To answer this Q, you'd have to understand the bone conduction vs air conduction comparison.
 - Basically, the normal ear anatomy allows for air conduction > bone conduction
 - In Sensorineural hearing loss, the anatomy is preserved, so also air conduction > bone conduction.
 - The only difference is the sound processing is globally reduced; you have hearing loss yes, but you still hear better via air conduction when compared to bone conduction.
 - Examples are Presbycusis (age-related), Noise-Induced, Meniere's disease, Ototoxic drugs, and Acoustic Neuromas.
 - In Conductive hearing loss, the anatomy is fucked up (due to involvement of the ossicles themselves or due to presence of something preventing/slowing down air conduction), which causes bone conduction > air conduction.
 - Example of Ossicles involvement is Otosclerosis (Choice E)
 - Examples of slowing down air conduction are Otitis Media with Effusion, Tympanic membrane perforation, Cholesteatoma, or even Impaction of ear wax.
 - What is the difference between Weber & Rinne Test?

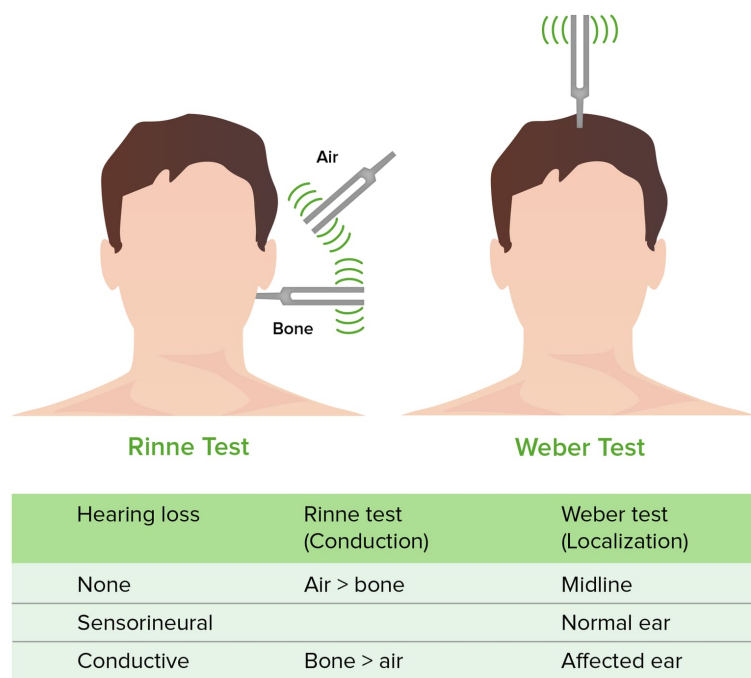
I remember which is which by remembering that Weber sounds similar to Whether

 - "In Weber test we put the tuning fork on our head to test whether it localized to an ear or not."

? What are the HY ototoxic drugs USMLE love?

▼ Answer

Aminoglycosides (Gentamycin is a favorite), Cisplatin, and Loop diuretics



Otosclerosis Rapid Review:
 Pathophysiology: **Abnormal bone remodeling** of the ossicles, which causes replacement of normal bone with **woven bone**, thus resulting in **fixation of these bones** → **decreased transmission of sound vibrations**
 How is affected the most? **Middle-Aged Females**
 Presentation: **Bilateral but asymmetrical Conductive hearing loss** (starts noticing hearing loss in one ear more than the other) +/- tinnitus. **NO pain & NO vertigo.**
 Findings:

- CHL: **BC > AC**
- **Normal Tympanic Membrane**
 - USMLE has this rare sign on a Q somewhere called **Schwartz's sign**, which is basically **reddish tympanic membrane seen sometimes in active bone remodeling of Otosclerosis**
 - Red because the newly synthesized woven spongy bone is **highly vascularized**



Q34

A 24-year-old woman comes to the physician because of a 2-week history of small purple spots over her legs. She feels well otherwise. Three months ago, she underwent splenectomy for immune thrombocytopenic purpura. Her temperature is 37.5°C (99.5°F), pulse is 60/min and regular, respirations are 14/min, and blood pressure is 120/75 mm Hg. Physical examination shows a well-healed surgical scar. The lungs are clear. Cardiac and abdominal examinations show no abnormalities. Laboratory studies show:

Hemoglobin	13.5 g/dL
Hematocrit	40%
Leukocyte count	10,000/mm ³
Platelet count	25,000/mm ³
Partial thromboplastin time	29 sec

Platelet counts done preoperatively, 1 week postoperatively, and 6 weeks postoperatively were 20,000/mm³, 100,000/mm³, and 220,000/mm³, respectively. Today, a peripheral blood smear shows normal erythrocyte morphology and no Howell-Jolly bodies; a peripheral blood smear done 6 weeks postoperatively showed the presence of Howell-Jolly bodies. Which of the following best explains this patient's current laboratory findings?

- A. Accessory spleen
- B. Acute lymphocytic leukemia
- C. Heparin-induced thrombocytopenia
- D. Postoperative sepsis
- E. Primary megakaryocyte deficiency

▼ Explanation

- **Answer is A (Accessory spleen)**
 - **IMP Clues**
 - Small purple spots over her legs (petechiae)
 - Three months ago, she underwent splenectomy for ITP
 - PLT count now is 25,000 despite & Peripheral blood smear shows no Howell-Jolly bodies DESPITE PLTs being 220,000 + having Howell-Jolly bodies 6 weeks post-op

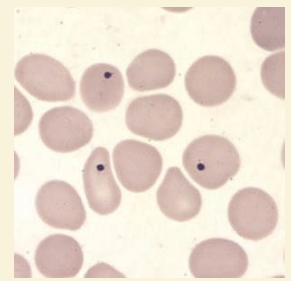
- **Dx → Immune Thrombocytopenic Purpura (ITP)**
 - Basically, this patient has **recurrence of ITP** due to the presence of an **accessory spleen (Choice A)**, let me explain.
 - As we know, ITP is **caused by antibodies against Glycoproteins IIb/IIIa on PLTs**
 - These now tagged platelets are **engulfed by splenic macrophages**, causing **thrombocytopenia**.
 - **After removal of the spleen (like in this patient), the tagged platelets are NOT destroyed → Increase in platelet count.**
 - Now if an **accessory spleen is present** and the patient gets an **ITP attack** again, the **tagged platelets will now be destroyed by the accessory spleen**.
 - Causing the above symptoms ⇒ **Thrombocytopenia** (with normal PT and PTT) and **Petechiae**.



Howell-Jolly Bodies:

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

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



What type of hypersensitivity reaction is ITP?

▼ Answer

Type 2 Hypersensitivity Reaction

Q35

A 35-year-old man comes to a new physician for a health maintenance examination. He has a history of intravenous drug use, but he has not used illicit drugs for 10 years. He admits to consuming six 12-oz beers daily. He takes no medications. He is not sexually active and has no interest in initiating a relationship. Physical examination shows gynecomastia, hypogonadism, and spider angiomas. There is no hepatosplenomegaly, ascites, or edema. Further evaluation is most likely to show metabolic dysfunction of which of the following organs?

- A. Adrenal glands
- B. Kidneys
- C. Liver
- D. Pituitary gland
- E. Thyroid gland

▼ Explanation

- **Answer is C (Liver)**
 - **IMP Clues**
 - He has history of IV drug use (Risk Factor for HCV)
 - Consumes six 12-oz beers daily (Alcoholic-Induced Liver Failure)
 - Gynecomastia + Hypogonadism + Spider angiomas (Seen in liver cirrhosis due to abnormal estrogen metabolism)
 - No hepatosplenomegaly (Liver is cirrhotic and shrunken), ascites, or edema (compensated liver cirrhosis)

• Dx → Liver Cirrhosis

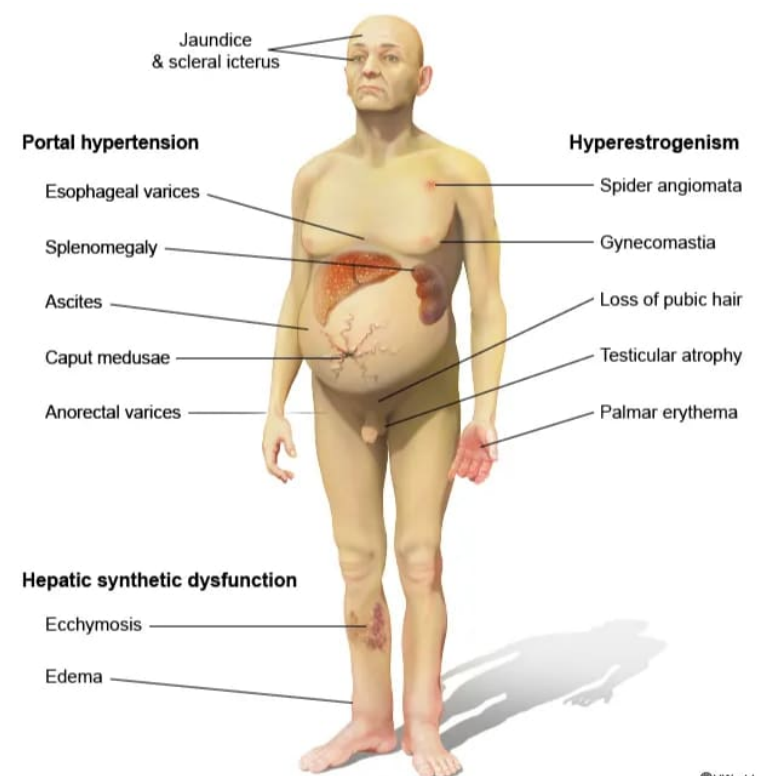
- Let's go through the mechanism of each sign in this patient:
 - **Decreased hepatic degradation of estrogen causes increased estrogen/testosterone ration:**
 - **Breast tissue growth stimulation ⇒ Gynecomastia**
 - **Decrease** in SHBG production, causing an **increase** in active portion of estrogen → **inhibition** of FSH and LH → **decreased** testosterone ⇒ **Hypogonadism**
 - **Estrogen causes vasodilation** of cutaneous arterioles ⇒ **Spider Angiomas & Palmer Erythema**



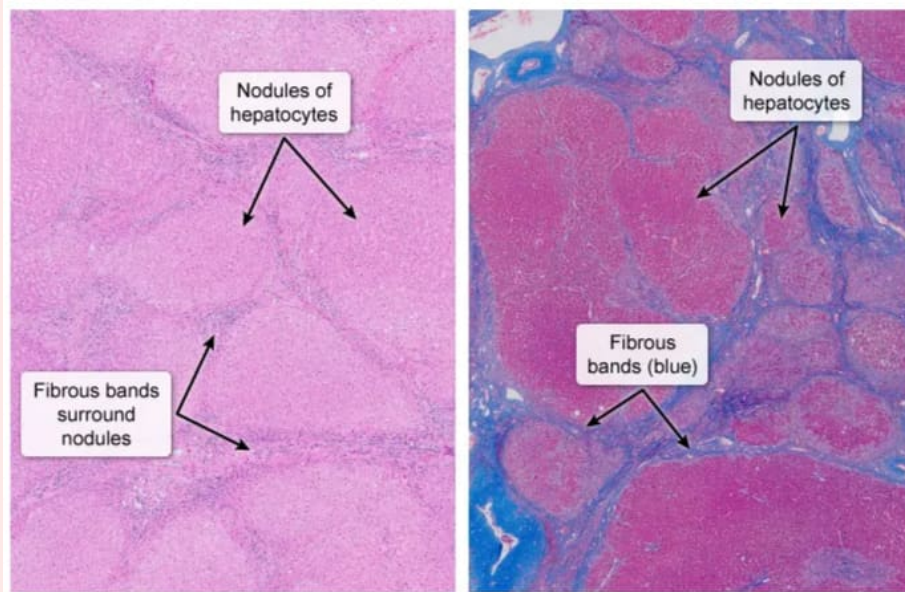
What 2 HY drugs cause gynecomastia on the USMLE?

▼ Answer

Spironolactone (Potassium-sparing diuretic) & **Cimetidine** (H2-Blocker)



Shown below is how cirrhosis looks under the microscope. USMLE can give you both stains below so know them



- USMLE sometimes refer to these as “**Regenerative Nodules surrounded by bands for fibrosis**”

Q36

A 10-year-old boy sustains an abrasion on his left knee. One week after the injury, epidermal cells cover many areas of the abraded skin. This stage of wound healing is best explained by the fact that epidermal cells belong to which of the following classes of proliferative activity?

- A. Labile cells
- B. Permanent cells
- C. Stable cells
- D. Terminal cells
- E. Transitional cells

▼ Explanation

- **Answer is A (Labile cells)**
 - **Labile Cells are cells that have the *highest* regenerative capacity.**
 - **Remains in G1 forever & NEVER enters G0**
 - HY Examples of Labile cells are **Skin epithelium, GI epithelium, Hair follicles, Bone marrow, and Germ cells.**
 - What are the other types of cells?
 - **Stable Cells go from G0 → G1 when stimulated** (so **moderate** regenerative capacity)
 - HY Examples are **Hepatocytes, Lymphocytes, Renal Tubular Cells, and Smooth muscle.**
 - Regenerates **if the structural framework is preserved:**
 - If the reticulin structure is preserved, Liver regenerates with **NO FIBROSIS**
 - If destroyed → **Fibrosis**
 - **Permanent Cells have NO regenerative capacity** (may regenerate from stem cells, but limited)
 - **Remains in G0 forever**
 - HY Examples are **RBCs, Neurons, and Skeletal & Cardiac muscles.**
 - Dead **Neurons** (Pos-Stroke) in CNS are replaced by **gliosis**.
 - Dead **Cardiocytes** (Post-MI) are replaced by **scar tissue**

⚠ Labile Cells are the most affected by chemo/anti-cancer drugs due to their **rapid turnover**.

- This is why patients on chemo/anti-cancer drugs develop **sores, infertility, neutropenia, and hair fall.**

? Patient takes chemo for cancer. Hair starts falling out, why?

▼ Answer
Hair Follicles have high turnover rates.

Q37

An 18-hour-old male newborn is 61 cm (24 in) long and weighs 5443 g (12 lb). His mother has type 1 diabetes mellitus. His serum glucose concentration is 20 mg/dL. Which of the following fetal conditions immediately prior to birth most likely precipitated the newborn's postnatal hypoglycemia?

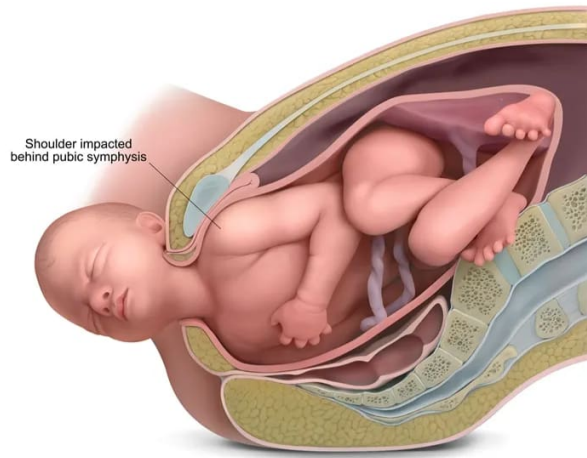
- A. Decreased gluconeogenesis
- B. Decreased glycogen concentration
- C. Decreased glycogen synthetase activity
- D. Decreased serum insulin concentration
- E. Increased serum insulin-like growth factor

▼ Explanation

- Answer is A (Decreased gluconeogenesis)
 - IMP Clues
 - 18-hour-old newborn weighs 5443 g (Macrosomic baby)
 - His mother has type 1 DM (most common cause of macrosomia)
 - His serum glucose concentration is 20mg/dl (Hypoglycemic)
 - Q asks which condition immediately prior to birth most likely precipitated the postnatal hypoglycemia
 - Dx → Fetal Post-Natal Hypoglycemia
 - Diabetic mother that has uncontrolled hyperglycemia → **glucose crosses placenta** into fetal circulation → baby's pancreas produces insulin in response to hyperglycemia.
 - Persistence of maternal hyperglycemia causes **persistent fetal hyperglycemia**, which causes **pancreatic beta-islets hyperplasia** → fetal hyperinsulinemia (Choice D)
 - What happens as a result?
 - Inhibition of gluconeogenesis (Choice A), lipolysis, and protein catabolism ⇒ Causes **Postnatal hypoglycemia** due to abrupt cessation of maternal glucose supply upon clamping the umbilical cord .
 - Increases glycogenesis (Choice C), Fat Storage, and protein anabolism ⇒ **Macrosomia**, which predisposes to **Shoulder Dystocia** [asked on NBME]
 - Other features seen are organomegaly and macroglossia.

? What glucose transporter is found in the placenta?

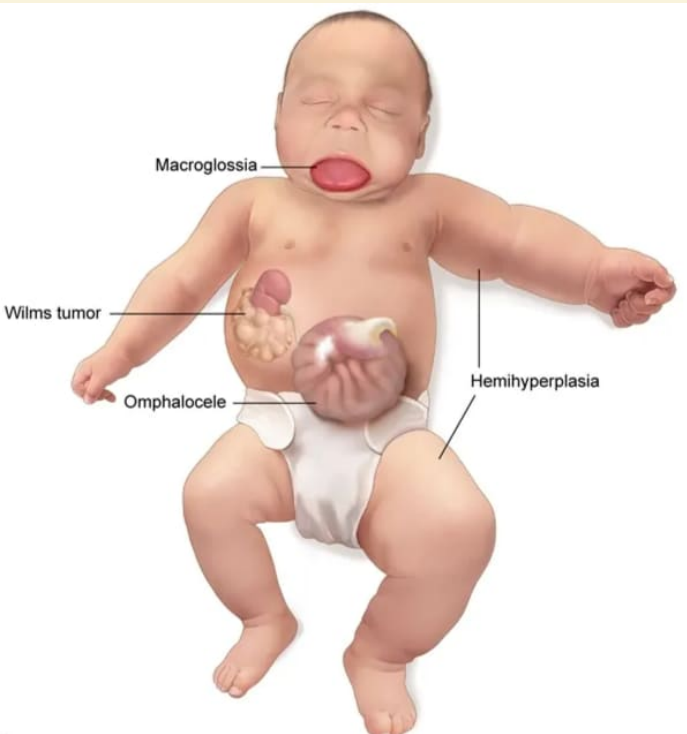
▼ Answer
GLUT-1 (The main key transporter)



Beckwith-Wiedemann Syndrome:

Pathophysiology: Congenital growth disorder characterized by **increased ILGF activity** caused by a mutation on **chromosome 11p15**
Presentation: **Macrosomia, Macroglossia, Hemihypertrophy, Omphalocele** or **Umbilical hernia, post-natal hypoglycemia, Wilms tumor, and hepatoblastoma**
How does USMLE present it?

1. They give you a newborn with macrosomia, macroglossia, hemihypertrophy... and asks for expected complication immediately after birth. Answer is **Hypoglycemia**.
 - Wilms Tumor is **Incorrect** as nephroblastoma presents a few years later, not at birth.
2. They give you a child with a smooth flank mass that doesn't cross the midline +/- red urine or hypertension. They then ask about the **pathophysiology**, the **postnatal hypoglycemia**, or **other features of the syndrome**. You get the idea.



! Remember that Wilms Tumor can be **sporadic** or part of genetic **syndromes**:

They all involve **chromosome 11**, as it has genes controlling **ILGF-1** expression.

1. **WAGR Syndrome** (Wilms Tumor, **Aniridia**, GU malformations, Retardation)
 - **Deletion** of chromosome **11p13** (**WT1**, a tumor suppressor gene)
2. **Denys-Drash Syndrome** (Wilms Tumor & pseudohermaphrodite)
 - **Mutation** of chromosome **11p13** (**WT1**, a tumor suppressor gene)
3. **Beckwith-Wiedemann Syndrome**
 - a. **Imprinting/Parental Uniparental disomy** of chromosome **11p15** (**WT2**)

Q38

A male newborn is delivered at 39 weeks' gestation after an uncomplicated pregnancy, labor, and delivery. Physical examination shows protrusion of a short segment of small intestine through the abdominal wall to the right of the umbilicus. There is no layer covering this intestine. Which of the following is the most likely diagnosis?

- A. Gastroschisis
- B. Midgut volvulus
- C. Omphalocele
- D. Umbilical hernia
- E. Urachal fistula

▼ Explanation

- Answer A (Gastroschisis)
 - IMP Clues
 - Protrusion of a short segment of small intestine through the abdominal wall (could be gastroschisis, omphalocele, or umbilical hernia)
 - To the right of the umbilicus (Either gastroschisis or omphalocele)
 - There is no layer covering this intestine (this is gastroschisis)

◦ Dx → Gastroschisis

- Full-thickness defect of the abdominal wall due to *failure of body folds fusion*, resulting in a *paraumbilical defect* → extrusion of the abdominal contents into the amniotic cavity

- **NOT** covered by peritoneum or amniotic membrane

- Differentiating between Gastroschisis, Omphalocele, and Umbilical Hernias is HY:

◦ Is it midline?

▪ Yes?

- **Covered by Skin?** ⇒ **Umbilical Hernia**
- **Covered by peritoneal/amniotic membrane?** ⇒ **Omphalocele**

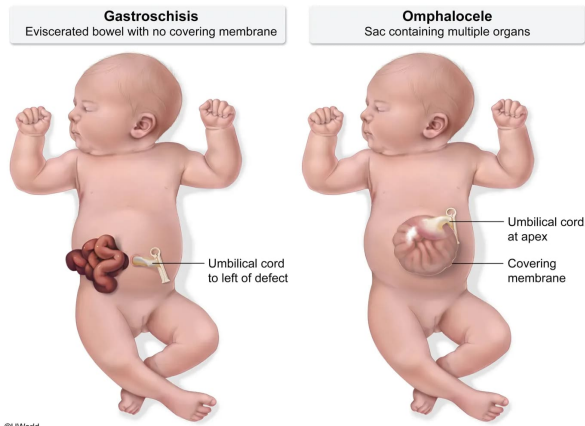
▪ No?

- **NOT covered by peritoneal/amniotic membrane?** ⇒ **Gastroschisis**



Remember that:

- **Congenital Umbilical Hernia** can be *sporadic/benign* but also can be HY hint to *congenital hypothyroidism*.
- **Gastroschisis** is usually an *isolated defect* with **NO** associated anomalies.
- **Omphalocele** is usually *associated with anomalies* (Edwards Syndrome, Patau Syndrome, and Beckwith-Wiedemann)



Q39

A 68-year-old woman has a 6-month history of weakness, fatigue, and weight loss associated with widespread autoimmune destruction of both adrenal glands. She has no other glandular dysfunction. Which of the following sets of findings in serum is most likely?

Choices	Na ⁺	K ⁺	pH
A	↑	↑	↑
B	↑	↑	↓
C	↑	↓	↑
D	↑	↓	↓
E	↓	↑	↑
F	↓	↑	↓
G	↓	↓	↑
H	↓	↓	↓

▼ Explanation

- Answer is F

- IMP Clues

- Weakness, Fatigue, and weight loss associate with autoimmune destruction of both adrenal glands
 - Q asks for most likely set of serum findings

- Dx → Autoimmune Adrenalitis

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

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

- **Presentation**

- 1. **Deficiency of Aldosterone:**

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

- **why?**

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

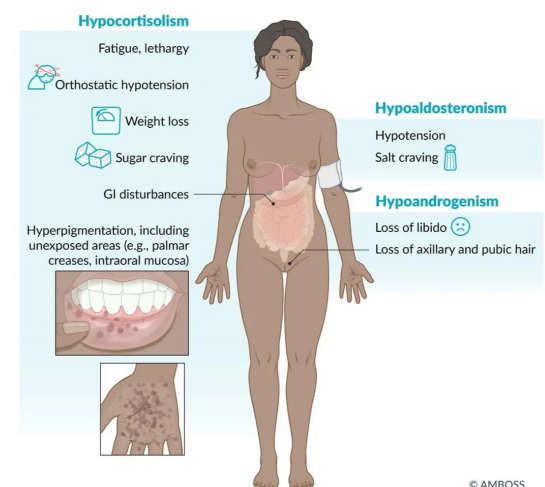
"Neat hack I learned is: Everything follows aldosterone *except* potassium it is the opposite"

- 2. **Deficiency of Cortisol:**

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

- **why?**

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



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

? What would be the expected renin levels in this patient?

▼ Answer

Increased Renin

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

Q40

A male newborn is delivered at term to a 30-year-old woman. The newborn has a malformed right upper extremity. The woman's husband, mother, and sister also are in the delivery room. Which of the following is the most appropriate initial action by the physician?

- A. Ask the mother and sister to leave the room and inform the parents of the abnormality
- B. Call for the hospital pediatricians to come to the delivery room immediately
- C. Conceal the abnormality but allow the parents to hold the baby
- D. Immediately consult with the hospital attorney
- E. Immediately inform the entire family of the abnormality in the delivery room

▼ Explanation

Answer is A (Ask the mother and sister to leave the room and inform the parents of the abnormality)

- Asking the mother and sister to leave is important to ensure that the sensitive news about the newborn is communicated privately to the **primary decision-makers (the parents)**.
 - This approach **respects the parents' autonomy** to ensure that they understand the information and decide when and how to share it with the extended family.
 - **This allows the physician to focus on the parents' immediate emotional and informational needs.**

Q41

A 31-year-old woman comes to the emergency department because of a headache. She is alert and appears anxious. Examination shows multiple contusions on the face and torso. Neurologic examination shows no abnormalities. When asked directly about domestic violence, she says that her husband assaulted her and that she is afraid for her life. She pleads with the physician not to allow her husband to enter the treatment area if he arrives in the emergency department. Within a few minutes, her husband arrives and tells the triage nurse that he is concerned about his wife. He says she is mentally unstable and has been threatening to harm herself. He insists that he be allowed into the treatment area with his wife. Which of the following is the most appropriate next step for the physician?

- A. Allow the patient's husband to join his wife in the treatment area, accompanied by hospital security staff
- B. Offer the patient's husband information about batterer intervention groups and ask him to leave
- C. Offer the patient's husband information about batterer intervention groups and tell him he must remain in the waiting area until his wife's evaluation is complete
- D. Tell the patient's husband that he is not allowed in the treatment area, and that he must remain in the waiting area

▼ Explanation

- Answer is D (Tell the patient's husband that he is not allowed in the treatment area, and that he must remain in the waiting area)
 - The Priority is the Patient's Safety
 - In cases of domestic violence, the physician's immediate and overriding concern is **the safety and autonomy of the patient**.
 - The patient stated that her husband assaulted her, fears for her life, and **pleaded** with the physician to keep him away.
 - This is a **direct request for protection that must be respected**.

Q42

A 50-year-old woman with idiopathic cardiomyopathy is evaluated by the physician prior to receiving a heart transplant. She immigrated to the USA from the Dominican Republic 20 years ago. Preoperative serologic studies show a positive *Strongyloides* antibody titer. This patient most likely acquired this infection via which of the following modes of transmission?

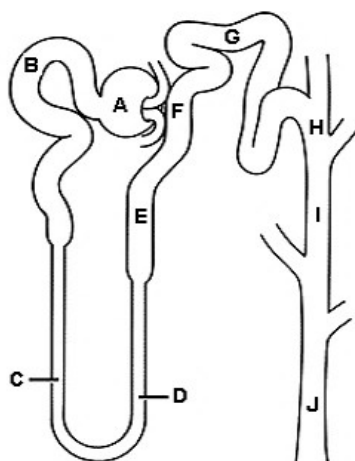
- A. Drinking water contaminated with larvae
- B. Eating watercress contaminated with metacercariae
- C. Ingestion of eggs from fecally contaminated soil
- D. Penetration of larvae from soil into the skin
- E. Person-to-person spread of eggs

▼ Explanation

- Answer is D (Penetration of larvae from soil into the skin)
 - Patient has positive *Strongyloides* antibody titer, and the Q asks about mode of transmission the patient acquired this infection from?
 - ***Strongyloides* is a nematode with a mode of transmission of percutaneous penetration of larvae (primarily via the feet)**

Q43

A 38-year-old woman with hypercalcemia, hypophosphatemia, and phosphaturia is diagnosed with primary hyperparathyroidism. Which of the following labeled segments of the nephron was most likely involved in the development of phosphaturia in this patient?



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

▼ Explanation

- Answer is B
 - Patient has primary hyperparathyroidism & Q asks for site involved in development of phosphaturia
 - This is honestly easy & pass level.
 - Phosphate is secreted in the PCT under the effects of PTH
- Let's Review Some Related HY Notes:
 - Effects of PTH:
 1. Increased bone resorption:
 - PTH stimulates **osteoblasts** → osteoblasts express **RANK-Ligand** → binds to nearby osteoclasts that express **RANK-Receptor** → **activation of osteoclasts** → bone resorption
 - USMLE refers to it as **"paracrine stimulation of osteoclasts by osteoblasts"** or **"increased osteoclasts maturation and activity"** [asked on NBME]
 2. Renal effects:
 - PTH causes **phosphorus secretion in PCT** → Hypophosphatemia & hyperphosphaturia
 - PTH causes **calcium reabsorption in DCT** → Hypercalcemia & hypercalciuria (yes, both are hyper-. Increased Ca in blood is filtered above threshold of reabsorption, so Calcium is still excreted by other mechanisms)
 - PTH causes **increased 1-alpha hydroxylase activity** → Increased conversion of 25-OH-Vitamin D into **1,25-OH-Vitamin D** (calcitriol)
 - PTH causes **increased urinary cAMP**
 3. Vitamin D effects:
 - On **Kidney** → **Increased** reabsorption of **BOTH** Calcium & Phosphate
 - On **Intestines** → **Increased** absorption of **BOTH** Calcium & Phosphate
 - On **Bones** → Balances resorption & mineralization

? What are the other HY things filtered in the PCT? How is this clinically relevant?

▼ Answer
Amino Acids, Glucose, Phosphate, and Bicarbonate

USMLE Like to test this concept plenty, so let's master it:

They give you a patient with glycosuria, aminoaciduria, phosphaturia and ask for what else is expected. Answer is **"decreased reabsorption of HCO3 in PCT"**

They give you a patient with glycosuria, aminoaciduria, phosphaturia, and metabolic acidosis and ask for Dx & Cause. Answer is **Fanconi Syndrome** caused by **ingestion of expired tetracyclines**

They give you glycosuria, aminoaciduria, phosphaturia, and metabolic acidosis and ask for expected type of renal tubular acidosis. Answer is **Type 2 RTA**.

They give you glycosuria, aminoaciduria, phosphaturia, and metabolic acidosis + crystals in the cornea. Dx is **Cystinosis** (Crystals in the Cornea + Fanconi Syndrome)

- Caused by defect in **Cystinosin** (lysosomal cystine transporter)



Remember that PCT carries the most amount of **Na/K ATPases**, so it is the most liable for **ATN** in the setting of **acute** ischemia.

Q44

A 43-year-old woman undergoing chemotherapy for acute myelogenous leukemia is given a blood transfusion for anemia. Shortly after the transfusion is initiated, she develops chest pain and shortness of breath. Her temperature is 39°C (102.2°F), pulse is 120/min, respirations are 24/min, and blood pressure is 80/50 mm Hg. The transfusion is immediately halted, and samples of the patient's blood and of the remaining untransfused blood are sent for analysis. Results show that the patient's blood group is O and the transfused blood group is A. Which of the following effectors is the most likely cause of the symptoms in this patient?

- A. Bacterial products
- B. Circulating immune complexes
- C. Mast cell mediators
- D. Preformed IgM antibodies
- E. Sensitized T lymphocytes

▼ Explanation

- Answer is D (Preformed IgM antibodies)
 - IMP Clues
 - Blood transfusion for anemia
 - Shortly after the transfusion is initiated, she develops chest pain and shortness of breath
 - Her Temperature is 39C + pulse is 120/min + respiration are 24/min + blood pressure is 80/50 mmHg
 - Results show that the patient's blood group is O and the transfused blood group is A
- Dx → Hemolytic ABO Mismatch
 - Caused by preformed IgM antibodies against donor's RBC antigens (A/B)
 - Preformed IgM antibodies bind to donor's RBCs, causing complement activation & RBC lysis
 - Presents as Fever/Chills + signs of severe hemolysis (Hypotension, Hemoglobinuria, dyspnea, and shock) MINUTES after transfusion
 - The time frame is super important & actually explained by the antibodies being "preformed"
 - Expected Lab Findings:
 - Coomb's test (or referred to as "Direct Antiglobulin test") is positive
 - Low Haptoglobin (haptoglobin picks up free Hb released by lysed RBCs, so becomes low as the bound type is increasing)
 - Hemoglobinemia & Hemoglobinuria (due to hemolysis)
 - Elevated LDH & Indirect hyperbilirubinemia

? What type of hypersensitivity is Hemolytic ABO mismatch?

▼ Answer

Type 2 Hypersensitivity Reaction

Q45

A 50-kg (110-lb) experimental animal receives 1 L of 5% saline intravenously. Which of the following changes in body fluid volume or osmolality is most likely in response to the 5% saline?

Choice	Intracellular Volume	Intracellular Osmolality	Extracellular Volume	Extracellular Osmolality
A	↓	↑	↑	↓
B	No change	↓	no change	↑
C	↑	↓	↓	↑
D	↓	↑	↓	↑
E	↓	no change	↑	no change
F	↓	↑	↑	↑

▼ Explanation

- Answer is F
 - Q says that 5% saline (which is hypertonic, as normal isotonic saline is 0.9%) is given intravenously & Q asks us for the Intracellular vs Extracellular osmolality and volume.
 - As know from our biology classes, water moves from area of low osmolality to high osmolality
 - Infusion of 1L IV saline causes increased extracellular Volume
 - The infused saline is 5% (hypertonic), so increases extracellular space osmolality.
 - High extracellular space osmolality causes → shift of fluid from intracellular space into extracellular space → lower intracellular volume
 - Now that the intracellular space is relatively fluid-depleted, the intracellular solutes are relatively increased, slightly raising the intracellular space osmolality.
 - So, final result is:
 - Increased Extracellular Volume & Osmolality
 - Decreased Intracellular Volume
 - Increased Intracellular Osmolality

Q46

A 32-year-old woman comes to the physician after the result of a home pregnancy test was found to be positive. Her last menstrual period was 8 weeks ago. Menses had occurred at irregular 24- to 35-day intervals since menarche at the age of 13 years. Transvaginal ultrasonography confirms a single viable intrauterine pregnancy with an embryo that dates to 6 weeks from the last menstrual period. A single transaxial ultrasound image of the uterus is shown; the arrow indicates a cystic structure. Which of the following best describes this structure?



- A. Amniotic cavity
- B. Chorionic cavity
- C. Gestational sac
- D. Rhombencephalon
- E. Yolk sac

▼ Explanation

- Answer is E
 - To be honest you either know the US or you don't.
 - Not HY and as far as I can remember this is the only Q on NBME that tests US knowledge of fetuses.
 - The Arrow points to the **Yolk Sac (Choice E)**, while the other "mass" is the **fetus**.
 - They are connected by a **very thin structure (the vitelline duct)**

Just showing you how a normal ultrasound looks like for the sake of understanding what you're looking at:



Q47

A previously healthy 32-year-old man is brought to the emergency department by friends 45 minutes after the sudden onset of severe headache, seizures, left-sided weakness, and nausea that began while they were attending a party. His friends believe there may have been drugs at the party. On arrival, he is alert and cooperative. He appears to be in pain. His pulse is 120/min, respirations are 16/min, and blood pressure is 160/100 mm Hg. Neurologic examination shows bilateral dilated pupils, hyperreflexia, and mild hemiparesis of the left side. He is oriented to person, place, and time. A CT scan of the head shows a 1.5-cm hemorrhage in the right basal ganglia. Which of the following is the most appropriate next step in diagnosis?

- A. Echocardiography
- B. Lumbar puncture
- C. Measurement of plasma free metanephrine concentration
- D. Measurement of urine 5-hydroxyindoleacetic acid concentration
- E. Toxicology screening

▼ Explanation

- Answer E (Toxicology screening)
 - IMP Clues
 - Severe headache, seizures, left-sided weakness, and nausea that began while attending a party (perfect place for drugs)
 - His friends believe there may have been drugs at the party

- His pulse is 120/min + blood pressure is 160/100 (hypertensive) + bilateral dilated pupils (sympathetic activation)
- CT scan of the head shows a 1.5-cm hemorrhage in the right basal ganglia (Intracerebral hemorrhage)

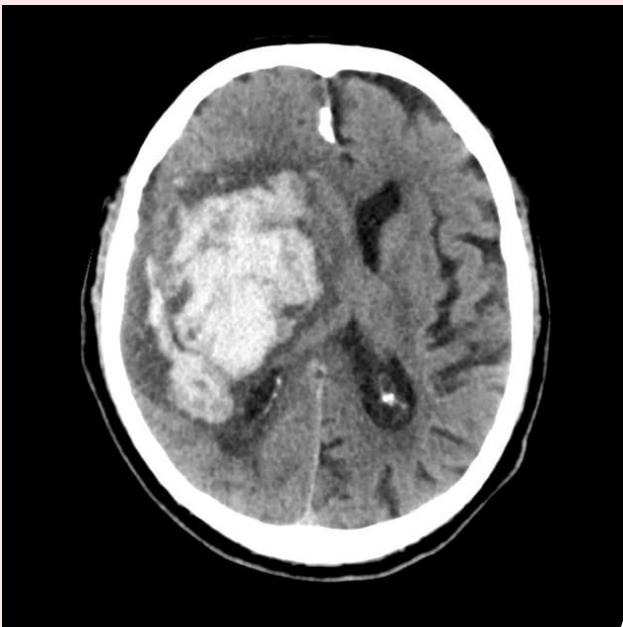
• Dx → Cocaine

- Cocaine causes reuptake inhibition of catecholamines → Massive sympathetic activation → increased heart rate and severe vasoconstriction → acute severe Hypertension
 - The acute severe rise in blood pressure causes rupture of the small arteries in the brain ⇒ Intracerebral Hemorrhage
 - Most common site lenticulostriate arteries of the basal ganglia
- Features
 - Tachycardia and Hypertension (due to sympathetic overstimulation)
 - Mydriasis (due to sympathetic overstimulation)
 - Headache, Weakness, hyperreflexia, vomiting, seizures, AMS (due to Intracerebral Hemorrhage)
 - Chest Pain, MI, Aortic Dissection (due to severe vasoconstriction) [asked on NBME]
 - Nasal Septum Perforation (due to severe vasoconstriction → ischemia) [asked on NBME]

? What other drugs can cause similar presentation?

▼ Answer
Sympathomimetic Drugs (MDMA - Methylphenidate - Amphetamine)

CT scan of Intracerebral Hemorrhage (Basal Ganglia):



Q48

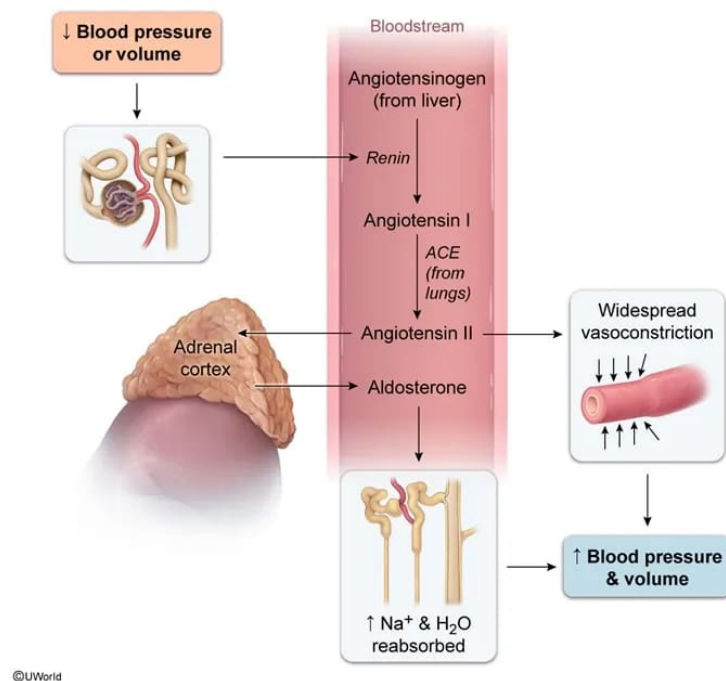
A 27-year-old woman has headaches and blurred vision. She does not smoke, drink, or use illegal drugs. Temperature is 37°C (98.6°F), and blood pressure is 196/142 mm Hg. Physical examination shows papilledema and bilateral costovertebral angle bruits. Which of the following serum concentrations is most likely to be increased?

- A. Angiotensin
- B. Catecholamines
- C. Erythropoietin
- D. Serotonin
- E. Thyroxine (T₄)

▼ Explanation

- Answer is A (Angiotensin)
 - IMP Clues
 - 27-year-old woman has headache and blurred vision
 - Blood pressure is 196/142 mmHg
 - Papilledema and bilateral costovertebral angle bruits
 - Q asks for which of the following would have an increased serum concentration

- Dx → Fibromuscular Dysplasia (FMD)
 - Can sometimes be referred to as **"Renal Artery Dysplasia"** on NBMEs
 - It is not a dysplasia really, it is **hyperplasia of the tunica media**
 - It is an **autoimmune disease that affects classically middle-aged women with NO hx of cardiovascular disease**
 - Causes the **"string of beads"** appearance on CT angiography
 - My opinion, knowing the CT scans will not help you as much as looking for risk factors like Age, hx of CVD, or other HY findings.
 - Hyperplasia of renal artery tunica media causes **decreased renal flow, which causes activation of RAAS**:
 - **High Renin** → Conversion of angiotensinogen to AT-I → AT-I is converted to AT-II via ACE, which causes:
 1. Vasoconstriction of renal efferent arterioles → **maintains GFR**
 2. Vasoconstriction of systemic arterioles → **hypertension** (headache, blurred vision, papilledema)
 3. Activation of Zona Glomerulosa → **aldosterone Secretion**
 - Causes **increased Na & Water reabsorption**, in addition to potassium & hydrogen **secretion**.



You will get this type of Q on every NBME, so let's run through what you need to know

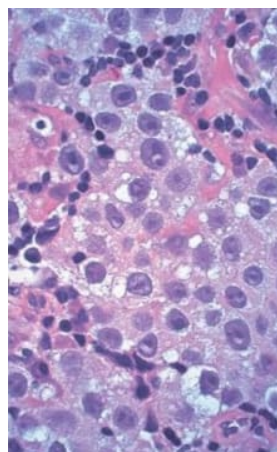
- **50-60y Male OR Female** + hx of cardiovascular disease / atherosclerosis / smoking?
 - Dx → Atherosclerosis
 - Vignettes can be tricky by saying **"BMI is 35"** or **"a carotid bruit is heard on examination"** instead of atherosclerosis.
 - BMI is high usually means he's atherosclerotic especially in this age group
 - If a patient has a carotid bruit, which is due to atherosclerosis, chances are he also has atherosclerotic arteries in other sites (Renal Artery)
- **20-40y F** + **NO** hx of cardiovascular disease / atherosclerosis / smoking?
 - Dx → FMD
- **20-40y F** + was given ACEi/ARBs + Creatinine levels have risen. What is diagnosis?
 - Dx → FMD
- **64M** + was given ACEi/ARBs + Creatinine levels have risen. What is diagnosis?
 - Dx → Atherosclerotic Renal Artery
- **55F** + was given ACEi/ARBs + Creatinine levels have risen. What is diagnosis?
 - Dx → Atherosclerotic Renal Artery

Reason is in FMD or Atherosclerosis, the renal blood supply is **decreased**, but the body adapts by **producing renin & AT-2**, which causes **vasoconstriction** of the **efferent renal arterioles** → **maintains GFR**

If **ACEi/ARBs** are administered, **efferent arterioles dilate** → **decreased GFR** → **creatinine rises**.

Q49

A 25-year-old man has an orchiectomy for a recently detected testicular neoplasm. A biopsy specimen from the neoplasm is shown. Which of the following are the most likely cells of origin of this neoplasm?



- A. Fibroblasts
- B. Germ cells

- C. Leydig cells
- D. Rhabdomyoblasts
- E. Sertoli cells

▼ Explanation

- **Answer is B (Germ cells)**

- 25-year-old man has an orchiectomy for recently detected testicular neoplasm
- Biopsy specimen from the neoplasm is shown
- Q asks for site of origin

- **Dx → Seminoma**

- Most common testicular **germ cell** tumor in **adults & teens** (patient here is 25)
- Presents as **painless testicular enlargement/firm mass**
- Gross appearance: **Solid** Homogenous mass with **NO hemorrhage/necrosis**

⚠ **Embryonal Carcinoma is a *painful* mass with *hemorrhage & necrosis***

- Microscopic appearance: **Fried Egg Appearance**, which is basically a *large central nucleus surrounded by clear cytoplasm*
- HY Associations: **Klinefelter Syndrome & Cryptorchidism** (undescended testes) **[asked on NBME]**
- Tumor Marker: **Placental ALP**

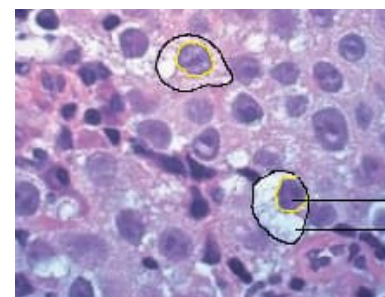


Primary testicular tumors originate from one of two things: Germ Cells (the vast majority) or **Sex Cord-Stromal Cells** (way less common)

- **Germ Cell Tumors** are **seminomas, yolk sac tumors, choriocarcinomas, teratomas, and embryonal carcinomas**
- **Sex Cord-Stromal Cell Tumors** are the **Sertoli-Leydig Cell Tumors**

So, if you have no idea of what you are looking at, going with **Germ Cells (Choice B)** is the wiser choice.

"I tried my best, okay??"



Large nuclei "Yolk"
Clear Cytoplasm "Egg White"

Q50

A 14-year-old boy with a tibial fracture is fitted with a leg cast and progresses satisfactorily for 6 weeks. One week after the first cast has been replaced, he has pain and numbness in the foot of the casted extremity. There is decreased sensation to pinprick on the anterolateral aspect of the leg and dorsum of the foot. The most likely cause is nerve compression by a tight cast at which of the following sites?

- A. Lateral malleolus
- B. Medial malleolus
- C. Medial tibial condyle
- D. Neck of the fibula
- E. Tibial tuberosity

▼ Explanation

- **Answer is D (Neck of the fibula)**

- IMP Clues
 - There is decreased sensation to pinprick on the anterolateral aspect of the leg & dorsum of the foot
 - Q asks for the site of nerve compression causing these symptoms

- **Common Fibular (Peroneal) Nerve**

- One of the HY lower limb nerves, so worth knowing:

- Branch of the **Sciatic Nerve**

- Course: Arises near at the posterior thigh near the popliteal fossa & **wraps around the neck of fibula** then divides into 2 branches

1. **Superficial Fibular (Peroneal)**

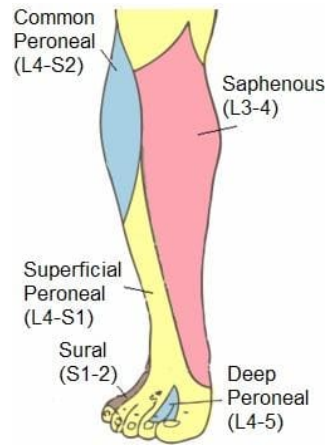
Nerve:

- Responsible for **Foot Eversion** & weak Plantarflexion
- Provides sensation to the **Dorsum of the Foot** (*except web space between 1st & 2nd toes*)

2. **Deep Fibular (Peroneal)**

Nerve:

- a. Responsible for **Foot Dorsiflexion**
- b. Provides sensation to the **web space between 1st & 2nd toes on the dorsum of the foot**



The Common Peroneal Nerve itself supplies the upper anterolateral leg!



Peroneal Nerve Injuries:

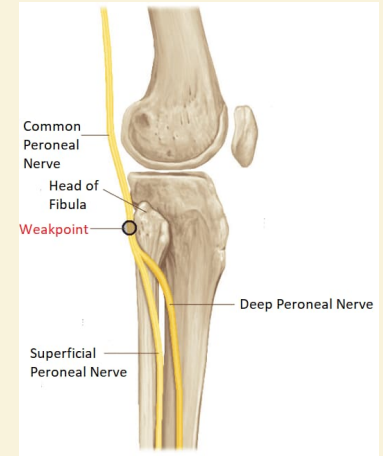
Common Peroneal Nerve Injury

- Causes:

- **Fibular Neck Fracture**
- **Tight Leg Cast**
- **Prolonged Leg Crossing**

- Presentation:

- Numbness & Pinprick sensation on **anterolateral aspect of leg and dorsum of foot**
- Loss of **Eversion**
- Loss of **Dorsiflexion**



USMLE can give you isolated peroneal nerve branch injury:

- **Isolated Loss of Dorsiflexion?**

- ⇒ **Deep Peroneal Nerve Injury**

- **Isolated Loss of Eversion?**

- ⇒ **Superficial Peroneal Nerve Injury**



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