



NBME EXPLANATIONS

NBME 23 Block 4

from CrackNBME

23-Block 4

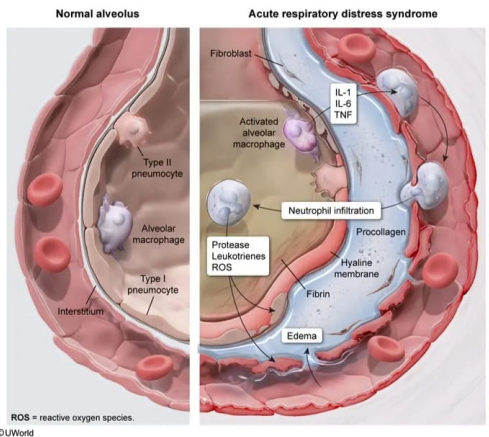
Q1

A 43-year-old woman sustains multiple fractures and lacerations in an automobile collision. On the second hospital day she develops tachypnea, tachycardia, and cyanosis. An initial x-ray of the chest shows no abnormalities, but a subsequent x-ray shows diffuse consolidation of both lungs. Despite intensive therapy she dies on the fourth hospital day. Which of the following is most likely on examination of the lungs at autopsy?

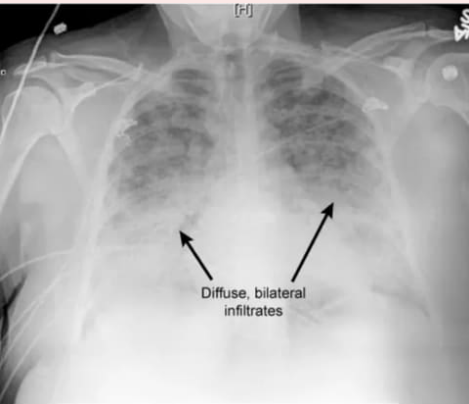
- A. Bronchiectasis
- B. Bronchiolitis obliterans
- C. Hyaline membranes
- D. Interstitial fibrosis
- E. Lobar pneumonia

▼ Explanation

- Answer is C (Hyaline membranes)
 - IMP Clues
 - Hx of automobile collision
 - Tachypnea + Tachycardia + cyanosis (Respiratory distress)
 - Subsequent x-ray shows diffuse consolidation of both lung (Diffuse bilateral Consolidation of Ground glass opacities is buzzy)
 - Q asks for most likely finding of lung autopsy?
- Dx → Acute Respiratory Distress Syndrome (ARDS)
 - ARDS is caused by many conditions (most HY to know are **sepsis, trauma, pancreatitis, drowning, transfusion reactions, or direct lung injury**), which cause **increased vascular permeability**.
 - This results in **migration of neutrophils, necrosis of pneumocytes**, and **extravasation of exudate into the alveoli** ⇒ **Proteinaceous debris (aka protein-rich fluid/fibrin) in alveoli + Hyaline membrane formation**
 - This results in **pulmonary edema (non-cardiogenic), disruption of surfactant, and V/Q mismatch**
 - V/Q mismatch (shunting) is due to the presence of fluid in alveoli, alveolar collapse, and disruption of surfactant
 - V/Q mismatch causes **increased A-a gradient [asked on NBME]** → hypoxia → tachypnea & cyanosis
 - The presence of fluids in the lung causes the “characteristic” **diffuse bilateral ground glass opacity** (consolidation)



Picture below shows diffuse bilateral ground glass opacity:



What are expected arrows of the following?
[Surface Protein D, A-a gradient, FEV1/FVC ratio, Compliance, PCWP]

- ▼ Answer
- **INCREASED** Surface Protein D
 - **INCREASED** A-a gradient
 - **INCREASED/NORMAL** FEV1/FVC ratio (Restrictive pattern)
 - **DECREASED** Compliance (surfactant is disrupted)
 - **NORMAL** PCWP (non-cardiogenic pulmonary edema)

Q2

A 42-year-old woman comes to the physician because of a 2-year history of fatigue and abnormally heavy, prolonged menses. She has not had abdominal or pelvic pain, pain with urination or increased urinary frequency, changes in bowel habits, or weight loss. Pelvic examination shows a normal-sized uterus with no adnexal masses. Her hemoglobin concentration is 9.4 g/dL. All other laboratory studies are within the reference ranges. Examination of an endometrial biopsy specimen shows simple glandular hyperplasia without atypia. Which of the following best describes the pathogenesis of this patient's endometrial disorder?

- A. Activation of G protein coupled receptor by guanosine triphosphate
- B. Binding of permeable ligand to nuclear transcription factor
- C. Cytokine-induced activation of surface receptor and Janus kinase proteins
- D. Dimerization of surface receptor with intrinsic tyrosine kinase activity
- E. Overexpression of epidermal growth factor receptor

▼ Explanation

- Answer is B (Binding of permeable ligand to nuclear transcription factor)

- IMP Clues

- Examination of an endometrial biopsy specimen shows simple glandular hyperplasia without atypia
- Q asks for which of the following best describes the pathogenesis of this patient?

- Dx → Endometrial Hyperplasia

- The endometrium grows in response to estrogen, which induces the **proliferative phase** in the physiological menstrual cycle.
 - The presence of **progesterone opposes estrogen's effects & prevents uncontrolled proliferation.**
 - How does both Estrogen & Progesterone work?
 - **Estrogen & Progesterone act via intracellular receptors (in the cytosol) then is translocated into the nucleus for it to act on transcription factors.**
- Disorders that cause **unopposed** hyperestrogenic states predispose to endometrial hyperplasia:
 - **PCOS [asked on NBME]**
 - **Estrogen-Secreting Tumors** (Vague abdominal pain with an adnexal mass, which may present as endometrial hyperplasia in an older female or precocious puberty in a younger one)
 - **Estrogen-only Pills**
 - **Tamoxifen** (SERM that acts as estrogen antagonist on breasts but estrogen agonist on endometrium & bone)

Let's Review the 2nd Messengers:

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

Q3

A 65-year-old man who is a farmer comes to the physician because of skin lesions that have been present on his face, arms, and upper trunk for the past several years. Biopsies show most lesions to be actinic keratoses, but one is a squamous cell carcinoma. Which of the following is most likely responsible for the development of squamous cell carcinoma in this patient?

- A. Decreased function of skin as a barrier to carcinogens
- B. Disruption of DNA strands secondary to ionization effect
- C. Increased conversion of 25-dihydroxycholecalciferol to 1,25-dihydroxycholecalciferol
- D. Increased mitotic activity through stimulation of melanocytes
- E. Increased susceptibility of skin to trauma

▼ Explanation

- Answer is B (Disruption of DNA strands secondary to ionization effect)

- IMP Clues

- Farmer (High sun exposure)
- Skin lesions on his face, arms, and upper trunk (sun exposed areas)
- Biopsy shows lesions to be actinic keratosis, but one is squamous cell carcinoma

- Dx → Actinic Keratosis

- also named on the USMLE as "Solar Keratosis"
- **Scaly / rough** lesions with a "sandpaper feel" on **sun exposed areas**, usually found on **farmers / construction workers / fishermen**
 - Why?
 - **Chronic UV radiation induces DNA damage in keratinocytes**, causing mutations that result in abnormal cell cycle regulations.
 - Overtime, this causes uncontrolled cell proliferation, causing **abnormal keratinocytes accumulation & formation of actinic keratosis.**



What are people with Actinic Keratosis at risk of developing?

▼ Answer

Squamous Cell Carcinoma of skin.

- **Over more time, the abnormal cell cycle regulations predispose to SCC**

UVA vs UVB?

? What would be seen on biopsy of this patient's SCC?

▼ Answer

Keratin pearls with intracellular bridges

- UVA → **ROS generation** & collagen breakdown → **Photoaging** (wrinkles, dermal thinning, solar elastosis) [asked on NBME]
- UVB → **Ionizing Radiation** that causes **pyrimidine dimers** [asked on NBME] → p53 mutation → keratinocytes dysplasia → SCC formation

Q4

A 52-year-old man comes to the physician because of inability to achieve an erection 6 weeks after undergoing operative removal of a tumor on the distal portion of the rectum. During the excision, the tumor was found to be extensively attached to the posterior aspect of the prostate. Damage to which of the following nerves is the most likely cause of this patient's symptoms?

- A. Gray rami from the sympathetic chain
- B. Pelvic splanchnics
- C. Pudendal
- D. Superior hypogastric
- E. Ventral rami of S2-4

▼ Explanation

- Answer is B (Pelvic splanchnic)

- IMP Clues

- Inability to achieve an erection (Impotence)
- Tumor was found to be extensively attached to the posterior aspect of the prostate (Site is key!)

- Q asks damage to what nerve caused this patient's symptoms?

Picture on the **right** shows the related anatomy. This is so HY so know it.

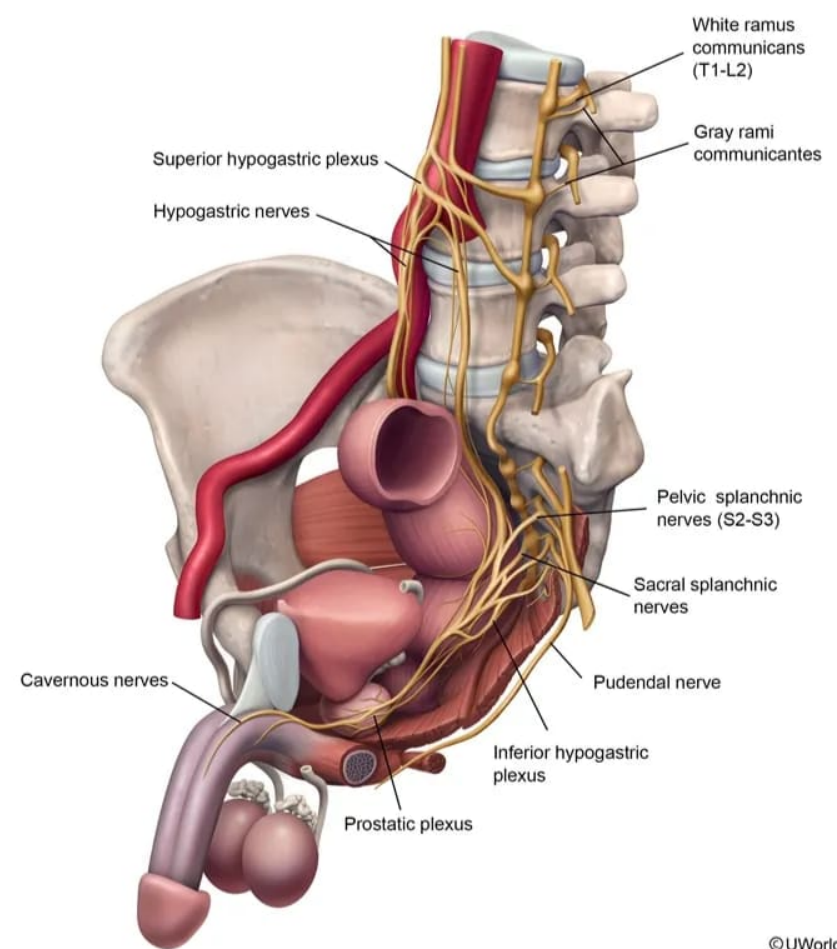
- Pelvic Splanchnic Nerves on the **posterior aspect** of the prostate injury causes:

- **Impotence** (Pelvic Splanchnic → Inferior Hypogastric → Cavernous Nerves)
- **Urine Retention & Overflow Incontinence** (Loss of Parasympathetic innervation to Detrusor muscle & Urethral Sphincter)
- **Loss of Defecation Reflex, Severe Constipation, and Fecal Impaction** (Loss of Parasympathetic innervation to rectum)

- USMLE assesses this in **prostate cancer & distal rectum surgeries complications**.



USMLE sometime tries to be sneaky and asks what is the nerve on the **LATERAL** aspect of the prostate that when injures causes impotence; answer is **Cavernous nerve**.



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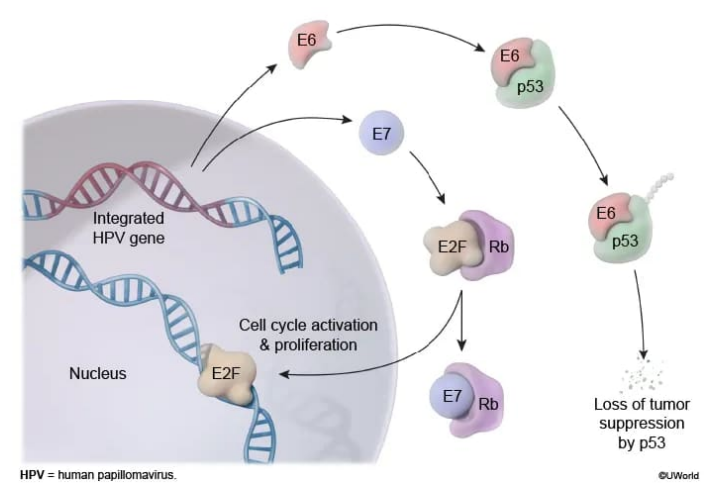
Q5

A 56-year-old woman comes to the physician for a health maintenance examination. Physical examination shows no abnormalities. Results of a Pap smear show epithelial cell abnormalities, including high-grade squamous intraepithelial lesions. Which of the following mechanisms is the most likely underlying cause of the lesions in this patient?

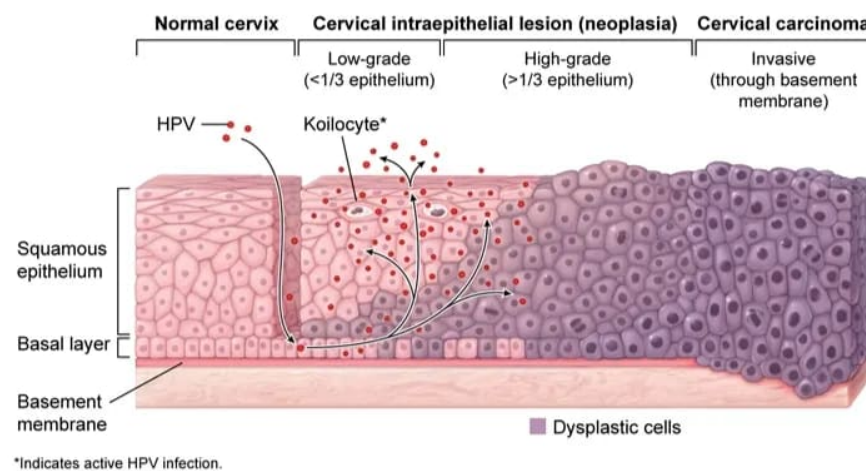
- A. Integration of a microbial genome into the host genome to induce a cellular proto-oncogene
- B. Microbe-induced chromosomal translocation
- C. Microbe-induced chronic inflammatory response
- D. Microbial oncoprotein that interferes with tumor suppressor proteins
- E. Microbial transcription factor that induces cellular proto-oncogenes

▼ Explanation

- **Answer is D (Microbial oncoprotein that interferes with tumor suppressor proteins)**
 - **IMP Clues**
 - Pap smear shows high-grade squamous intraepithelial lesions (HSIL is HPV on the USMLE)
 - **Dx → High-grade Squamous Intraepithelial Lesions (HSIL) secondary to HPV Infection**
 - **HPV infection is the greatest risk factor for Cervical Intraepithelial Neoplasms (CIN)**
 - USMLE can refer to HPV as **“Multiple Sexual Partners”**, **“Early age of sexual intercourse”**, or **“Unprotected sex”** as HPV is a STD
 - What is the pathophysiology?
 - **E6 protein** ⇒ Inactivation **TP53 (tumor suppressor gene)** via **Ubiquitin-mediated proteolysis** → **Decreased** apoptosis
 - **E7 protein** ⇒ Increased phosphorylation of **Rb** → Rb separates from E2F → **E2F** then **causes cell cycle activation & proliferation** (mitosis)



Note that the CIN starts down & extends upwards & Carcinoma is characterized by invasion of basement membrane!



Q6

A 45-year-old man is brought to the physician by his parents because he is reclusive, has "weird ideas," and still wants to live at home. He is dressed in several layers of clothes. During the interview, he is cooperative but he has poor eye contact and seems uninterested in the interview. He says, "I believe some people can read other people's minds. I carry these crystals to help me realize self-actualization." He has no delusions or hallucinations. This patient most likely has which of the following personality disorders?

- Borderline
- Dependent
- Histrionic
- Narcissistic
- Schizoid
- Schizotypal

▼ **Explanation**

- **Answer is E (Schizotypal)**
 - **IMP Clues**
 - Reclusive
 - Weird Ideas + Dressed in several layers of clothes + Believes he can read people's mind + carry crystals to help self-actualization
 - He has poor eye contact & seems uninterested in the interview
 - Has no delusions or hallucinations
 - **Dx → Schizotypal**
 - **On the USMLE, Schizotypal is a person that dresses wildly & thinks wildly.**
 - Qs might say a patient that has **“multiple layers of clothes”** (dress wildly), **“deck of card that can read the future”**, or **“he believes he can read other people's minds”** (thinks wildly).
 - He is **NOT** delusional, he's just **schizotypal**.

A 45-year-old woman with coronary artery disease and anemia comes to the physician for assessment of her cardiac perfusion. Transthoracic color Doppler echocardiography is done. Results show that blood flow in the anterior interventricular (left anterior descending) branch of the coronary artery is 30 mL/min. Arterial blood oxygen concentration is 0.15 mL O₂/mL. Based on this information, which of the following most closely approximates the myocardial oxygen supply to the left ventricle in this patient (in mL O₂/min)?

- ▼ **Explanation**

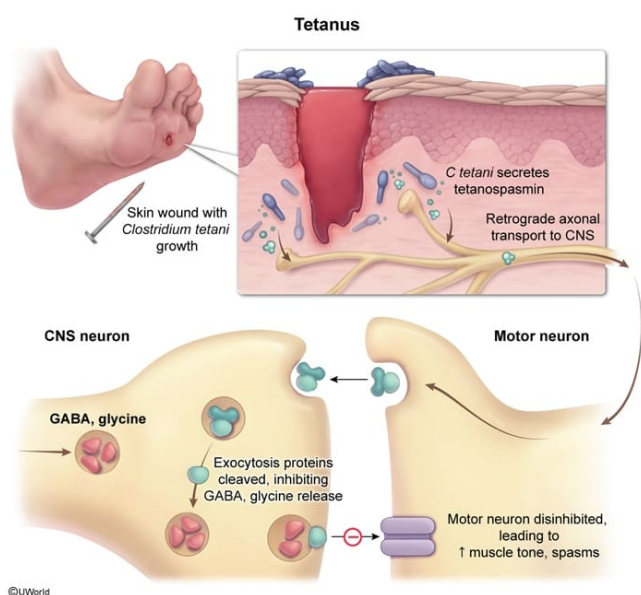
- A 48-year-old man who is a farmer in a remote area of India develops muscle spasms, trismus, and seizures 1 week after sustaining a puncture wound to his hand from a dirty farm tool. Which of the following best describes the mechanism of action of the toxin causing this disease?**

- ▼ **Explanation**

- Tetanus toxin (tetanospasmin) causes decreased *presynaptic* release of *GABA and Glycine* by inhibiting SNARE proteins (SNAP25, Syntaxin, Synaptobrevin) [asked on NBME]
 - **GABA & Glycine** are **inhibitory** neurotransmitters, so their inhibition would cause persistent stimulation ⇒ **Spastic Paralysis, Trismus, risus sardonicus, opisthotonos**
 - **Decreased presynaptic release of neurotransmitters causes blocking of postsynaptic inhibition of spinal motor neurons (Choice D)**

▼ Answer

- Another HY Toxoid Vaccine is the **Diphtheria vaccine**.



Note that **neonatal tetanus** occurs through an **infected umbilical stump** in non-immunized mothers.

? What other toxin cleaves SNARE?

▼ Answer

Botulinum Toxin (Protease) cleaves SNARE

- Decreased **Acetylcholine** release at NMJ
- Acetylcholine is excitatory, so inhibition of release causes paralysis (**Flaccid Paralysis**; classically **descending**)

? What cells are Glycine & GABA normally release from?

▼ Answer

Renshaw Cells

Q9

A 52-year-old man comes to the physician because of severe recurrent abdominal pain for 6 years. He has a 3-month history of bulky, foul-smelling stools that float; he has had a 9-kg (20-lb) weight loss during this period. He has a 20-year history of alcoholism. Abdominal examination shows tenderness and left upper quadrant localization of the pain. Which of the following lipids is most likely to be found in an excessive amount in the feces of this patient?

- Cholesterol
- Linoleic acid
- Oleic acid
- Palmitic acid
- Triglyceride

▼ Explanation

- Answer is E (Triglyceride)

◦ IMP Clues

- Severe recurrent abdominal pain for 6 years (Pain of recurrent pancreatitis)
- 3-month history of bulky, foul-smelling stools that float (Steatorrhea)
- 9-kg weight loss (due to malabsorption)
- 20-year history of alcoholism (The cause of the pancreatitis)
- Q asks which of the following lipids would most likely be seen in excessive amounts 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**

- Fats normally absorbed from GI tract by lipases are **triglycerides (Choice E)**
- Giving this patient **Pancrelipase** (pancreatic enzymes replacement) will cause absorption of fat & 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**.
 - Answer is **Pancrelipase**, which is basically a mixture of pancreatic digestive enzymes (lipases, amylases, proteases)
 - If the patient is started on pancreatic enzymes replacement, **fats will be absorbed** → **resolution of steatorrhea**
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**.
 - Answer is **Pancreatic Insufficiency due to inspissated pancreatic secretions**.



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

Q10

Unlike the DNA polymerases found in *Escherichia coli*, RNA polymerase from this bacterium lacks proofreading activity. Which of the following is the most likely reason that the lack of proofreading activity in RNA polymerase does not compromise the survival of the species?

- A. Messenger RNAs are too small to be affected by transcription errors
- B. Messenger RNAs containing mutations are not translated
- C. Mistakes in transcription are not transmitted to progeny
- D. RNA repair enzymes usually correct errors made by RNA polymerase during transcription
- E. The fidelity of RNA polymerase exceeds that of DNA polymerases

▼ Explanation

- **Answer is C (Mistakes in transcription are not transmitted to progeny)**

- Basically, Qs RNA polymerase lacks proofreading activity. Why doesn't this "lack of proofreading" don't compromise the survival of the whole bacterial species "progeny"
- **Well, RNA Polymerases synthesize RNA from DNA**
 - If RNA is mutated, RNA is not synthesized → proteins are not made → bacteria has defective proteins +/- dies if essential proteins.
 - **DNA is intact**, so progeny **don't inherit** any abnormal DNA
 - RNA polymerases are **NOT** inherited (**Choice C**)
- **DNA Polymerase, on the other hand, synthesized new complementary DNA strand from the template DNA**
 - Mutations affect DNA structure, and are **passed to progeny** → **compromises survival of species**

Q11

A 35-year-old man comes to the physician because of a tremor and difficulty initiating body movements since starting haloperidol therapy for schizophrenia 6 weeks ago. Physical examination shows masked facies and a resting tremor. In addition to decreasing the dose of haloperidol, it is most appropriate to prescribe which of the following types of medication?

- A. Anticholinergic agent
- B. Antidepressant

- C. High-potency antipsychotic agent
- D. Mood stabilizer
- E. Stimulant

▼ Explanation

- Answer is A (Anticholinergic agent)
 - IMP Clues
 - Tremors and difficulty initiating body movements since starting haloperidol therapy for schizophrenia
 - 6 weeks ago
 - Masked facies and a resting tremor

- Dx → Bradykinesia
 - One of the extrapyramidal side-effects of antipsychotics & dopamine antagonists
 - Dopamine blocking effect of antipsychotic (Haloperidol) causes Parkinson-like symptoms
 - Slow movement, rigidity, resting tremors, mask face
 - Treatment is via benztropine, an anticholinergic, (Choice A) OR amantadine (dopamine agonist)

? What are the 2 HY uses of benztropine?

▼ Answer

1. Acute Dystonia due to antipsychotic use
2. Cogwheel Rigidity in Parkinson Disease



THE DIFFERENCE IS HY:

Rigidity + NO Fever ⇒ Acute Dystonia

- Treatment is benztropine or diphenhydramine

Rigidity + Fever ⇒ Neuroleptic Malignant Syndrome

- Treatment is Dantrolene

Extrapyramidal Effects of antipsychotic therapy:

- Within Hours → Acute Dystonia
 - Sudden muscle contraction WITH NO FEVER
 - Oculogyric Crisis, Torticollis, Opisthotonus
 - Treatment is benztropine or diphenhydramine
- Within Days → Akathisia
 - Restlessness
 - Treatment is beta blocker or BDZ
- Within Weeks → Bradykinesia
 - Parkinsonism
 - Rigidity, Slow movement, mask face, resting tremors
 - Treatment is benztropine or amantadine
- Within Months → Tardive Dyskinesia
 - Choreiform, repetitive involuntary movement
 - Treatment is STOP & switch to atypical antipsychotic

Q12

Which of the following is present in integral plasma membrane-associated proteins but is absent from secreted proteins?

- A. N-linked glycosylation site
- B. O-linked glycosylation site
- C. Phosphorylation site
- D. Signal sequence
- E. Transmembrane region

▼ Explanation

- Answer is E (Transmembrane region)
 - Integral Plasma proteins are the proteins found embedded in the cell membrane (bilipid layer), so they must have a transmembrane region (Choice E)
 - As the cell membrane is made up of lipids, the protein must be lipophilic & hydrophobic [asked on NBME]
 - Examples of these proteins are transporters, channels, receptors, Na/K ATPases, and Cell adhesion proteins
 - Secreted Proteins are proteins that are synthesized in the cell but secreted outside
 - As these proteins will be transported in extracellular space, the proteins must be hydrophilic & lipophobic
 - Examples of these proteins are hormones, enzymes, and antibodies

Q13

A study is conducted to examine the effectiveness of a newly developed antihypertensive drug (Drug X). Subjects to be enrolled in the study must have moderate systemic hypertension; approximately 100 to 200 subjects will be tested. Drug X is most likely in which of the following phases of drug development?

- A. Phase 1
- B. Phase 2
- C. Phase 3
- D. Phase 4

▼ Explanation

- **Answer is B (Phase 2)**
 - **Phase 2** mainly tests *Efficacy & Safety*, which is tested on **< 100 (10^2)** of diseases patients.
 - **What about the other phases?**
 - **Phase 1** mainly tests *safety*, which is tested on **<10 (10^1)** healthy or diseases patients.
 - **Phase 3** compares **between the new drug & existing treatments** on **100s** of people (10^3).
 - **If a drug is on the market**, this means it already had the FDA approval and is now in **stage 4**.

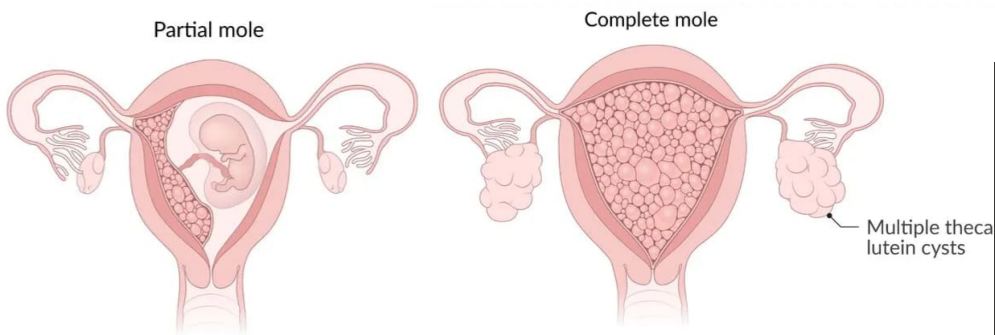
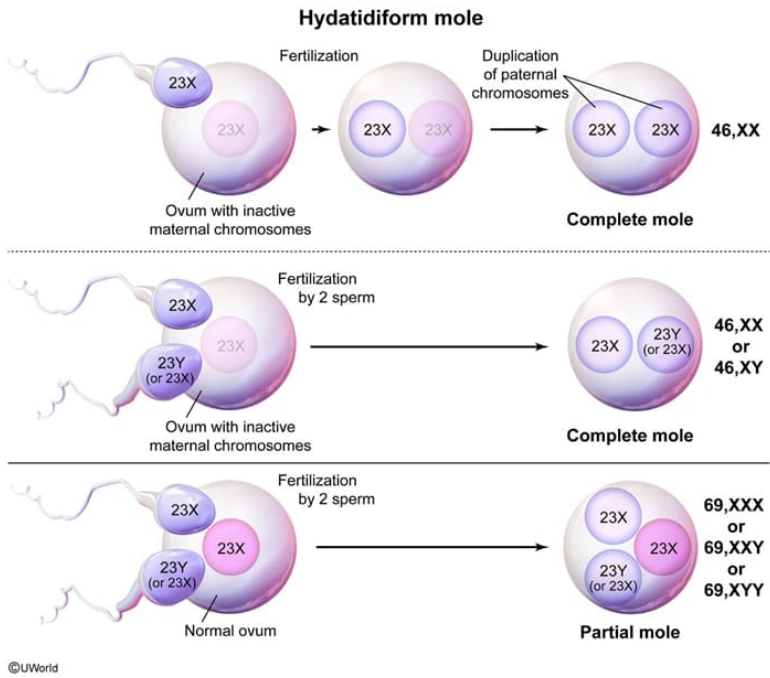
Q14

A 22-year-old woman at 12 weeks' gestation comes to the physician because of a 3-hour history of vaginal bleeding. Physical examination shows a uterus consistent in size with a 16-week gestation. Ultrasonography shows multiple grapelike intrauterine structures and no fetus. The patient undergoes removal of the abnormal tissue by dilatation and curettage. Which of the following properties of the tissue best correlates with the grapelike structures identified during ultrasonography?

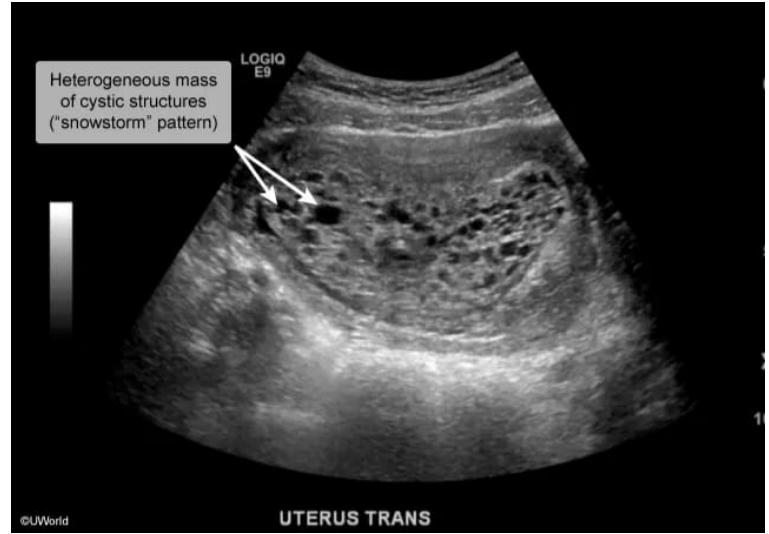
- A. Ball-like masses of proliferating decidua
- B. Hydropic villi with central cisterns
- C. Markedly dilated fetal blood vessels
- D. Sheetlike masses of syncytiotrophoblast
- E. Tortuous loops of umbilical cord

▼ Explanation

- **Answer is B (Hydropic villi with central cisterns)**
 - **IMP Clues**
 - 12 weeks' gestation + examination shows a uterus size consistent with a 16-week gestation (Uterine level > GA is consistent with hydatidiform mole)
 - Multiple grapelike intrauterine structures and no fetus
- **Dx → Hydatidiform Mole**
 - A type of Gestational Trophoblastic Disease (GTD), which is basically **abnormal villous trophoblastic tissue growths**
 - Results from **abnormal fertilization** → **abnormal placental trophoblastic proliferation** → abnormal fetal development
 - **What is placental trophoblastic proliferation?**
 - **Trophoblasts cells are the cells that form the outer layer of the blastocytes (which goes on & becomes embryo) and the placenta**
 - This Forms the massive **"clusters of grapes"**, also known as **"hydropic villi"**
 - **b-hCG is produced from the syncytiotrophoblast layer [asked on NBME]** → This is why GTDs have super high b-hCG levels
 - **Types of GTD?**
 - Complete Mole → **NO Fetus, just clusters of grapes**
 - Partial Mole → **Fetus is present with clusters of grapes**



How would complete mole look like on ultrasonography?
"Snowstorm" appearance of "clusters of grapes" with NO fetus:



Q15

A 54-year-old woman comes to the physician because of a 1-week history of pain in her right shoulder. The pain is more severe when she lifts objects over her head, and it is affecting her work at a retail store where she is responsible for stocking shelves. She also has difficulty sleeping at night because of increased pain when she lies on her right side. She has no history of major medical illness. Physical examination shows tenderness of the right deltoid region. There is full passive range of motion but decreased active range of motion to abduction. Abduction and passive shoulder flexion over the head produce pain. During strength testing, the patient has pain and weakness with abduction, particularly with simultaneous shoulder internal rotation. Which of the following muscles is most likely affected in this patient?

- A. Deltoid
- B. Subscapularis
- C. Supraspinatus
- D. Teres minor
- E. Trapezius

▼ **Explanation**

• **Answer is C (Supraspinatus)**

◦ **IMP Clues**

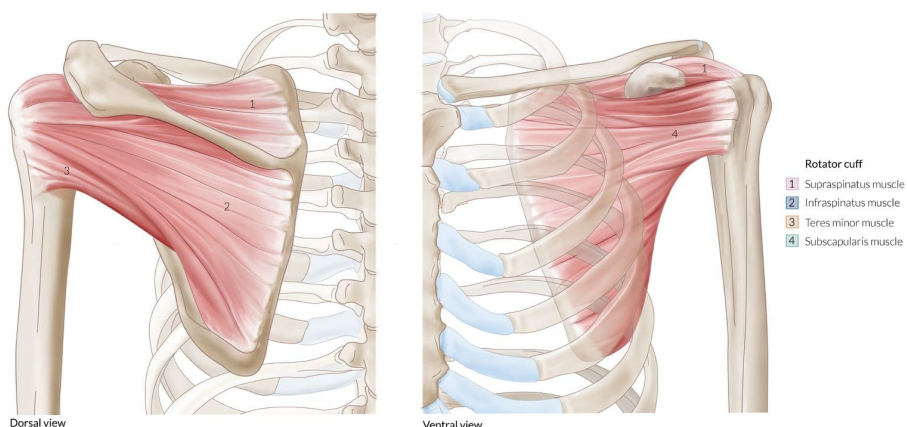
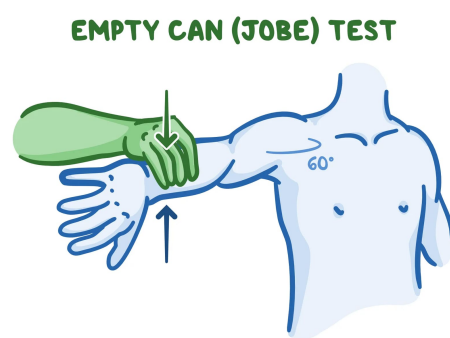
- Decreased active range of motion to abduction
- Abduction and passive shoulder flexion over the head produce pain
- Patient has pain and weakness with abduction, particularly with simultaneous shoulder internal rotation (Empty can test btw)

• **Dx → Supraspinatus Tendinopathy**

- The **supraspinatus muscle** is one of the **shoulder rotator cuff muscles**.
 - **It is the most common rotator cuff injury.**
 - 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**

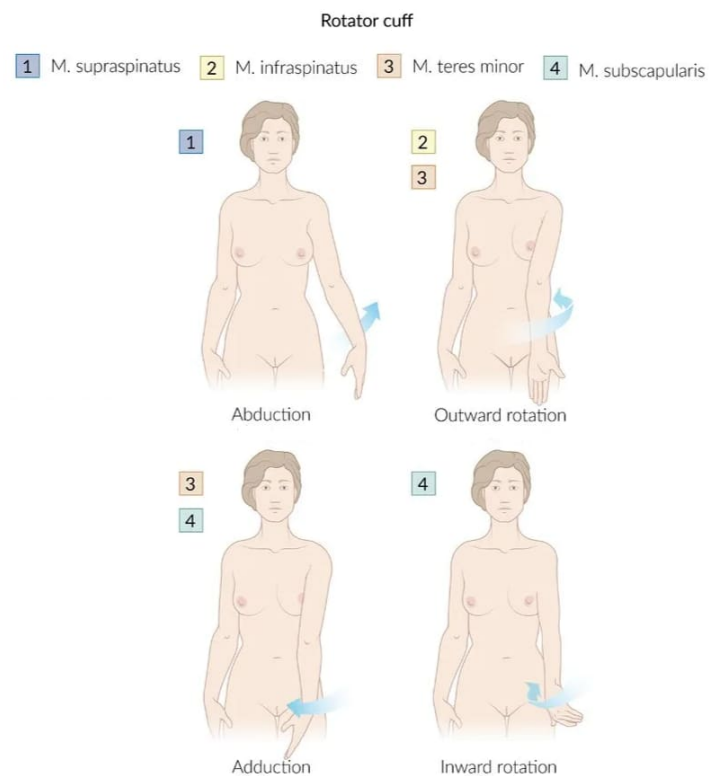
- Action → **External Rotation**
- Nerve Supply → **Suprascapular nerve**

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)



Q16

A 5-year-old boy who is undergoing induction chemotherapy for acute lymphoblastic leukemia has a 2-day history of fever, cough, and shortness of breath. His temperature is 38.8°C (101.8°F), and respirations are 46/min. Physical examination shows cyanosis and a generalized vesicular rash. Crackles are heard in both lung fields. A chest x-ray shows extensive nodular infiltrates in both lung fields. The most likely cause of his condition is infection with which of the following viruses?

- A. Adenovirus
- B. Influenza virus
- C. Measles virus
- D. Parainfluenza virus
- E. Varicella-zoster virus

▼ Explanation

• Answer is E (Varicella-Zoster Virus)

◦ IMP Clues

- Undergoing induction chemotherapy for acute lymphoblastic leukemia (Immunocompromised patient)
- Generalized vesicular rash (Shingles rash)
- Crackles are heard in both lung fields + CXR shows extensive nodular infiltrates in both lung fields (pneumonia)

• Dx → Varicella-Zoster Virus Reactivation

- USMLE always tests this concept: **Immunocompromised patients are susceptible to reactivation of herpesviruses family.**

- Primary infection of VZV is **chickenpox**. The Virus then remains latent in the **dorsal root ganglion [asked on NBMEs]**. Once immunosuppressed, sick, or stressed, **VZV reactivates as shingles rash, encephalitis, or pneumonia**

- **Shingles Rash** → Painful, burning, itching **vesicular lesions** in **dermatomal distribution** that later crust & form ulcers [Note that in severely immunocompromised patients, it can present as **widespread/generalized rash**]

- **Tzanck test** → Smear of vesicular fluid showing **multinucleated giant cells** (seen in VZV & HSV)

- Treatment → **Acyclovir** (HSV/VZV DNA Polymerase inhibitor)



? What is the cause of Acyclovir resistance?

▼ Answer

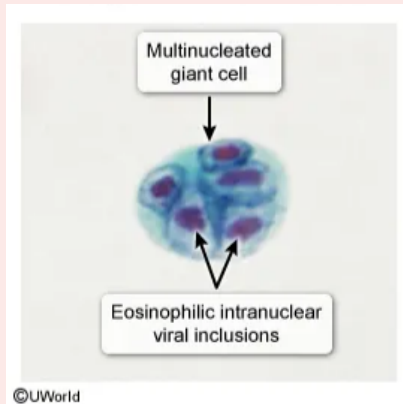
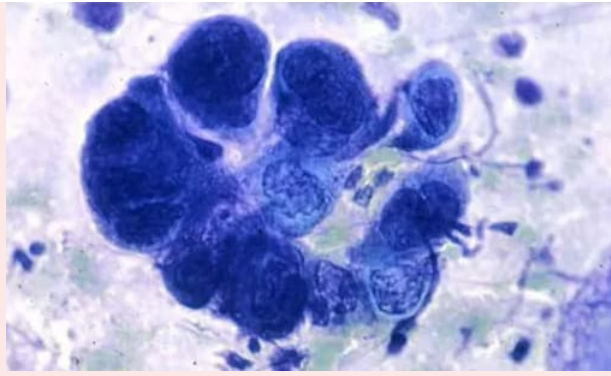
Altered/Absent Thymidine Kinase

Tzanck Smear:

? Where does HSV1/2 remain latent at?

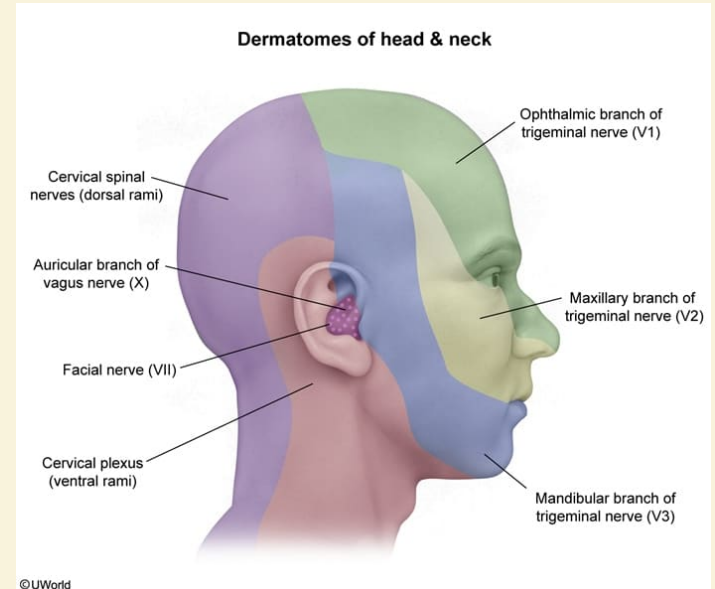
▼ Answer

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



VZV Reactivation in the **ophthalmic division (V1)** can cause **VZV Keratitis (Herpes Zoster Ophthalmicus)**, which is characterized by **pseudodendritic corneal ulcer**, **vesicular lesions**, and **pain** in V1 dermatome.

- Presence of vesicular lesions on **tip of nose (Hutchinson's Sign)** indicated **nasociliary branch involvement** & is associated with **high risk of keratitis**.



! Ramsay Hunt Syndrome (Herpes Zoster Oticus) is reactivation of VZV in the **geniculate ganglion of Facial nerve**, resulting in **ipsilateral ⇒ facial pain, ear pain, and vesicular rash on the external ear canal, pinna, or ear drum**.

Q17

A 25-year-old woman and her 25-year-old husband come to the physician for counseling prior to conception. They both are of Vietnamese descent. Previous screening showed a mean corpuscular volume of less than 80 μm^3 in both; hemoglobin electrophoresis showed no abnormalities. This couple's offspring is at greatest risk for which of the following diseases?

- A. Hemoglobin H
- B. Hemoglobin S
- C. Hemoglobin SC
- D. α -Thalassemia trait
- E. β -Thalassemia

▼ Explanation

- **Answer is D (α -Thalassemia trait)**
 - **IMP Clues**
 - Vietnamese descent (cis pattern)
 - Previous screening showed a MCV of less than 80 (Microcytic anemia)
 - Hemoglobin electrophoresis showed no abnormalities (alpha thalassemia trait)
- Q asks for the couple's offspring is at greatest risk of developing which of the following?
 - Both parents have **alpha thalassemia trait (mild microcytic anemia)**, who have **deletion of 2 alpha globulin chain**.
 - Father $\Rightarrow - - / aa$
 - Mother $\Rightarrow - - / aa$
 - Possible combinations are:
 - **25% $\rightarrow aa/aa$ (Normal)**
 - **50% $\rightarrow - - / aa$ (alpha Thalassemia trait)**
 - **25% $\rightarrow - - / -$ (alpha Thalassemia major)**

? What would be the expected outcome of the parents where Africans?

▼ Answer

Transmission would be in a **trans** pattern instead:

- Father $\Rightarrow - a / - a$
- Mother $\Rightarrow - a / - a$

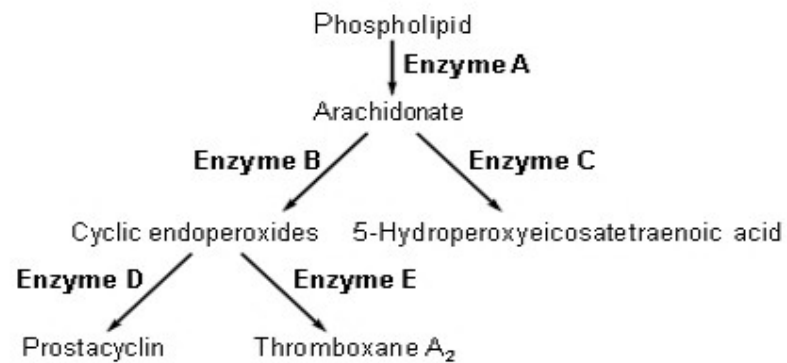
Possible Combinations:

- **100% $\rightarrow - a / - a$ (**alpha thalassemia trait**)**

- Q asks for **GREATEST** risk, 50% chance of getting alpha thalassemia trait (Choice D)

Q18

A 15-year-old boy has nasal polyps and develops bronchospasms after taking a drug. The drug is most likely to inhibit which of the following enzymes in the biochemical scheme shown?



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

▼ Explanation

• Answer is B

◦ IMP Clues

- Nasal polyps and bronchospasms after taking a drug
- Biochemical scheme shows Arachidonic acid pathway

• Dx → Samter's Triad (Aspirin-Exacerbated Respiratory Disease)

◦ Triad is Nasal Polyps, Aspirin-Induced Asthma, and Aspirin-Induced Hypersensitivity

▪ How does it happen?

- Aspirin & NSAIDs inhibit COX (inhibits PGs synthesis) → all the arachidonic acid is *shunted into Leukotrienes* (via LOX) → bronchoconstriction → Asthma in susceptible patients.

◦ Treatment is Zileuton (5-LOX inhibitor) OR Montelukast & Zafirlukast (Leukotrienes Receptor antagonists)

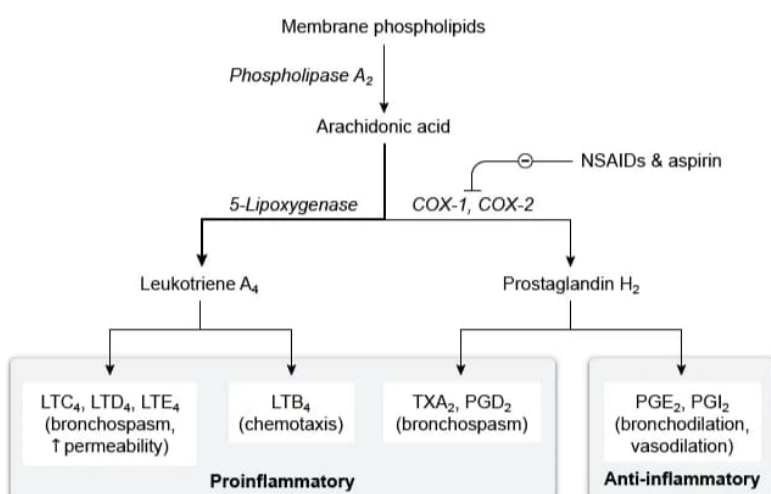
? What type of hypersensitivity is AERD?

▼ Answer

Pseudoallergic Reaction (**NOT** IgE-mediated reaction)

This distinction is super HY.

- Overproduction of leukotrienes (LTC₄, LTD₄, LTE₄) → increases mast cell & eosinophils activation → Airway inflammation & bronchoconstriction
- **NOT** IgE-mediated & **NOT** type 1 hypersensitivity reaction.
 - This is why concurrent urticaria & angioedema are rare: Pseudoallergy is mediated by LTs **NOT** histamine or bradykinin.



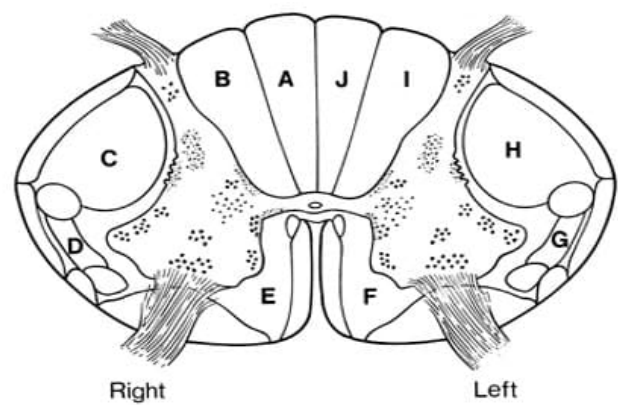
Let's Review some HY points regarding Arachidonic Pathway:

- What Inhibits Phospholipase A2 → **Glucocorticoids**
- What Leukotriene is unique → **LTB₄** (one of the chemotaxis molecules; they attract neutrophils to site of inflammation)
 - Chemotactic Molecules on the USMLE are **LTB₄, C5b, IL-8, PAF, and Kallikrein**
- Difference between Aspirin & other NSAIDs → Aspirin is **irreversible** and **noncompetitive**
 - Other NSAIDs are reversible & competitive.
- Difference between NSAIDs & Acetaminophen → Acetaminophen is a **CENTRAL** COX inhibitor
- What are COX 1 Functions → **Integrity of Gastric Mucosa** & **TXA₂ formation for PLT aggregation**
- What are COX 2 Functions → **Inflammation** & **Vasodilation**

- What is Celecoxib ⇒ **Selective COX-2 inhibitor**
 - **Decreases inflammation while maintaining gastric mucosa integrity**
 - Used in **patients with gastric ulcers** who need to be on anti-inflammatory medications
 - HY disadvantage ⇒ **Higher risk of thrombosis** (TXA2 + vasoconstriction), so use carefully in patients with cardiovascular or cerebrovascular diseases.

Q19

A 34-year-old woman is brought to the emergency department 30 minutes after being involved in a motor vehicle collision. Sensation to pain is decreased over the left lower extremity. Which of the following labeled regions on the diagram of the spinal cord shown is most likely damaged 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 D
 - IMP Clues
 - Sensation to pain is decreased over the left lower extremity
 - Q asks for which region of the spinal cord is damaged in this patient

• Spinal Cord Tracts

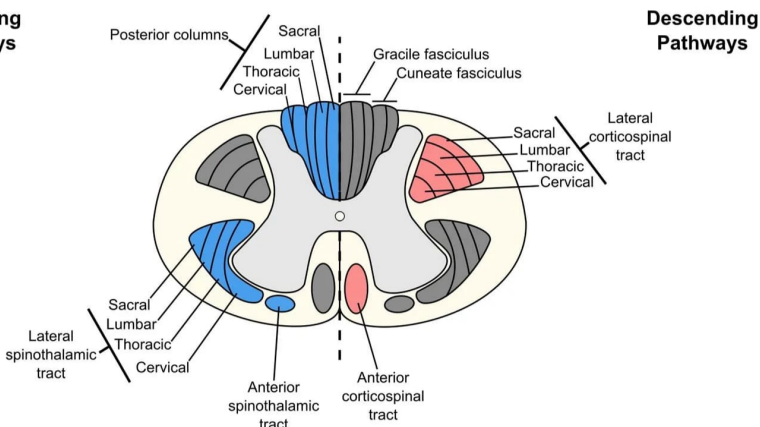
Knowing the names, functions, and sites of the spinal cord tracts are pass-level. Let's master them

- This patient has **decreases sensation to pain** ⇒ Spinothalamic Tract (Choices D & G)
 - Is it right or left side?
 - Pain is on the left extremity & spinothalamic tract crosses in the spinal cord, so **contralateral** tract ⇒ Right Spinothalamic Tract (Choice D)

The 4 main HY tracts you need to know for the USMLE are:

- 3 Ascending tracts:
 1. Spinothalamic Tract ⇒ conveys pain, temperature, and crude touch sensations
 - Crosses in **spinal cord**, so **spinal cord lesions cause CONTRALATERAL deficits** (loss of pain & temperature sensation)
 2. Dorsal Column ⇒ conveys fine touch, vibration, and **CONCIOUS** [asked on NBME] proprioception

Ascending Pathways



- Crosses in **medulla**, so **spinal cord lesions cause *IPILATERAL* deficits** (loss of vibration sense & **high-steppage gait/ataxia** with **positive Romberg sign**) [*asked on NBME*]
- Made up of two parts: **Gracile** Fasciculus that conveys sensations of **Lower Limb** & **Cuneate** Fasciculus that conveys sensations of **Upper Limb**

3. Spinocerebellar Tract ⇒ conveys **UNCONCIOUS** [*asked on NBME*] proprioception

- **Doesn't cross**, so **ALL lesions cause *IPILATERAL* deficits** (**ataxia** with **negative Romberg sign**) [*asked on NBME*]

• 1 Descending Tract:

1. Corticospinal Tract ⇒ Controls Voluntary Motor movement (Pyramidal Tract)

- Crosses in the **medulla**, so **spinal cord lesions cause *IPILATERAL* deficits** (Weakness/Paralysis & Hypertonicity)



MYELIN STAINS **BLACK**

- IF **NOT BLACK** → Unmyelinated/Demyelinated
- **Nerve fibers that convey pain & temperature sensation are NON-MYELINATED**. USMLE give you an EM microscopy picture of a myelinated (surrounded by a black layer) & unmyelinated (with no surrounding black layer) with an "X" on the unmyelinated nerve. The Q then asks for function of the labeled "X" nerve.
 - Answer was "**Conveys pain and temperature sensation**".

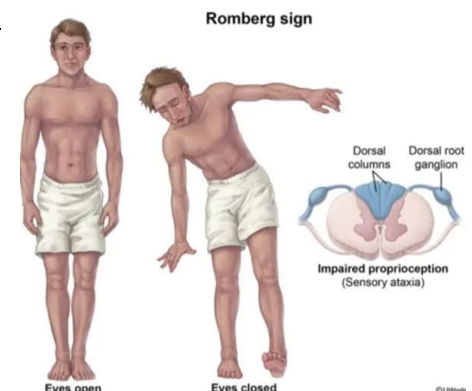
2 Main Types of Ataxias you need to differentiate:

1. Sensory Ataxia

- Caused by **Dorsal Column lesion** or **Peripheral Neuropathy**
- **Positive Romberg Sign**

2. Cerebellar Ataxia

- Caused by **Cerebellar lesion** or **Spinocerebellar tract lesion**
- **Negative Romberg Sign**



Q20

A 30-year-old man with HIV infection comes to the office for a follow-up examination. He is asymptomatic and takes no medications. His CD4+ T-lymphocyte count is 158/mm³ (N>500), and plasma HIV viral load is 180,000 copies/mL. He is prescribed antiretroviral therapy, including ritonavir and another protease inhibitor (PI). Which of the following best explains the effectiveness of ritonavir in combination with a second PI in this patient?

- It decreases the increased serum amylase activities caused by other PIs
- It decreases the risk for pancreatitis
- It increases plasma concentrations of other PIs also metabolized by cytochrome P450
- It significantly shortens intervals between dosages of PIs
- It slows the rate of lipodystrophy associated with administration of other PIs

▼ Explanation

- **Answer is C (It increases plasma concentrations of other PIs also metabolized by cytochrome P450)**
 - Easy but important concept: HIV drugs & their side effects.
 - **Ritonavir (a protease inhibitor, "-navir") has a unique side effect → CYP3A4 inhibitor**
 - Used mainly as a pharmacokinetic booster used with other anti-retroviral drugs to **potentiate their drug levels & effects**.
 - Shares the same side effects of all other protease inhibitors → **Lipodystrophy** (cushingoid appearance), **hyperglycemia** (Insulin Resistance & DM), and **hypertriglyceridemia** [*asked on NBME*]
 - **What is a protease?**
 - **Protease** is HIV's enzyme used to **cleave proteins into their mature functional form**.
 - If inhibited, **immature and non-infectious virions** are produced

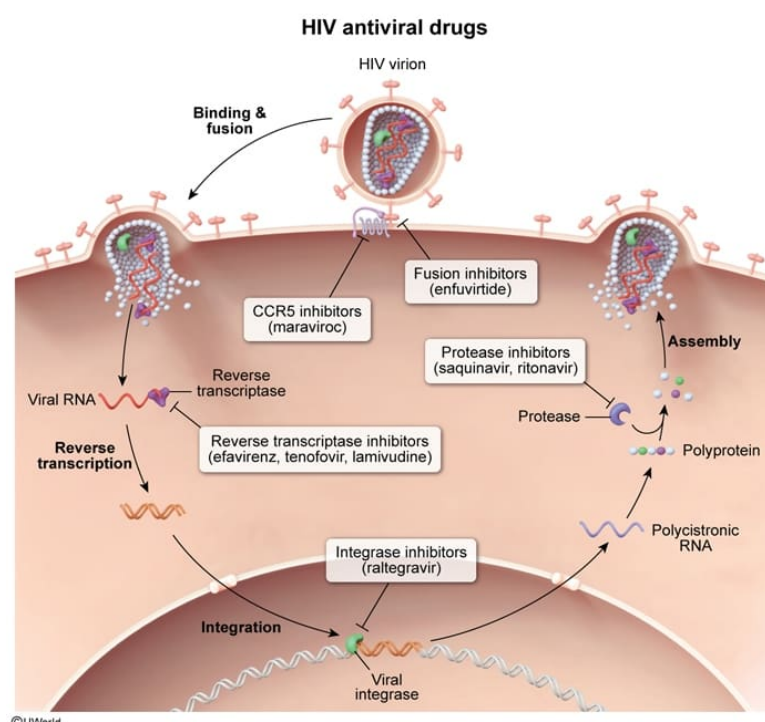
HIV Drugs Overview:

1. NRTIs [Require intracellular phosphorylation to be active]

- MOA: Inhibit Reverse Transcriptase **Competitively** (inhibits synthesis of viral DNA from RNA) [*asked on NBME*]
- **Common Side Effects: Lactic Acidosis & Bone Marrow Suppression**
- **UNIQUE NRTIs:**
 - Zidovudine** → Most notorious for **bone marrow suppression** [*asked on NBME*] & **given intrapartum to HIV+ pregnant women to prevent maternal-to-fetal transmission**
 - Didanosine** → **Pancreatitis** [*asked on NBME*]
 - Abacavir** → **Hypersensitivity in HLA-B5701 positive patients**, so test for HLA-B5701 before initiating ttt [*asked on NBME*]
 - Emtricitabine** → **Hyperpigmentation** of palms & soles
 - Didanosine, Stavudine, and Zalcitabine** → Most notorious for **Peripheral Neuropathy**

2. NNRTIs [DON'T require intracellular phosphorylation to be active]

- MOA: Inhibit Reverse Transcriptase **Allosterically** (inhibits synthesis of viral DNA from RNA) [*asked on NBME*]
- **Common Side Effects: Rash & Hepatotoxicity**
- **UNIQUE NNRTIs:**
 - Efavirenz** → **Vivid Dreams** [*asked on NBME*]
 - Others** → **Nevirapine & Doravirine**



3. Protease Inhibitors ("-navir")

- **MOA:** Inhibits **HIV proteins cleavage & maturation into functional proteins**
- **Common Side Effects:** **Lipodystrophy** (cushingoid appearance), **Hyperglycemia** (Insulin Resistance & DM), and **Hypertriglyceridemia** [asked on NBME]
- **UNIQUE Protease Inhibitors:**
 - **Ritonavir** → **CYP3A4 inhibitor** (increases other anti-retroviral drugs levels in blood, potentiating their effects) [asked on NBME]
 - **Indinavir** → **Nephrolithiasis**

4. Integrase Inhibitors ("-tegra-", e.g. Raltegravir or Dolutegravir)

- **MOA:** Inhibits **HIV DNA integration into host's genome**

5. Entry Inhibitors:

a. Maraviroc (CCR5 antagonist)

- **MOA:** Inhibits HIV **docking** & entry by blocking **gp120** with Chemokine-Cysteine-Cysteine Receptor 5 (**CCR5**) of CD4 cell [asked on NBME]

b. Enfuvirtide (Fusion Inhibitor)

- **MOA:** Inhibits HIV **fusion** with CD4 cell membrane & entry by binding to HIV **gp41**

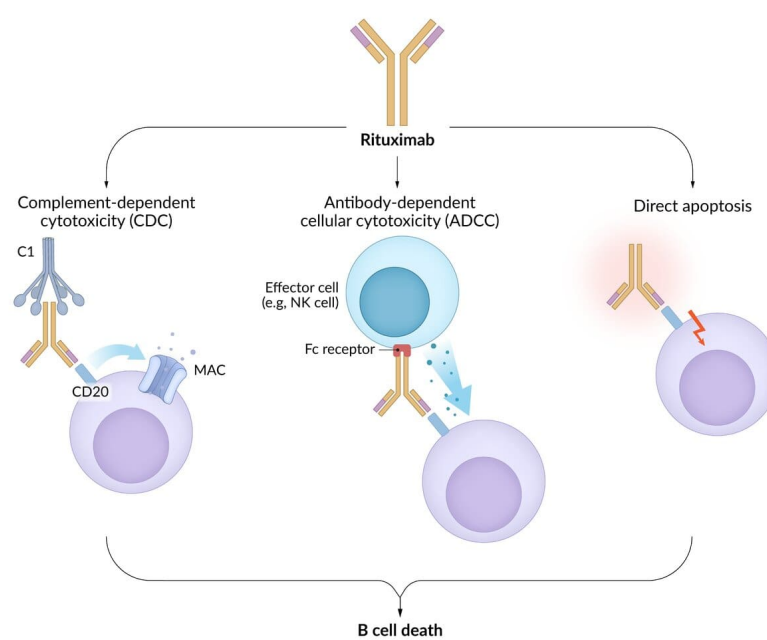
Q21

A 40-year-old woman with a history of low-grade follicular B-cell lymphoma comes to the physician for a follow-up examination. One week ago, she completed a 4-month course of rituximab and is in complete remission. She appears well. This patient is at increased risk for which of the following conditions as a result of her treatment?

- Bacterial pneumonia
- Bone marrow failure
- Development of a solid tumor
- Hematopoietic malignancy
- Serum sickness

▼ Explanation

- **Answer is A (Bacterial pneumonia)**
 - Q asks what Rituximab increases risk of which of the following?
 - **Rituximab is anti-CD20 monoclonal antibody.**
 - CD20 is a membrane protein found on the surface of B-cells through its maturation.
 - It helps in **B-cell activation, proliferation, and differentiation.**
 - **Rituximab blocks CD20 membrane protein → prevents B-cell activation, proliferation, and differentiation**
 - This causes B-cell depletion via:
 - Complement-dependent Cytotoxicity** OR
 - Antibody-dependent Cellular Cytotoxicity** OR
 - Direct Apoptosis**
 - **As a result, B-cell deficiency causes hypogammaglobulinemia and increases risk of bacterial infections.**
 - Additionally, patients taking rituximab are at increased risk of reactivation of 2 buzzy viruses:
 - JC Virus Reactivation** (causes Progressive Multifocal Leukoencephalopathy)
 - Hepatitis B Virus Reactivation**



Q22

A 26-year-old man who is a Peace Corps volunteer comes to the physician because of a 2-day history of nausea after eating and profuse, watery diarrhea without blood. There has been no fever or chills. He returned from a 1-year assignment in Haiti 1 day ago. His temperature is 37.9°C (100.2°F), pulse is 120/min, respirations are 20/min, and blood pressure is 90/60 mm Hg. Physical examination shows dry mucous membranes. Stool culture grows an oxidase-positive, curved, gram-negative bacillus. Which of the following is the most appropriate immediate treatment for this patient?

- A. Bismuth subsalicylate
- B. Ivermectin
- C. Metronidazole
- D. Nitazoxanide
- E. 0.9% Saline

▼ Explanation

• Answer is E (0.9% Saline)

◦ IMP Clues

- Profuse water diarrhea without blood + No fever or chills (Non-invasive)
- He returned from Haiti 1 day ago (Not USA = Not clean, according to USMLE)
- Pulse is 120/min and Blood pressure is 90/60 mmHg + dry mucous membrane (dehydrated)
- Oxidase-positive, curved, gram-negative bacillus (V.cholerae)

• Dx → Cholera

- Cholera caused by **Vibrio Cholerae**
- **Comma-shaped, Oxidase-positive, highly-motile, gram-negative rod** that is transmitted via **fecal-oral route and contaminated water**.
- **ACID-LABILE** (so increased risk in patients on **PPIs**, or **with achlorhydria**)
- Once in the intestines, it **attaches (NO invasion, hence no erythrocytes & leukocytes in stool) & releases Cholera Toxin**
 - **Cholera Toxin activates adenylate cyclase & increases cAMP**, causing excessive chloride secretion and decreased sodium reabsorption ⇒ **PROFUSE WATERY DIARRHEA**
 - USMLE likes the buzzy **"Rice Water Stools,"** or **"Grey and Turbid Stools."**
- Treatment is simply **ORS (Oral Rehydration Solution)**
 - Sometimes, in severe cases **IV hydration** can be used



Q23

A male newborn has a myelomeningocele that involves the vertebral arches of L2-5. Physical examination also shows bilateral clubfeet. Which of the following developmental processes is most likely affected in this newborn?

- A. Axis specification
- B. Closure of the caudal neuropore
- C. Closure of the rostral neuropore
- D. Development of the apical ectodermal ridge
- E. Development of the notochord
- F. Development of the zone of polarizing activity
- G. Polarity specification
- H. Scheduled apoptosis

▼ Explanation

• Answer is B (Closure of the caudal neuropore)

- Newborn has myelomeningocele (a Neural Tube Defect) and the Q ask for the responsible affected developmental process.
 - For USMLE, all you need to know is the following:
 - **Neural Tube Defects → Abnormal Closure of Caudal Neuropore (Lower End of spinal cord)**
 - **Anencephaly → Abnormal Closure of Rostral Neuropore (Head)**
 - Do I need to know any time frames?
 - Just knowing that **at 3-4 weeks, the fetus is most susceptible to congenital malformations, especially neural tube defects**

- Do I need to know the markers?
 - **AFP** is increased in amniotic fluid & maternal serum
 - **AChE** is increased in amniotic fluid

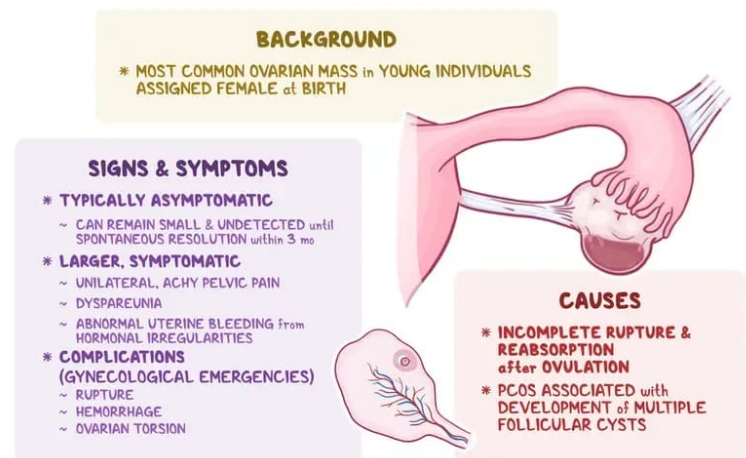
Q24

An asymptomatic 30-year-old woman comes to the physician for a health maintenance examination. Physical examination shows a nontender adnexal mass on the left. Ultrasonography confirms the presence of a single 6-cm fluid-filled cyst. Which of the following is the most likely cause of this ovarian cyst?

- A. Anovulation
- B. Ectopic pregnancy
- C. Endometriosis
- D. Ovarian malignancy
- E. Pelvic inflammatory disease

▼ Explanation

- **Answer is A (Anovulation)**
 - **IMP Clues**
 - Asymptomatic 30-year-old women
 - Nontender adnexal mass on the left
 - US confirms presence of single 6-cm fluid-filled cyst
- **Dx → Follicular Cyst (type of functional cysts)**
 - Normally, what happens is **FSH stimulation causes follicular growth then at ovulation, the follicle ruptures** causing liberation of the ova
 - **If the patient is *non-ovulatory* (no LH surge) → Follicles fail to rupture → fluid accumulates inside causing a *follicular cyst*.**
 - Ultrasound would show a **simple thin-walled fluid filled cyst**.



Q25

Physical analysis of the isolated genomic DNA from a mutant strain of Escherichia coli shows that it can now be digested into numerous small fragments with a restriction endonuclease (Mbo I) that recognizes the GATC sequence. The DNA from the wild-type parental strain is resistant to digestion with this restriction endonuclease. The mutation that causes this type of phenotype is most likely to occur in the gene encoding which of the following activities?

- A. DNase
- B. Gyrase
- C. Helicase
- D. Ligase
- E. Methylase

▼ Explanation

- **Answer is E (Methylase)**
 - Bullshit Biochemistry. Just memorize the following facts:
 - **Restriction endonuclease cut specific sequences (for example Mbo I cuts GATC sequence) if they are unmethylated**
 - **Methylase (Choice E) adds methyl groups to the sequences, so protects it from cutting**
 - **If methylase is muted (like in this Q), restriction endonuclease (Mbo I) cuts all of the unprotected sequences**

Q26

A 61-year-old man comes to the emergency department because of severe abdominal pain for 1 hour. He has polycythemia vera and has frequently missed appointments to have his hematocrit monitored. His most recent examination 2 weeks ago showed no abnormalities. Physical examination shows mild scleral icterus. Abdominal examination shows a tender, enlarged liver, a moderately enlarged spleen, and ascites. Which of the following is the most likely diagnosis?

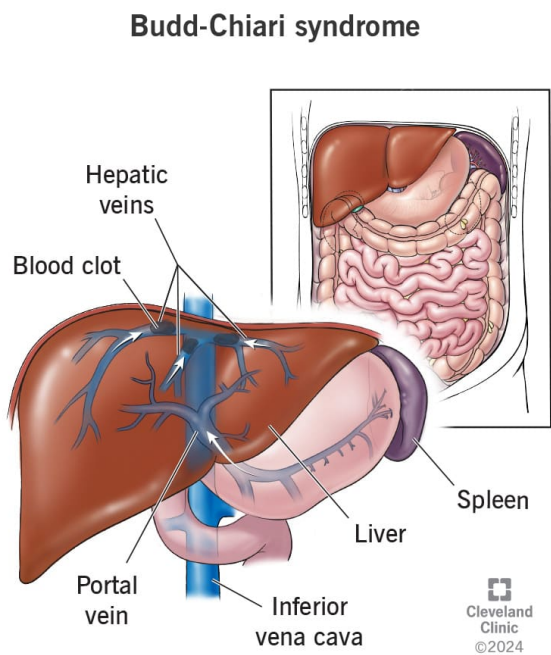
- A. Budd-Chiari syndrome
- B. Hepatic cirrhosis
- C. Pancreatic carcinoma
- D. Portal vein thrombosis
- E. Primary hemochromatosis

▼ Explanation

- Answer is A (Budd-Chiari syndrome)
 - IMP Clues
 - Severe abdominal pain
 - He has polycythemia vera
 - Mild scleral icterus + tender enlarged liver + moderately enlarged spleen + ascites
 - Dx → Budd-Chiari Syndrome
 - Hepatic Vein Thrombosis/Obstruction caused by Polycythemia Vera (most commonly), malignancy, and COCs/Pregnancy
 - Characterized by Triad → Hepatomegaly + Ascites + Abdominal pain/tenderness
 - Additional features are jaundice, splenomegaly, elevated transaminases & bilirubin, LCF (causing prolonged INR/PTT & hepatic encephalopathy), and variceal bleeding.
 - Diagnosed by Doppler US showing decreased hepatic vein flow

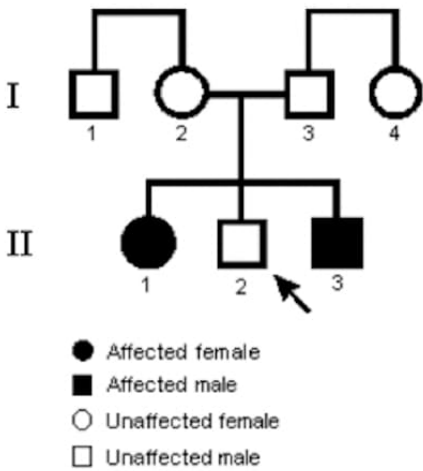
? What is the pathophysiology of Polycythemia Vera?

▼ Answer
JAK2 mutation



Q27

A couple comes to the physician for counseling prior to conception. The man has two siblings with cystic fibrosis. Assuming that the carrier frequency for this disorder in the general population is 1/25, which of the following best approximates the recurrence risk that the individual identified by the arrow in the pedigree shown will have a child with cystic fibrosis?



- A. 1/100
- B. 1/150
- C. 1/200
- D. 1/1500
- E. 1/2000

▼ Explanation

- **Answer is B (1/150)**
 - **IMP Clues**
 - The man has 2 siblings with cystic fibrosis
 - Carrier frequency in general population is 1/25
 - Q wants to know the incidence that this man's child will have cystic fibrosis?
 - **The man's probability that he is a carrier is 2/3**
 - Why?
 - **AR** disorder, so it can be **AA, Aa, Aa, aa**
 - He is **not aa**, as he is not affected → So the possible options are **AA, Aa, Aa**
 - We want to know **the probability that he is a carrier (Aa) → so 2/3**
 - **The General population carrier frequency is 1/25**
 - **The probability that the child gets an AR disorder is 1/4 (aa)**
 - So, total $2/3 \times 1/25 \times 1/4 = 2/300 = 1/150$ (Choice B)

Q28

A 34-year-old woman with a 5-year history of hepatitis C comes to the physician because of progressive fatigue during the past month. Her vital signs are within normal limits. Her liver is not palpable. Serum studies show:

Albumin	3 g/dL
Total bilirubin	1.8 mg/dL
Alkaline phosphatase	68 U/L
AST	33 U/L
ALT	38 U/L

Her serum α -fetoprotein concentration is within the reference range. A liver biopsy specimen is most likely to show which of the following?

- A. Hepatocellular carcinoma
- B. Infiltration of lymphocytes, plasma cells, and macrophages
- C. Infiltration of neutrophils and eosinophils
- D. Palisading lymphocytes and giant cells
- E. Normal hepatic histology

▼ Explanation

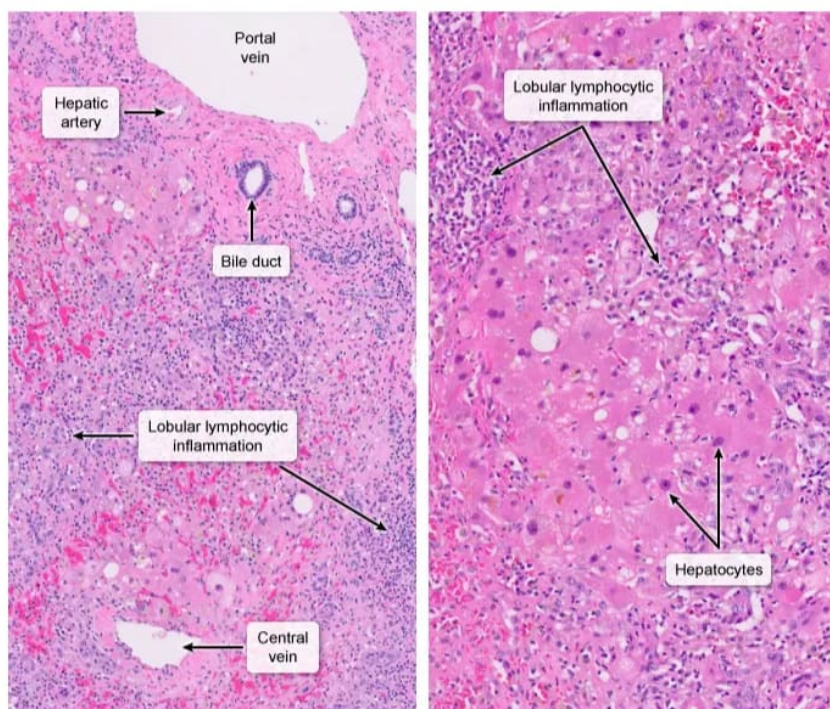
- **Answer is B (Infiltration of lymphocytes, plasma cells, and macrophages)**
 - **IMP Clues**
 - 5-year history of hepatitis C
 - Serum α -fetoprotein concentration is within reference range (excluding HCC)
 - **Dx → Chronic HCV Infection**
 - HCV infection is characterized by the **presence of lymphocytic infiltration and features of hepatocyte injury**
 - Feature of hepatocyte injury include **ballooning of hepatocytes, piecemeal necrosis, and apoptosis (Councilman bodies) [asked on NBME]**
 - **Macrophages** come in and phagocytose any cellular debris present
 - **It is super HY to understand that Lymphocytes are the cells of chronic inflammation, so their presence = Chronic.**

? What is the cause of hepatocyte injury in viral hepatitis?

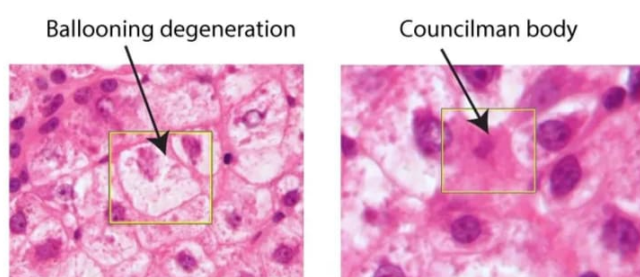
▼ Answer

Apoptosis

- USMLE loves to test this concept: Hepatocyte injury in viral hepatitis is caused by **Cytotoxic CD8+ T-cell-mediated Apoptosis**



Picture below shows Councilman Body & Hepatocyte Ballooning:



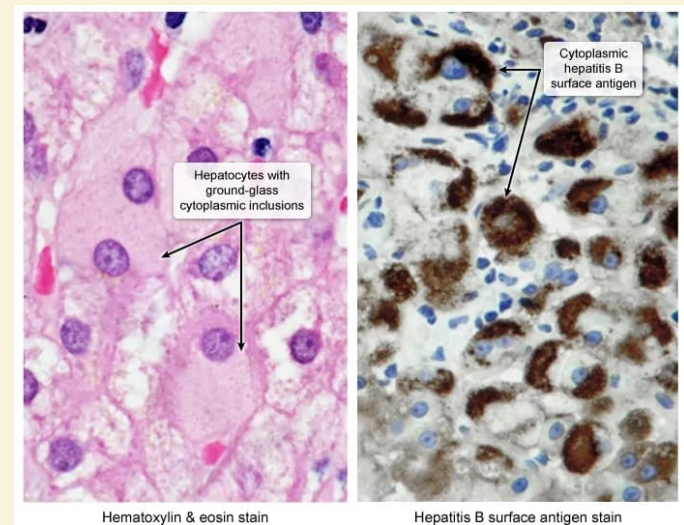
Disease that are highly associated with HCV infection:

- **Liver Cirrhosis** (which progresses to **HCC**)
- **Mixed Cryoglobulinemia** (Palpable purpura, glomerulonephritis, and peripheral neuropathy)
- **Porphyria Cutanea Tarda** (Heme pathway enzyme **uroporphyrinogen decarboxylase deficiency** → **photosensitivity & skin hyperpigmentation**)
- **Lichen Planus**
- **MPGN** (Nephritic Syndrome)

? What's buzzy in HBV's biopsy?

▼ Answer

Ground-Glass hepatocytes



Q29

An 11-year-old boy is brought to the physician by his mother because she recently found him naked in bed with his 4-year-old male cousin. The cousin was crying. Neither will talk to her about the incident, but she and her family are very concerned that something is wrong. The mother describes her son as quiet and says that he is rarely in trouble. She adds that his school performance has declined during the past 2 months. It is most appropriate for this patient to be evaluated for which of the following?

- Attention-deficit/hyperactivity disorder
- Conduct disorder
- Major depressive disorder
- Precocious puberty
- Sexual abuse

▼ Explanation

- **Answer is E (Sexual Abuse)**
 - Signs of sexual abuse in children presents as the following:
 - **Genital OR Rectal Bleeding**
 - **STDs or Discharge**
 - **Developmentally inappropriate knowledge of sexual activity**
 - **Engagement in developmentally inappropriate play** (what we have here)
 - These behaviors **are learned** (not normally explored by children), which means that **the child had *previously experienced sexual abuse* (Choice E)**

Q30

An investigator is studying the adverse effects of a proteasome inhibitor, bortezomib, on immune responses. Bortezomib is administered to a group of patients with relapsed multiple myeloma, and immune responses are observed. Which of the following immunologic processes is primarily affected by this drug?

- Activation of the complement cascade
- Activation of perforin

- C. Presentation of antigens to CD8+ T lymphocytes
- D. Secretion of histamine by mast cells
- E. Secretion of interleukin-1 (IL-1) by macrophages

▼ Explanation

- **Answer is C (Presentation of antigens to CD8+ T lymphocytes)**
 - First, we need to discuss what are proteasomes:
 - They are cellular proteins that assist in **protein degradation & antigen-presentation**:
 1. **Degrades Misfolded/Truncated proteins (via ubiquitination)**
 2. **Prevents their accumulation & prevents induction of apoptosis**
 3. **Generates peptides from intracellular proteins/antigens for MHC 1 presentation**
 - Now, if we inhibit the proteasomes by Bortezomib (proteasome inhibitor):
 - **Truncated/Misfolded proteins are NOT degraded & accumulate → Cellular Stress → Induction of Apoptosis**
 - **NO peptides are presented to MHC 1 class & NO antigen presentation to CD8+ cells**

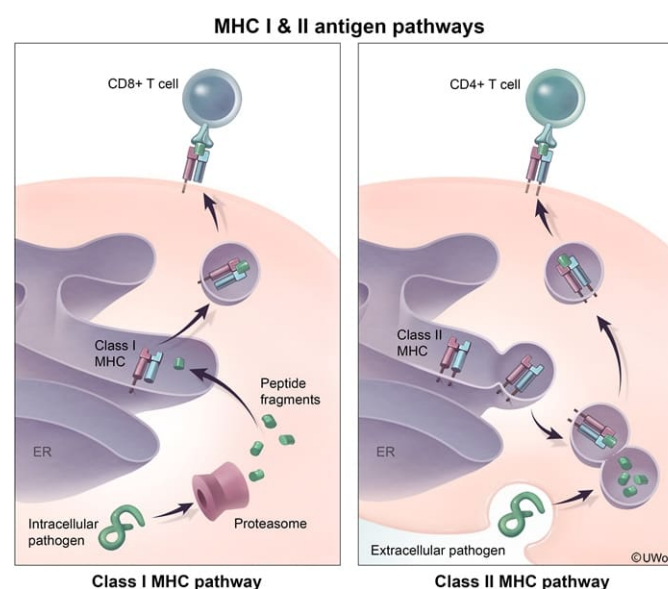
? What are the 2 main uses of Bortezomib?

▼ Answer

Multiple Myeloma & Mantle Cell Lymphoma

- Both are associated with massive misfolded protein accumulation

Picture below shows difference between MHC Class 1 vs MHC Class 2 antigen presentation:



Note how Proteasomes are involved in MHC 1 antigen presentation process.

Q31

A 20-year-old man is brought to the emergency department by his friend 8 hours after the acute onset of confusion following an all-night dance party. His pulse is 140/min, and blood pressure is 180/110 mm Hg. Physical examination shows pale, cold extremities. There is no diaphoresis. An ECG shows sinus tachycardia. This patient most likely ingested which of the following substances?

- A. Ketamine
- B. Levodopa
- C. LSD
- D. Marijuana
- E. 3,4-Methylenedioxymethamphetamine (MDMA)

▼ Explanation

- **Answer is E (3,4-Methylenedioxymethamphetamine (MDMA))**
 - **IMP Clues**
 - Following an all-night dance party (most likely drugs were used)
 - Acute Onset Confusion
 - Pulse is 140/min and Blood Pressure is 180/110 + Tachycardia
 - Pale, cold extremities
 - **Dx → MDMA Ecstasy Intoxication**
 - **Mechanism:** **Induces reversal of monoamine transporters → Increases neurotransmitter release (Serotonin & Catecholamines) → Sympathetic Overstimulation**
 - **Features:**
 - **Increased Catecholamines:**
 - **Euphoria & Hallucinations & Distorted perception**
 - **Hyperactivity & Disinhibition & Bruxism (teeth grinding)**
 - **Hypertension, Tachycardia, Hyperthermia, and mydriasis**
 - Hyperthermia + increased muscle contraction ⇒ **Increased Creatine Kinase** due to muscle breakdown

Q32

A medical student is caring for a 72-year-old man who has been admitted to the hospital because of a lung mass. Biopsy shows carcinoma, but the resident physician instructs the student not to inform the patient of the results until after the oncologist has evaluated the patient the next day. The next morning the patient asks the student, "What did my biopsy show?" Which of the following responses is most appropriate?

- A. "Everything is okay."
- B. "I don't know, but the oncologist will be seeing you later today."
- C. "It was positive for cancer."
- D. "Let me get the resident physician so we can go over the results."
- E. "The results are not back yet."

▼ Explanation

- Answer is D ("Let me get the resident physician so we can go over the results.")
 - Let's go through the choices:
 - Choice A ⇒ This is straight **lying**. Everything is not okay. He has carcinoma.
 - Choice B ⇒ This is also **lying**. You do know the biopsy results AND this choice come out a little dismissive.
 - Choice C ⇒ You are **not authorized** to reveal the results alone AND **you don't have sufficient information** to answer the patient's questions.
 - Choice D ⇒ **Most ethically correct answer. You are not dismissing the patient question, and you are getting the resident, who will have the sufficient information to answer the parent's question.**
 - Choice E ⇒ This is also **lying**.

Q33

A 68-year-old woman comes to the office because of a 3-month history of increased daytime and nighttime urination and pain of her low back. She had cervical cancer 15 years ago, at which time she underwent hysterectomy with bilateral salpingo-oophorectomy. She also received external beam radiation to the pelvis. Physical examination shows no palpable abdominal masses. Laboratory studies show increased serum concentrations of urea nitrogen and creatinine and decreased urine osmolality. Renal ultrasonography shows bilateral hydronephrosis and hydroureter, with distal ureteral narrowing bilaterally. Which of the following best explains the findings in this patient?

- A. Recurrent cervical carcinoma
- B. Retroperitoneal fibrosis
- C. Urethral condyloma
- D. Urethral transitional cell papilloma
- E. Urothelial carcinoma

▼ Explanation

- Answer is B (Retroperitoneal fibrosis)
 - Patient here underwent hysterectomy with bilateral salpingo-oophorectomy (the cervix is removed, so recurrence of cervical cancer is unlikely as there is no cervix present (**Choice A**))
 - After which, she received **radiation to the pelvis**.
 - Radiation causes **endarteritis obliterans and fibrosis**.
 - The **ureters are retroperitoneal organ**.
 - Q says **BILATERAL hydronephrosis & hydroureter**, meaning that **BOTH ureters** must be compressed. This excludes unlikely causes (**Choices C, D, and E**).
 - **Both ureters are retroperitoneal organs & the presence of history of radiation make the most likely cause of these findings Retroperitoneal Fibrosis (Choice B)**

Q34

A researcher is asked to prospectively investigate the prevalence and incidence of decubitus ulcers in 100 residents of a nursing care facility during a 2-year period. At the beginning of the study, 10 residents are found to have decubitus ulcers. During the first year, five additional residents develop decubitus ulcers, and another 10

residents develop decubitus ulcers during the second year. Three of the previously noted ulcers have completely healed by the end of the 2-year period. National standards for nursing care facilities mandate that the prevalence of decubitus ulcers should be less than 20% of the total residents in the facility, and the incidence of new decubitus ulcers should be less than 50 per 1000 patient years. Which of the following is the most appropriate conclusion regarding the prevalence and incidence of decubitus ulcers in this population at the end of the 2-year period?

Choices	Prevalence	Incidence
A.	Above the standard	above the standard
B.	Above the standard	below the standard
C.	Below the standard	above the standard
D.	Below the standard	below the standard

▼ Explanation

- Answer is A
 - Our Values:
 - At the beginning of the study = 10 residents have decubitus ulcers ⇒ Initial Prevalence = 10/100 = 10%
 - During the first year, 5 additional residents develop decubitus ulcers ⇒ Incidence = 5/90 = 5.55%
 - During the second years, 10 additional residents develop decubitus ulcers ⇒ Incidence = 10/80 = 12.5%
 - 3 residents have completely healed by the end of the 2-year period ⇒ Prevalence after 2 years ⇒ 10 + 5+ 10 - 3 ⇒ 22/100 = 22%
 - National Standards:
 - Prevalence should be less than 20%
 - Incidence should be less than 5%
 - Answer:
 - Prevalence in this facility (22%) is above the national standard (less than 20%)
 - Incidence in first year (5.55%) and second year (12.5%) are above the national standard (less than 5%)
 - Answer is Choice A

Q35

A 55-year-old man who has a 10-year history of type 2 diabetes mellitus comes to the physician because of fecal incontinence. Which of the following additional symptoms is most likely in this patient?

- A. Dysuria
- B. Impotence
- C. Inability to climb stairs
- D. Nighttime leg cramps
- E. Sciatica

▼ Explanation

- Answer is B (Impotence)
 - IMP Clues
 - 10-year history of type 2 diabetes mellitus
 - Fecal incontinence
 - Dx → Autonomic Neuropathy
 - Long-standing DM causes diabetic neuropathy, causing the classical peripheral neuropathy & glove-and-stock paresthesia
 - The same way peripheral nerves get affected by long standing DM, autonomic nerve can also be affected ⇒ Autonomic Neuropathy
 - Neuropathy of Pelvic Splanchnic Nerve ⇒ Impotence & Urinary Incontinence
 - Neuropathy of Inferior Hypogastric Plexus ⇒ Reduced Internal anal sphincter tone, resulting in Fecal Incontinence
 - Additionally, peripheral neuropathy of pudendal nerve ⇒ Reduced External anal sphincter tone
 - Additional HY Features of Autonomic Neuropathy:
 - Neuropathy of Sympathetic Fibers of the heart ⇒ Silent MI & Orthostatic Hypotension
 - Vagus Nerve Neuropathy:
 - Loss of parasympathetic tone of the heart ⇒ Resting Tachycardia



Pathophysiology of Diabetic Neuropathy:

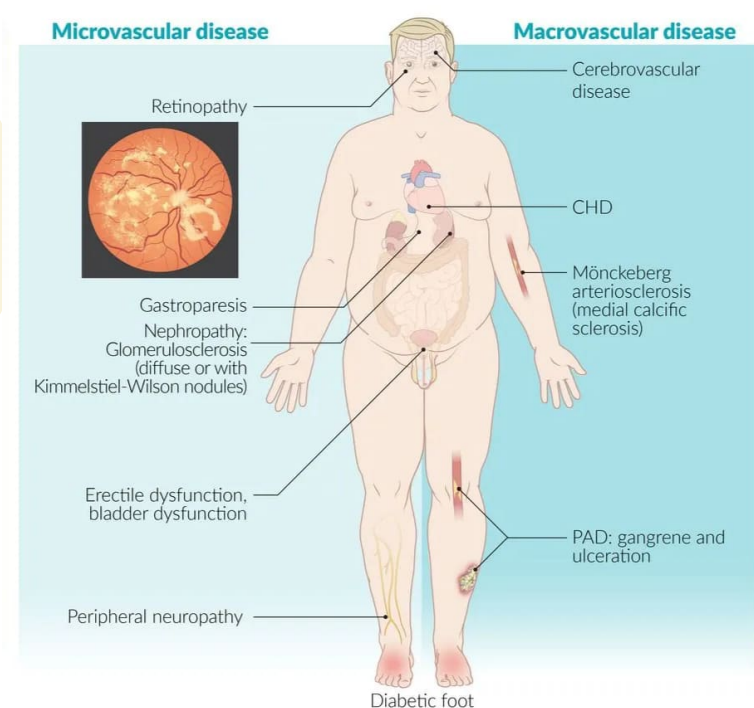
1. Advanced glycation end products (AGEs) trigger neural inflammation and small vessel changes
2. Hyperglycemia-induced ROS formation causes direct DNA damage and reduced NO bioavailability
3. Microangiopathic Changes (hyalinization of endoneural arterioles)
4. Sorbitol Accumulation causes impaired mitochondrial function

- Loss of parasympathetic tone of the GI ⇒ **Gastroparesis** *[asked on NBME]*

? What type of nerves are affected initially in diabetic neuropathy?

▼ Answer

Unmyelinated Distal Long Nerves (sensory & autonomic) are most vulnerable to metabolic damage



Q36

A 65-year-old woman has the recent appearance of a lesion at the site of a peripheral scar on the lung. The scar developed at the site of a pulmonary infarct 20 years ago. It was not present on her last x-ray 2 years ago. She has not smoked cigarettes for the past 20 years. A lobectomy is done. Which of the following is the most likely type of malignancy?

- A. Adenocarcinoma
- B. Malignant lymphoma
- C. Metastatic carcinoma
- D. Small cell carcinoma
- E. Squamous cell carcinoma

▼ Explanation

- Answer is A (Adenocarcinoma)

◦ IMP Clues

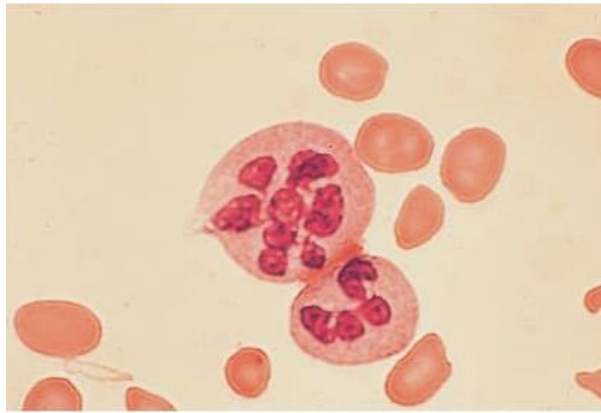
- Peripheral Scar (Site is important in differentiating lung cancers)
- Scar (adenocarcinoma commonly rise from sites of lung scarring, usually called "scar carcinoma")
- She has not smoked cigarettes for the past 20 years (smoking status is also one of the important aspects in differentiating lung cancers)

◦ Dx → Lung Adenocarcinoma

- Approaching Lung malignancies is often confusing, so let's get through the HY points you need to know for the USMLE.
- Adenocarcinoma is the **most common lung tumor**
 - **WEAKLY** associated with smoking (associated with **radon exposure** though)
 - Site → **Peripheral** (can present as **apical lesion** → **Pancoast tumor** or **SVC Syndrome** or **Brachiocephalic Syndrome**)
 - HY Paraneoplastic Syndromes:
 - **Hypercoagulability** (can present as **thrombosis** or **migratory thrombophlebitis** [Trousseau sign])
 - **Dermatomyositis** (violaceous eyelids rash + Shawl distribution rash + Gottron's papules + proximal muscle weakness)
 - **Hypertrophic Osteoarthropathy** (clubbing + joint pain + new bone formation, due to **fibrovascular proliferation**)
- Biopsy would show **glandular tissue morphology**

Q37

An otherwise healthy 82-year-old man is brought to the physician by his wife because of a 6-month history of progressive numbness and tingling in his toes bilaterally. His wife says that he also has had mildly increased short-term memory difficulties during this period. He has not been examined by a physician for the past 3 years. His vital signs are within normal limits. Physical examination shows normal muscle mass and tone. Muscle strength is 5/5 in the lower extremities. Patellar and calcaneal (Achilles) deep tendon reflexes are normal. Sensation to pinprick is decreased in the lower extremities below the level of the knees. He walks with a wide-based gait. Laboratory studies show a hemoglobin concentration of 9 g/dL, hematocrit of 28%, and platelet count of 175,000/mm³. A photomicrograph of a peripheral blood smear is shown. Which of the following is the most likely diagnosis?



- A. Anterior cord syndrome
- B. Central cord syndrome
- C. Hemicord syndrome
- D. Posterior cord syndrome
- E. Segmentary syndrome

▼ Explanation

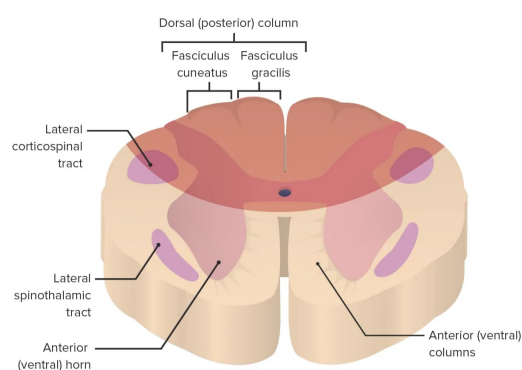
• Answer is D (Posterior Cord Syndrome)

◦ IMP Clues

- Progressive numbness and tingling in his toes bilaterally + sensation to pinprick is decreased (so fine sensation is affected, Dorsal Column)
- Memory difficulties (Psychiatric/memory affection)
- Normal mass mass & tone + intact muscle strength + deep tendon reflexes are normal (excludes affection of motor nerves/UMNL)
- Wide-base gait (could be due to Dorsal column affection or Spinocerebellar tract affection)
- Hemoglobin concentration of 9 + Hct 28% (anemic) + smear shows hypersegmented neutrophils (seals the deal)

• Dx → Posterior Cord Syndrome

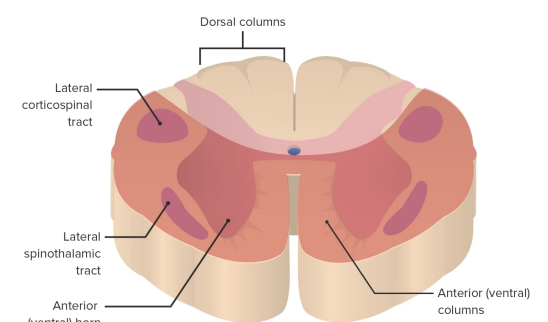
- This patient has **Vitamin B12 deficiency** (anemia + neurological, think Vitamin B12 or Vitamin E)
- **Anemia + hypersegmented neutrophils on smear is either B9 (folic acid) deficiency or B12 deficiency. Only B12 has the neurological symptoms.**
- **Subacute combined degeneration Triad is:**
 1. Affection of **Dorsal Column** (Vibration, Proprioception, Fine touch/sensation)
 2. Affection of **Spinocerebellar tract** (Ataxia)
 3. Affection of **Corticospinal tract** (Motor affection) [NOT PRESENT HERE]



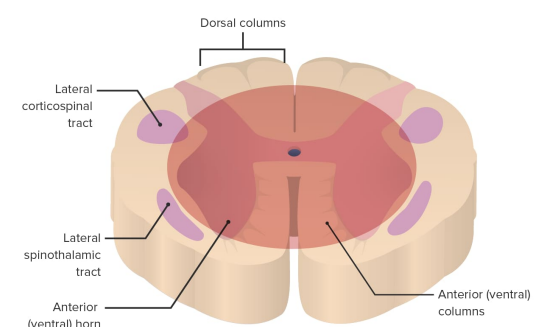
- In this Q, we have affection of the Dorsal column +/- spinocerebellar tract which cause the symptoms we have. The disease hasn't yet progressed to affect the corticospinal tract, which would cause the patient to have motor dysfunction.
- What the hell is "Posterior Cord Syndrome"?
 - We said that the dorsal column is affected, **the site of the dorsal column is the posterior aspect of the spinal cord, hence the name "posterior cord syndrome"**
- What else can cause "Posterior Cord Syndrome"?
 - **Occlusion of the Posterior Spinal artery**
 - **Tabes Dorsalis of tertiary Syphilis**

Let's review the other conditions as they are HY:

- **Choice A → Anterior Cord Syndrome** is caused by **Anterior spinal artery occlusion**.
 - **Presents as loss of all spinal cord functions EXCEPT DORSAL COLUMN:**
 - **Bilateral** loss of **motor function** below lesion
 - **Bilateral** loss of **pain & temperature** sensation below lesion



- **Choice B → Central Cord Syndrome** is associated with **syringomyelia**.
 - Syringomyelia is associated with **Chiari I malformation & trauma [asked on NBME]**
 - Presents as:
 - **Bilateral** loss of **temperature & pain sensation (Spinothalamic tract)** in **cape distribution** (upper chest, shoulders, arms, and hands). Lower limb may be affected but will be less severe.
 - **+/- motor power (Corticospinal tract)**



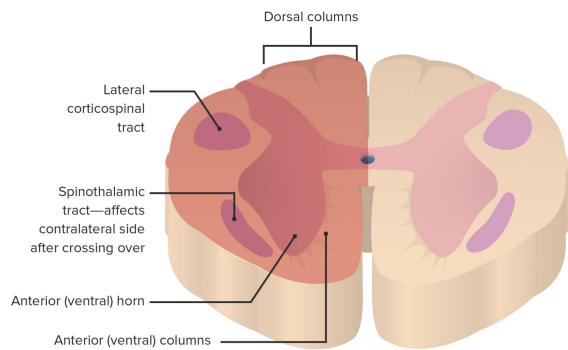
- **Choice C → Hemicord Syndrome is Brown-Sequard Syndrome**
 - Medical books always mention "stab wounds" as the etiology but **on the USMLE, SLE and viral infections are the common etiologies.**
 - Presents as:

? What are the HY Vitamin B12 complications?

▼ Answer

1. Hematological → **Macrocytic anemia (MCV > 100) + hypersegmented Neutrophils**
2. Neurological → **SCD & Memory affection**
3. Psychological → **Depression & Psychiatric symptoms**
4. Biochemical → **HIGH** Homocysteine & **HIGH** Methylmalonic acid
 - Vitamin B9 → **HIGH** Homocysteine & **NORMAL** Methylmalonic acid

- **Ipsilateral** loss of **vibration & proprioception (Dorsal Column)**
- **Ipsilateral** loss of **motor function (Corticospinal Tract)**
- **Contralateral** loss of **pain & temperature (Spinothalamic tract)**



Q38

A 39-year-old man comes to the physician because of darkening of his skin and fatigue during the past 4 months. He has a 3-year history of type 1 diabetes mellitus treated with insulin. Physical examination shows hepatomegaly and testicular atrophy. Serum studies show:

Na ⁺	138 mEq/L
K ⁺	4.1 mEq/L
AST	45 U/L
ALT	74 U/L
Testosterone	7 nmol/L (N=10–35)

Which of the following serum concentrations is most likely to be abnormal in this patient?

- A. Adrenocorticotrophic hormone
- B. Cortisol
- C. Ferritin
- D. Thyroid-stimulating hormone
- E. Uric acid

▼ Explanation

- **Answer is C (Ferritin)**
 - **IMP Clues**
 - Darkening of his skin (Could be hemochromatosis(it is), or increased ACTH secretion)
 - Type 1 DM + Hepatomegaly + testicular atrophy (hemosiderin deposition in skin, pancreas, liver, and testes causes dysfunction)
 - Testosterone 7nmol/L (Low, could be due to hypothalamic, pituitary, or testicular dysfunction 2ry to hemosiderin deposition)
 - Q asks which serum concentration is most likely to be abnormal in this patient?
 - **Dx → Hemochromatosis**
 - **AR**; mutation of **HFE gene** on **chromosome 6**
 - MOA → **Increased intestinal absorption of Iron** [asked on NBME]
 - **How?**
 - **Decreased** **Hepcidin** causes **increase** **ferroportin** → **increased** **intestinal iron absorption**
 - **Iron overload causes:**
 - **Deposits in skin** → **Hyperpigmentation / Bronze skin**
 - **Deposition in liver** → **Hepatomegaly, hepatitis & can progress to HCC**
 - **Deposits in tail of pancreas** → **DM & hypoglycemia**
 - Deposition in joints → **pseudogout (HY)**
 - Deposition in heart → **Cardiomyopathy** (Both dilated & restrictive cardiomyopathy)
 - **Deposition in testes, pituitary, hypothalamus** → **hypogonadism & infertility**
 - **Diagnosis**
 - **Ferritin > 300 ng/dl** (reflects huge amount of stored iron)
 - **Transferrin** decreased (availability of iron transporters decrease due to their being so much iron floating around)

Q39

A 65-year-old woman develops deep venous thrombosis of the right lower extremity 10 days after she underwent a right hip replacement. She has been receiving subcutaneous anticoagulant therapy since the procedure. Her platelet count is now 75,000/mm³, compared with 300,000/mm³ 10 days ago. Which of the following is the most likely underlying cause of this patient's condition?

- A. Acute myeloblastic leukemia
- B. Henoch-Schönlein purpura
- C. Heparin-induced thrombocytopenia
- D. Immune thrombocytopenic purpura
- E. Thrombotic thrombocytopenic purpura

▼ Explanation

- Answer is C (Heparin-induced thrombocytopenia)
 - IMP Clues
 - Woman with DVT after hip replacement surgery 10 days ago + has been receiving subcutaneous anticoagulant therapy (SC anticoagulant on the USMLE = Heparin; Oral anticoagulant = Warfarin)
 - Her platelets count is now 75,000 compared with 300,000/mm³ 10 days ago (10 days ago she started heparin & her PLT count was normal at the time, now it is decreased so it must be related)
 - Q asks for underlying cause of thrombocytopenia
- Dx → Heparin-Induced Thrombocytopenia (HIT)
 - This condition is super HY and all over the NBMEs
 - Heparin-induced thrombocytopenia is **decreased platelet count that occurs after heparin administration.**
 - MOA: **Autoantibodies against heparin-platelet factor 4 complex (PF4), which bind to the PLTs.**
 - **Causing the spleen to destroy these "tagged" PLTs ⇒ THROMBOCYTOPENIA**
 - USMLE can ask about the MOA as "anti-platelet production" or "destruction of platelets by spleen"
 - Treatment is to **STOP the heparin + administer Direct-Thrombin inhibitors (Factor 2 inhibitors)** like *Dabigatran, Lepirudin, Bivalirudin, or Argatroban.*
 - **WARFARIN IS INCORRECT.**

? Which of the following has a similar etiology as HIT?

A) Serum Sickness
B) Graves' Disease
C) Poison Ivy dermatitis
D) Hay Fever

▼ Answer

B) Grave's Disease (Type 2 HS)

Other Choices:

- A → Type 3 HS
- C → Type 4 HS
- D → Type 1 HS

Q40

A 47-year-old woman with multiple sclerosis is brought to the physician because of a 2-day history of bilateral lower extremity numbness. Muscle strength is 5/5 in the upper extremities. There is spastic paraparesis of the lower extremities. Deep tendon reflexes are brisk in the lower extremities, and there is sustained clonus at the ankles. Babinski sign is present bilaterally. Proprioception and sensation to vibration are diminished in the toes. Sensation to pinprick and temperature are normal. When asked to stand with her eyes closed and arms extended outward, the patient is unable to maintain balance. This patient's symptoms of abnormal sensation are most likely caused by damage to which of the following tracts?

- A. Dorsal spinocerebellar
- B. Fasciculus cuneatus
- C. Fasciculus gracilis
- D. Spinothalamic
- E. Ventral spinocerebellar

▼ Explanation

- Answer is C (Fasciculus Gracilis)
 - IMP Clues
 - MS + Deep tendon reflexes are brisk in the lower extremities + sustained clonus + Babinski sign (UMNL)
 - Proprioception and sensation to vibration are diminished in his toes (Dorsal column affected)
 - Sensation to pinprick and temperature are normal (Intact spinothalamic tract)
 - When asked to stand with her eyes closed and arm extended out, the patient is unable to maintain balance (ataxia + positive Romberg sign = Dorsal column affection; ataxia + negative Romberg sign = Cerebellar pathology)
 - Q asks the abnormal sensation in this patient is due to damage of which tract?

- We know that it is Dorsal Column. Dorsal column is made up of **2 tracts**
 - **Fasciculus Gracilis (medial)** → Conveys the proprioception and vibration sense from the **lower limb**
 - Mnemonic I use to remember that **Gracilis is the tract for the lower limb** is that we have a **muscle called the Gracilis muscle in our legs**.
 - **Fasciculus Cuneate (lateral)** → Conveys the proprioception and vibration sense from the **upper limb**
- Q says that "Proprioception and sensation to vibration are diminished in his **toes**", **so the lower limb is affected** → **Fasciculus Gracilis is our answer (Choice B)**

Q41

A 32-year-old woman comes to the emergency department after taking 40 1-mg tablets of alprazolam. She says that her boyfriend threatened to leave her, and she feels "empty." She drinks several six-packs of beer weekly and uses cocaine daily. She has outbursts of rage whether or not she is intoxicated. Which of the following is the most likely personality disorder?

- A. Antisocial
- B. Borderline
- C. Dependent
- D. Narcissistic

▼ **Explanation**

- **Answer is B (Borderline)**
 - **IMP Clues**
 - 40 1-mg tablets of alprazolam (Suicidal activity)
 - She says that her boyfriend threatened to leave her (Unstable personal relationships) + she feels empty (unstable self-image)
 - She has outbursts of rage whether or not she is intoxicated (unstable emotions)
 - **Dx → Borderline Disorder**
 - Patients have **Unstable relationships, self-image, emotions, and impulsivity**
 - Maybe associated with **suicidal behaviors**

Q42

A 62-year-old woman is brought to the emergency department 30 minutes after her husband found her on the bedroom floor, awake but unable to move her arms or legs. She has a history of type 2 diabetes mellitus, hypertension, and hyperlipidemia. Her current medications are insulin, clonidine, and simvastatin. Her blood pressure is 173/95 mm Hg. Horizontal eye movements are impaired bilaterally; vertical eye movements are intact. Her speech is dysarthric. Examination of the extremities shows quadriplegia. An MRI of the brain is most likely to show a lesion at which of the following locations?

- A. Medulla
- B. Midbrain
- C. Pons
- D. Putamen
- E. Thalamus

▼ **Explanation**

- **Answer is C (Pons)**
 - Awake but unable to move her arms or legs + Examination of the extremities shows quadriplegia (so quadriplegia, duh)
 - History of T2DM + hypertension + BP is 173/95 mmHg + hyperlipidemia (most definitely this is due to a stroke that caused quadriplegia, ringing any bells yet?)
 - Horizontal eye movement impaired + vertical eye movements are intact (will yap about this finding in details below, if you're a neuroscience nerd)
- **Dx → Locked-in Syndrome**
 - Most commonly caused by **basilar artery stroke** (which supply the Pons [Choice C])
 - This causes the patient to be literally locked in → **Can't move (Quadriplegia), Can't talk (Dysarthria), Can't look side-to-side (impaired horizontal eye movement)**.
 - Can also be caused by **Central Pontine Myelinolysis**

- **When you correct hyponatremia quickly with hypertonic saline** → Water leaves the tissues rapidly → causing shrinkage and apoptosis of cells → **Central Pontine Myelinolysis** ⇒ **Locked-in Syndrome**

? What would happen if you correct hypernatremia quickly with hypotonic saline?

▼ **Answer**

Cerebral Edema - Water enters tissue rapidly → Edema of cells → Cerebral Edema

Correcting **hyp**Onatremia quickly = **p**Ontine (central pontine myelinolysis)

Correcting **Hyp**Ernatremia quickly = **E**dema (cerebral edema)

[For Nerds]

Why is horizontal eye movement impaired in Locked-in Syndrome while vertical movement is intact?

- **Horizontal gaze** is mediated by **centers found in the pons**, specifically the *paramedian pontine reticular formation* & the *abducens nerve nuclei* ⇒ Together **they mediate the horizontal eye movements**.
 - Another nerdy detail is that the **basilar artery supplies the ventral pons**, so centers in the **dorsal pons are spared**: **The Reticular Formation is there & is spared** → **Patient is awake but can't move**. Get it?
- **Vertical gaze** is mediated by **centers found in the midbrain**, which are **spared** in **basilar artery strokes**.
 - Other spared actions are **blinking**

The End Result of Locked-In Syndrome is:

1. **Can't** move (Quadriplegia)
2. **Can't** talk well (Dysarthria)
3. **Can't** look side-to-side (impaired horizontal gaze)
4. **IS** awake & alert
5. **CAN** BLINK
6. **CAN** look up-and-down

Q43

A 13-year-old girl is brought to the office because of a 1-day history of itchy red spots on her face and neck. She returned 1 day ago from a trip to a neighboring state for a swim meet. Her team had stayed at a hotel where she and several of her teammates noted small bugs in their beds. She captured three of these and brought them home. Her mother put them in alcohol to kill them and brought them to the physician's office. The bugs are shown in the photographs. This patient is at increased risk for infection with which of the following as a result of these findings?



- A. Cytomegalovirus
- B. Herpes simplex virus
- C. HIV
- D. Staphylococcus aureus
- E. Streptococcus pneumoniae

▼ **Explanation**

- **Answer is D (Staphylococcus aureus)**
 - **IMP Clues**
 - Itchy red spots on her face and neck for 1 day (sounds like a rash of some sort)
 - Returned from a trip 1 day ago + stayed at hotel where they note small bug in their beds (so hx of travel + bed bugs + rash appeared in that time frame so must be related)

- Picture given shows bed bugs (scientific name is Cimex Lectularius, "lectularius" in Latin means literally "of the bed", so bed bugs)
- Q asks what is the patient at increased risk of?
 - These are **bed bugs**. They are blood-feeding insects that usually affect **travelers, and the users of used unwashed bed sheets**.
 - **Bite is *painless* and causes red "spots" with a central hemorrhagic punctum in a cluster or linear distribution that appear after waking up** (the bugs were hammering you while you sleep)
 - Bites resolve spontaneously in a week or so.
- The bites are painless, yes, **but they are *extremely itchy***.
- This causes you to use your fingernails and scratch the skin surface → **damaging the skin protective layer → opens way for secondary bacterial infection.**
 - Most common bacteria that cause skin infections, especially secondary infections?
 - **Staphylococcus aureus (Choice D)**
 - *"Basically, what this Q is assessing is that bed bugs are common in travelers, the bites themselves are not a risk, but what we worry about is 2ry bacterial infection, which is most commonly caused by Staph aureus. Easy."*

Q44

A 64-year-old woman is found dead at the foot of her basement steps. A photograph of the liver obtained at autopsy is shown. Which of the following is the most likely diagnosis?



- A. Abscess
- B. Cirrhosis
- C. Focal nodular hyperplasia
- D. Hepatitis B infection
- E. Infarct
- F. Metastatic breast cancer

▼ **Explanation**

- **Answer is F (Metastatic breast cancer)**

- **IMP Clues**

- 64-year-old woman (Post-menopausal age is risk factor for some cancers)
- Liver autopsy picture shows multiple lesions (knowing multiple lesions = usually metastasis is how you answer this Q)

- **Dx → Metastatic breast cancer**

- All you need to know to answer this Q is, when ever you see **multiple lesions** in **commonly "metastasized to" organs (liver, spine, lung, brain)**, especially in **older patients** or patients with evident **risk factors** ⇒ **THINK OF METASTASIS.**

- USMLE assess this all the time in different ways:

- **65M + acute back pain + XRAY shows multiple *osteoblastic* lesions?**
 - Answer ⇒ Metastatic *prostate* cancer
- **72M + jaundice + CT shows *multiple hepatic* lesions?**
 - Answer ⇒ Metastatic *colon* cancer
- **62F + hx of breast cancer + CXR shows *multiple lung* lesions?**
 - Answer ⇒ Metastatic *breast* cancer
- **32F + hx of mole + MRI shows *multiple brain lesions* OR seizures?**
 - Answer ⇒ Metastatic *choriocarcinoma*

▮ **All these Qs & more are found all over the NBMEs. Get used to vague vignettes & using what you have.**

Q45

A 16-month-old boy is brought to the physician for a follow-up examination. He has had recurrent bacterial infections since the age of 8 months. Findings on a complete blood count, including leukocyte differential, are within the reference ranges. Further testing of the patient's leukocytes shows normal oxidative burst. His serum immunoglobulin concentrations are uniformly decreased. Which of the following additional findings is most likely in this patient?

- A. Absence of germinal centers in lymph nodes
- B. Absent neutrophil chemotaxis
- C. Decreased CD4+ T-lymphocyte count
- D. Decreased complement concentrations
- E. Impaired intracellular bactericidal activities in neutrophils

▼ Explanation

- Answer is A (Absence of germinal centers in lymph nodes)

- IMP Clues

- Recurrent bacterial infections since the age of 8 months (remember that mother's IgG last in babies for around 6 months, this is why many hereditary immunodeficiencies, especially ones where the abnormalities in B-cells/Igs, present after 6 months)
- Leukocyte differential are within the reference ranges + normal oxidative burst (This excludes any neutrophil associated pathologies or dysfunction like CGD)
- His serum immunoglobulin concentrations are uniformly decreased (all of them are decreased, this means the pathology is from the source. What is the source? B-cells.)
- Q asks what additional finding is expected in this patient?

- Dx → Bruton Agammaglobulinemia (X-Linked Agammaglobulinemia)

- X-Linked Recessive Disorder, characterized by **isolated B-cell deficiency**
 - **No B-cells = No plasma cells = No immunoglobulins/antibodies = No humoral Immunity**
- Presents as **recurrent BACTERIAL infections** starting for 6 months of age
 - Maternal IgGs are present in the first 6 months
 - **If the vignette has bacterial + viral/fungal infections too → NOT XLA.**
- Physical Examination shows **ABSENT/SCANTY tonsils & lymph nodes**
 - Germinal centers of lymph nodes / tonsillar tissue is made up of B-cells.
 - This piece of info is super HY guys. Previous NBME had the exact same presentation but said "No tonsillar tissue" → answer was "Bruton Agammaglobulinemia."



HY PHRASES YOU MUST KNOW

"ABSENT/SCANTY tonsils," "ABSENT/SCANTY lymph nodes," or "ABSENT Germinal Centers in lymph nodes"

- **B-cells are absent** ⇒ think **Bruton XLA**
- Presents with **ONLY BACTERIAL INFECTIONS**

"ABSENT Thymic Shadow," or "Candida Skin Test/PDD shows no induration or erythema"

- **T-Cells are absent** ⇒ think **Thymic aplasia as in DiGeorge Syndrome**
- Presents as **ONLY FUNGAL / VIRAL / PROTOZOA INFECTIONS**

If Both

- **B-cells & T-cells are absent** ⇒ think **Severe Combined Immunodeficiency**
- Presents as **BACTERIAL INFECTIONS + FUNGAL / VIRAL / PROTOZOA INFECTIONS**

Q46

A 56-year-old woman comes to the physician because of a 3-week history of increasing weakness of her arms and legs. She has smoked 1 pack of cigarettes daily for 30 years. Physical examination shows pronounced weakness of the hip girdle muscles and lesser weakness of the shoulder girdle muscles, both of which improve with repetitive testing. A chest x-ray shows a hilar lung mass. Electromyography is compatible with a malfunction of the neuromuscular junction. Impairment of which of the following is the most likely cause of these findings?

- A. Acetylcholinesterase
- B. Binding of acetylcholine on the postsynaptic membrane
- C. Direct depolarization of muscle fibers by Ca^{2+}
- D. Postsynaptic membrane potential
- E. Presynaptic release of acetylcholine

▼ Explanation

- Answer is E (Presynaptic release of acetylcholine)

- **IMP Clues**
 - Smoked 1 pack of cigarettes daily for 30 years (Smoking is a very HY risk factor/association)
 - Weakness of the hip girdle muscles and weakness of the shoulder girdle muscles (proximal muscle weakness bro, why the yapping)
 - Both of which improve with repetitive testing (Bingo, this is the Highest Yield sentence we need)
 - CXR shows a hilar lung mass (the SCLC)
 - Q tells us that this is a NMJ malfunction and asks us for the cause.

• **Dx → Lambert Eaton Syndrome**

- Etiology → Antibodies against **pre-synaptic** voltage-gated **calcium** channels
 - normally, Action potential → pre-synaptic voltage-gated calcium channels → Calcium influx → release of ACh vesicles into synapses → binds to ACh Receptors → Muscle contraction
- Behavior → Weakness **improves** with **repeated movements**
 - mMore APs → APs overcome number of calcium channels → Calcium influx → ACh released from vesicles into synapses → Muscles contraction
 - Qs can say **“swings chair multiple times before getting up”** instead of repeated movements.
- Associated Tumors → **SCLC AND Prostate Cancer**
- **Response to Tensilon test (edrophonium) → NO** improvement

? 42F+ muscle weakness + diplopia / ptosis / weakness at end of day. CT shows a mediastinal mass. Which embryological origin is the mass derived from?

▼ **Answer**

Third Pharyngeal Pouch - Great 3rd order Q from me I know.
Basically, I assessed that you know that the **diagnosis is MG**. Then, I assessed that you know that **MG is associated with Thymoma**. Then I assessed if you knew where is the **Thymus derived from**. Is that Important? Yes.
DiGeorge Syndrome is HY (hypocalcemia + T-cell deficiency) caused by **deletion in the gene (22q11)** that causes malformation of **3rd pharyngeal pouch** (gives up **inferior parathyroid glands & thymus**) and **4th pharyngeal pouch** (gives us **superior parathyroid gland**)

Myasthenia Gravis

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

Q47

A 31-year-old primigravid woman at 28 weeks' gestation comes to the physician because of a 1-week history of a nonproductive cough. Her temperature is 38.6°C (101.4°F), pulse is 88/min, respirations are 24/min, and blood pressure is 128/88 mm Hg. Laboratory studies and a chest x-ray show evidence of interstitial pneumonia. Tetracycline is contraindicated in this patient because of its toxicity to which of the following organs in the fetus?

- A. Bone
- B. Ear
- C. Eye
- D. Kidney
- E. Liver

▼ **Explanation**

- **Answer is A (Bone)**
 - Q asks why is tetracyclines contraindicated in pregnant women, for it affects what organ?
 - Easy pharmacology Q.
 - **Tetracyclines chelate calcium, hence why a common side effect of tetracyclines is teeth discoloration.**
 - It makes sense that it would be **contraindicated in pregnancy, as it would bind to bones and teeth of the fetus (where the calcium is) and cause deformities.**
 - USMLE also tests this concept somewhere by telling you that **“a guy takes his tetracyclines with milk, and asks you why isn’t the drug working.”** Answer is → **Calcium in milk chelates tetracyclines.**

Q48

Which of the following sets of serum findings is most likely in a 50-year-old man with recently diagnosed chronic renal failure?

Choices	Phosphate	Ca ²⁺	Parathyroid Hormone
A.	↑	↑	↑
B.	↑	↑	↓
C.	↑	↓	↑

Choices	Phosphate	Ca ²⁺	Parathyroid Hormone
D.	↑	↓	↓
E.	↓	↑	↑
F.	↓	↑	↓
G.	↓	↓	↑
H.	↓	↓	↓

▼ Explanation

- **Answer is C**
 - On the USMLE, **Renal Failure = Secondary Hyperparathyroidism**. Know this.
 - So Q is asking, what are the expected arrows of 2ry Hyperparathyroidism?
 - Kidney is fucked up, so can't do it work.
 - **Can't reabsorb Calcium → Hypocalcemia**
 - **Can't secrete Phosphate → Hyperphosphatemia**
 - **Hypocalcemia + Hyperphosphatemia ⇒ PTH increases**
 - PTH can't work on kidneys as they are failing. So, increased PTH doesn't do anything.

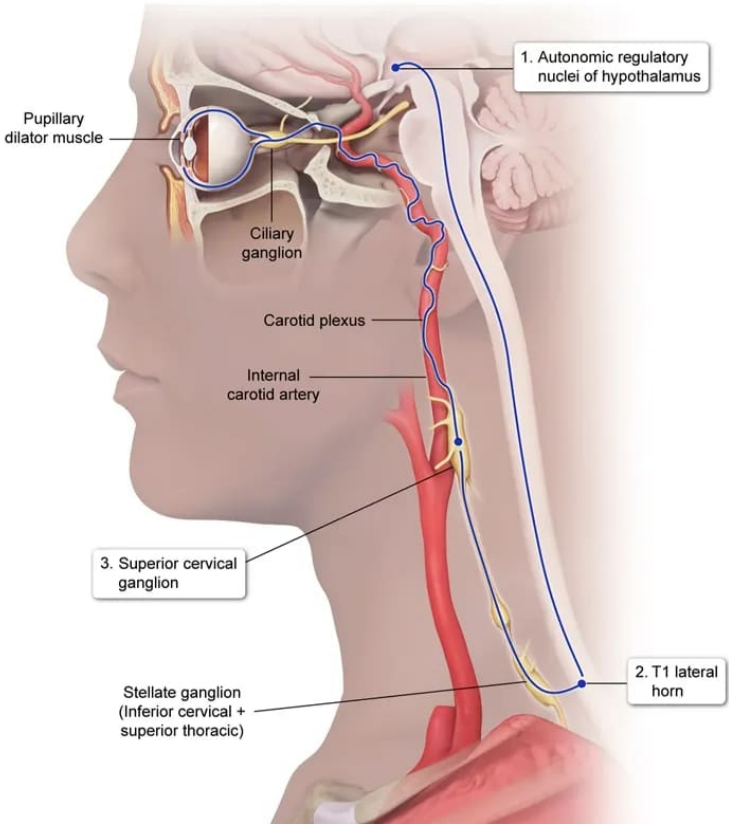
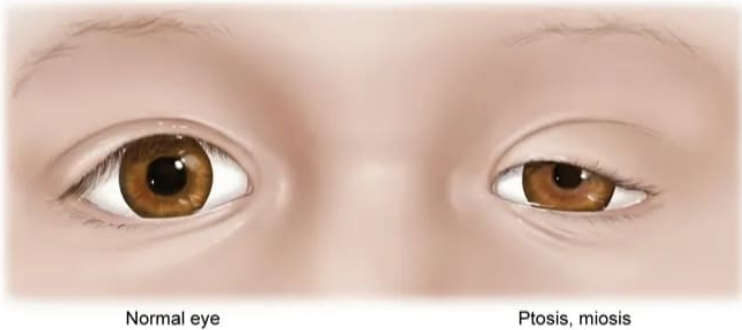
Q49

Electrical stimulation of the stellate ganglion is most likely to result in an increase in which of the following?

- A. Bronchoconstriction in the lung
- B. Glandular secretion in the esophagus
- C. Heart rate
- D. Peristalsis in the esophagus
- E. Vasodilation in the skin of the upper extremity

▼ Explanation

- **Answer is C (Heart rate)**
 - If you know what the stellate ganglion is, then this would be an easy Q.
 - **Stellate ganglia is a sympathetic ganglion that supplies the head, neck, upper limbs, and thorax.**
 - So, **increased stimulation of sympathetic system ⇒ Increased HR**
 - **What else should you know?**
 - Stellate ganglion is also involved in the **Oculosympathetic innervation** of the eye.
 - **Injury/Compression of Stellate Ganglion in cases of Pancoast tumor causes Horner Syndrome (Ptosis - Miosis - Anhidrosis)**



- If you didn't know what the stellate ganglion is, you could've answered the Q by just looking at the answer choices:
 - **Choices A, B, D, and E are Parasympathetic activities.**
 - Hence, leaving **Choice C** as the only **Sympathetic activity**.

Q50

Which of the following properties of integral membrane proteins results in their becoming anchored within the membrane?

- A. Disulfide bond formation between the protein and its phosphatidylinositol anchor
- B. Extensive hydrogen bonding of the amino acid side chains of the protein and the membrane phospholipid tails
- C. Extensive hydrophobic interactions between the amino acid side chains of the protein and the membrane phospholipid tails
- D. Formation of ionic bonds between the amino acid side chains and the phospholipid tails
- E. Formation of β -pleated sheet structures to maximize protein interactions with the phospholipid head group

▼ **Explanation**

- **Answer is C**

- This Q assess the features of integral proteins. There is like one other NBME Q regarding this topic, so if you hate cell biology, you can get away but just knowing the following:

- **Integral Membrane Proteins:**

- Location → **Embedded in membrane** (Spans membrane whole thickness)
- Binding → **Hydrophobic** (cell membrane phospholipid tails are hydrophobic, so to stay "within" must also be hydrophobic)

- **Now let's look at peripheral proteins in comparison:**

- Location → **Attached to membrane surface**
- Binding → **Hydrophilic** (attached to hydrophilic heads on the external of the the phospholipid membrane)



There was this Q on some NBME that asked for what would be found in integral proteins but is not found in peripheral proteins & they listed a cell biology garbage. Answer was **"Transmembrane region"**.

- It is the region that anchors the protein into the membrane, making it an integral protein.



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