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Question: 3467

Rifampicin binds the β -subunit of bacterial DNA-dependent RNA polymerase and sterically blocks the exit tunnel for nascent RNA. Which codon mutation within the *rpoB* gene is the most frequent molecular marker of rifampicin resistance used in rapid diagnostic assays?

- A. GyrA D94G substitution affecting DNA gyrase
- B. A1401G alteration in the 16S rRNA gene
- C. S531L substitution in the RNA polymerase β -subunit
- D. K65R mutation in reverse transcriptase

Answer: C

Explanation: The rifampicin-resistance-determining region of *rpoB* encodes amino acids that line the RNA exit channel. The S531L missense mutation alters a critical residue that contacts the drug, reducing binding affinity by several orders of magnitude while still permitting sufficient polymerase function for mycobacterial survival; this single nucleotide change accounts for the majority of clinically significant rifampicin-resistant isolates and is detected by line-probe and GeneXpert assays.

Question: 3468

Tissue bridges spanning the depths of a wound are pathognomonic of which category of mechanical injury?

- A. Laceration produced by blunt-force trauma
- B. Stab wound produced by a pointed instrument
- C. Incised wound produced by a sharp-edged weapon
- D. Chop wound produced by a heavy sharp weapon

Answer: A

Explanation: Blunt force tears the skin and deeper tissues irregularly, leaving strands of intact blood vessels, nerves and connective tissue that stretch across the wound depths. These bridges are never seen in cleanly divided sharp-force injuries.

Question: 3469

A 50-year-old female with long-standing type 2 diabetes mellitus presents for routine evaluation. Her best-corrected visual acuity is 20/30. Examination of the macula using optical coherence tomography reveals diffuse retinal thickening and intraretinal cystoid spaces within the outer plexiform and inner nuclear layers centered around the fovea, with no tractional component. Which of the following is the most appropriate first-line treatment intervention for this condition?

- A. Immediate grid-pattern thermal laser photocoagulation applied directly across the entire area of non-perfused macular zones
- B. Urgent pars plana vitrectomy with removal of the posterior hyaloid face and internal limiting membrane peeling
- C. Intravitreal injection of anti-vascular endothelial growth factor agents to reduce vascular permeability and macular edema
- D. Systemic administration of high-dose systemic corticosteroids combined with oral carbonic anhydrase inhibitors

Answer: C

Explanation: Diabetic macular edema driven by increased vascular permeability is primarily treated with intravitreal anti-VEGF medications as the first-line standard of care, which significantly superiorly improve visual outcomes compared to historical

grid laser photocoagulation. Focal laser is now reserved as a secondary or adjunctive treatment.

Question: 3470

A 62-year-old male with severe heart failure develops bilateral tender gynecomastia and sexual dysfunction after six months of medical therapy targeting the renin-angiotensin-aldosterone system. His physician decides to substitute the offending medication with eplerenone. What is the fundamental pharmacological difference between the old and new medication that resolves this side effect?

- A. Exhibits lower binding affinity for androgen and progesterone receptors, significantly reducing endocrine side effects.
- B. Has a substantially longer elimination half-life, allowing for less frequent dosing and reduced systemic tissue accumulation.
- C. Inhibits the epithelial sodium channel directly, bypassing the need for mineralocorticoid receptor binding completely.
- D. Requires conversion in the liver to active metabolites to exert its potassium-sparing and anti-fibrotic diuretic effects.

Answer: A

Explanation: The patient originally received spironolactone, a non-selective mineralocorticoid receptor antagonist. In addition to blocking aldosterone, spironolactone inadvertently binds to and antagonizes androgen receptors and acts as an agonist at progesterone receptors, leading to side effects like gynecomastia, impotence, and menstrual irregularities. Eplerenone is a highly selective mineralocorticoid receptor antagonist. Because it has minimal affinity for androgen and progesterone receptors, it maintains the mortality benefits in heart failure without causing the endocrine side effects.

Question: 3471

A diabetic patient develops clinically significant macular edema (CSME) with persistent fluid accumulation threatening the foveal center. Intravitreal pharmacotherapy targeting vascular endothelial growth factor is initiated. What is the primary molecular rationale for utilizing anti-VEGF agents in this condition?

- A. Inhibition of leukostasis and reduction of inflammatory cytokine expression within the outer plexiform layer
- B. Upregulation of tight junction proteins zonula occludens-1 within retinal pigment epithelial cells
- C. Neutralization of circulating and tissue-bound isoforms of VEGF to reduce vascular permeability and endothelial proliferation
- D. Stimulation of pericyte proliferation and stabilization of the capillary basement membrane architecture

Answer: C

Explanation: Vascular endothelial growth factor (VEGF) is a potent vasopermeability factor and mitogen upregulated in diabetic retinopathy due to retinal hypoxia. Anti-VEGF agents bind to and neutralize VEGF isoforms, reducing abnormal vascular permeability, resolving macular edema, and inhibiting regression or progression of retinal neovascularization.

Question: 3472

A patient receiving phenoxybenzamine for pheochromocytoma experiences profound orthostatic hypotension. Which pharmacologic property of the drug

accounts for the prolonged duration of this adverse effect?

- A. Partial agonist activity at α_2 -receptors that dampens sympathetic outflow
- B. Rapid redistribution into lipid stores followed by slow release
- C. Irreversible covalent alkylation of α -adrenergic receptors
- D. Competitive reversible antagonism at α_1 -receptors with short half-life

Answer: C

Explanation: Phenoxybenzamine forms a covalent bond with the α -receptor, producing non-competitive, irreversible blockade. New receptors must be synthesized before vascular tone recovers, resulting in prolonged orthostatic hypotension that can last 24–48 hours after a single dose.

Question: 3473

A 10-month-old infant with severe malnutrition and chronic diarrhea has flat small-bowel mucosa on biopsy and negative celiac serology. The most likely diagnosis is:

- A. Autoimmune enteropathy
- B. Cow's-milk protein allergy
- C. Celiac disease with false-negative serology
- D. Tropical sprue

Answer: B

Explanation: In young infants, especially those with severe malnutrition, cow's-milk protein allergy can produce a flat mucosal biopsy indistinguishable from celiac disease; negative celiac serology and clinical improvement after elimination of cow's-milk protein confirm the diagnosis.

Question: 3474

Which of the following best describes the key difference between innate and adaptive immunity?

- A. Adaptive responses are identical upon first and subsequent antigen exposure
- B. Innate responses are antigen-specific and generate long-lived memory cells
- C. Adaptive responses act within minutes and rely solely on phagocytosis
- D. Innate responses are rapid, non-specific, and lack immunologic memory

Answer: D

Explanation: Innate immunity provides immediate, broad protection through barriers, phagocytes, complement, and natural killer cells, but does not refine its recognition or retain memory. Adaptive immunity requires days to activate, is highly antigen-specific via T- and B-cell receptors, and generates memory cells that accelerate subsequent responses. This temporal and specificity dichotomy underpins the complementary roles of the two systems.

Question: 3475

A hematology panel indicates pure red cell aplasia. During normal adult erythropoiesis, which specific sequential transition marks the final stage before the extrusion of the nucleus to form a reticulocyte?

- A. The transformation of an orthochromatic normoblast into a circulating anucleated erythrocyte precursor
- B. The conversion of a myeloblast into a metamyelocyte within the vascular sinuses of the bone marrow
- C. The differentiation of a colony-forming unit-erythroid directly into a proerythroblast without cell division
- D. The maturation of a promegakaryoblast into a fully functional platelet-shedding megakaryocyte

Answer: A

Explanation: Erythropoiesis in the bone marrow proceeds through distinct morphological stages: proerythroblast, basophilic normoblast, polychromatophilic normoblast, and orthochromatic normoblast. The orthochromatic normoblast contains a condensed, pyknotic nucleus that is extruded from the cell, yielding a reticulocyte that enters the circulation.

Question: 3476

A patient with a progressive nasal fibrovascular conjunctival growth extending onto the cornea develops induced with-the-rule astigmatism and a vertical iron line at the advancing edge. What is the most accurate histopathological description of this lesion?

- A. Amyloid deposition within the substantia propria of the conjunctiva
- B. Elastotic degeneration of collagen with fibrovascular proliferation
- C. Squamous epithelial hyperplasia without stromal invasion
- D. Granulomatous inflammation surrounding foreign-body material

Answer: B

Explanation: Pterygium is characterized by elastotic degeneration of collagen within the substantia propria accompanied by fibrovascular proliferation that invades the cornea. The vertical iron line (Stocker's line) forms at the head due to tear-film disruption. This histological pattern differentiates true pterygium from pinguecula or neoplastic lesions.

Question: 3477

Active vitamin D (1, 25-dihydroxycholecalciferol) exerts its primary effects on calcium homeostasis by binding to an intracellular nuclear receptor. In the small intestine, what is the principal molecular mechanism by which this hormone enhances active calcium absorption across the brush border membrane?

- A. Direct activation of the brush border sodium-calcium exchanger protein
- B. Stimulation of basolateral calcium ATPase pump through direct phosphorylation
- C. Induction of paracellular tight junction permeability to divalent cations
- D. Upregulation of calbindin-D9k synthesis and apical calcium channels

Answer: D

Explanation: Calcitriol binds to the vitamin D receptor (VDR), altering gene transcription to increase the expression of apical calcium entry channels (such as TRPV6), intracellular calcium-binding proteins (calbindin-D9k) that ferry calcium across the enterocyte, and basolateral extrusion pumps (PMCA1b and NCX1), thereby optimizing mineral uptake.

Question: 3478

In the thorax the azygos vein arches over the root of which lung structure before entering the superior vena cava?

- A. Right pulmonary artery
- B. Right main bronchus
- C. Left main bronchus
- D. Left pulmonary artery

Answer: B

Explanation: The azygos vein ascends on the right side of the vertebral column and arches anteriorly over the right main bronchus at the level of the fourth thoracic vertebra to join the superior vena cava. This relationship is constant and of surgical importance during right pneumonectomy.

Question: 3479

A patient returning from a malaria-endemic zone presents with cyclical high-grade fever and chills. Microscopic evaluation of blood smears confirms *Plasmodium falciparum*. The physician prescribes Artemisinin-based Combination Therapy (ACT). What is the primary epidemiological rationale for using this combination therapy rather than artemisinin monotherapy?

- A. To decrease the financial cost of mass antimalarial treatment for public health programs.
- B. To provide simultaneous broad-spectrum treatment for potential co-infection with *Plasmodium vivax*.
- C. To delay the emergence and spread of artemisinin drug resistance in the parasite population.
- D. To reduce the acute hepatic toxicity and adverse effects directly associated with

artemisinin derivatives.

Answer: C

Explanation: Artemisinin derivatives are highly potent and rapidly clear parasite biomass, but they have a very short half-life. If used as monotherapy, surviving parasites are exposed to sub-therapeutic drug levels, which strongly selects for resistant mutations. By combining artemisinin with a longer-acting partner drug, the partner drug eliminates the remaining parasites, thereby delaying the emergence and spread of artemisinin resistance in endemic regions.

Question: 3480

A patient undergoing a hemodynamic study is administered phentolamine intravenously, followed ten minutes later by a high-dose intravenous bolus of epinephrine. The attending physician observes a paradoxical drop in systemic blood pressure rather than the expected elevation. Which receptor dynamic explains this "epinephrine reversal" phenomenon?

- A. Antagonism of alpha-1 receptors unmasks epinephrine-mediated beta-2 receptor vasodilation and subsequent hypotension.
- B. Downregulation of alpha-1 receptors leads to a blunted vasoconstrictive response to systemic catecholamines.
- C. Activation of presynaptic alpha-2 receptors decreases sympathetic outflow and subsequent norepinephrine release.
- D. Blockade of beta-1 receptors in the myocardium directly reduces cardiac output and systemic perfusion pressure.

Answer: A

Explanation: Epinephrine is a non-selective adrenergic agonist that activates both alpha (vasoconstrictive) and beta (vasodilatory and inotropic/chronotropic) receptors. Under normal circumstances, high-dose epinephrine produces a net pressor response due to dominant alpha-1 mediated vasoconstriction. When phentolamine (a non-selective alpha-antagonist) is administered first, the alpha-1 receptors are blocked. Subsequent epinephrine administration leads to unopposed beta-2 receptor activation in the vascular smooth muscle, causing profound vasodilation and a paradoxical decrease in blood pressure.

Question: 3481

During an experiment investigating autonomic regulation of cardiac output, stimulation of the vagus nerve results in a negative chronotropic effect. At the cellular level in the sinoatrial nodal cells, which specific ionic conductance change mediates this parasympathetic response?

- A. Upregulation of hyperpolarization-activated cyclic nucleotide-gated sodium influx currents
- B. Activation of G-protein coupled inwardly rectifying potassium channels coupled with suppression of funny current channels
- C. Blockade of transient L-type calcium channels leading to a prolonged phase 0 depolarization slope
- D. Enhancement of transient T-type calcium channel conductance combined with accelerated sarcoplasmic calcium uptake

Answer: B

Explanation: Parasympathetic stimulation releases acetylcholine, which binds to cardiac muscarinic M2 receptors. This activates a pertussis toxin-sensitive G-protein

whose beta-gamma subunits directly open acetylcholine-activated potassium channels, increasing potassium conductance and hyperpolarizing the cell. Simultaneously, the alpha subunit inhibits adenylyl cyclase, lowering cyclic adenosine monophosphate levels and suppressing the funny current channels that drive pacemaker depolarization, thereby slowing the heart rate.

Question: 3482

A 4-year-old child with steroid-sensitive nephrotic syndrome presents with sudden abdominal pain, fever, and hypotension. The most important immediate diagnostic consideration is:

- A. Acute appendicitis
- B. Renal-vein thrombosis
- C. Steroid-induced gastritis
- D. Primary peritonitis

Answer: D

Explanation: Children with nephrotic syndrome are profoundly immunocompromised because of urinary loss of immunoglobulins and complement factors, predisposing them to encapsulated bacterial infections, especially primary peritonitis caused by *Streptococcus pneumoniae*. Prompt blood and ascitic-fluid cultures and empiric antibiotics are mandatory.

Question: 3483

A 27-year-old woman is evaluated for acute pelvic inflammatory disease. She

reports severe nausea, vomiting, high fever, and right upper quadrant pleuritic pain radiating to the right shoulder. Transvaginal ultrasound shows no pelvic abscess, but liver function tests show mild transaminitis. What specific clinical syndrome explains these upper abdominal findings?

- A. Acute viral hepatitis type B presenting concurrently with ascending genital infection
- B. Acute cholecystitis secondary to obstructing gallstones within the cystic duct
- C. Subdiaphragmatic appendiceal perforation leading to localized peritoneal abscess
- D. Fitz-Hugh-Curtis syndrome characterized by perihepatic inflammation and capsular adhesions

Answer: D

Explanation: Fitz-Hugh-Curtis syndrome is an extra-pelvic complication of pelvic inflammatory disease caused by the direct spread or lymphatic translocation of pathogens—most notably *Chlamydia trachomatis* or *Neisseria gonorrhoeae*—onto the liver capsule, producing perihepatitis characterized by characteristic "violin-string" adhesions and right upper quadrant pain.

Question: 3484

A 6-month-old infant presents with fever, cough, wheezing, and increased work of breathing. Oxygen saturation is 92% on room air. Chest X-ray shows hyperinflation and peribronchial thickening. Which management step is most supported by evidence?

- A. Systemic corticosteroids
- B. Nebulized hypertonic saline in the emergency department
- C. Supportive care with oxygen and hydration

D. Nebulized salbutamol trial and continue if responsive

Answer: C

Explanation: Bronchiolitis (typically RSV) is managed with supportive care: oxygen to maintain saturation >90%, hydration, and nasal suctioning. Bronchodilators, steroids, and hypertonic saline are not routinely recommended in typical cases, though a single salbutamol trial may be considered in some guidelines. Evidence does not support routine use of these therapies.

Question: 3485

A 50-year-old woman is diagnosed with ductal carcinoma in situ (DCIS), 2.5 cm, ER-positive, margins negative after wide local excision. According to current surgical oncology guidelines, what margin width is considered adequate for DCIS treated with breast-conserving therapy plus radiotherapy?

- A. At least 5 mm
- B. No ink on tumor
- C. At least 1 mm
- D. At least 2 mm

Answer: D

Explanation: For pure DCIS treated with breast-conserving surgery and radiotherapy, a margin of at least 2 mm is recommended to reduce local recurrence. “No ink on tumor” is adequate for invasive cancer but not for pure DCIS. Margins of 1 mm are insufficient for DCIS. A 5-mm margin is not required and may lead to unnecessary re-excision.

Question: 3486

A 3-year-old boy presents with progressive proximal muscle weakness, difficulty climbing stairs, and frequent falls. Physical examination shows Gowers' sign and pseudohypertrophy of calf muscles. Creatine kinase level is 15,000 IU/L. Which genetic abnormality is most likely?

- A. Trinucleotide repeat expansion on chromosome 4
- B. Mutation in SMN1 gene on chromosome 5
- C. Deletion of dystrophin gene on X chromosome
- D. Trinucleotide repeat on chromosome 19

Answer: C

Explanation: This presentation is classic for Duchenne muscular dystrophy (DMD), an X-linked recessive disorder caused by mutations (most commonly deletions) in the dystrophin gene on Xp21. Dystrophin is essential for muscle membrane stability. Clinical features include onset between 2-5 years, proximal muscle weakness, Gowers' sign (using hands to push off thighs when rising from floor due to hip weakness), and calf pseudohypertrophy (fatty infiltration of muscle). CK is markedly elevated (10-100 times normal). Becker muscular dystrophy is a milder allelic variant with later onset. Spinal muscular atrophy (SMN1 mutation) presents with hypotonia and weakness but without pseudohypertrophy or such elevated CK. Myotonic dystrophy involves CTG repeats on chromosome 19.

Question: 3487

In the management of anticipated difficult airway, the LEMON assessment includes evaluation of the 3-3-2 rule. What does the “2” component specifically measure?

- A. Neck extension should permit two fingerbreadths of movement at the atlanto-occipital joint
- B. Mouth opening should allow insertion of at least two fingers between the incisors
- C. The distance from the hyoid bone to the thyroid notch should accommodate at least two fingerbreadths
- D. The thyromental distance should be at least two fingerbreadths

Answer: C

Explanation: The 3-3-2 rule assesses mouth opening (3 fingerbreadths), thyromental distance (3 fingerbreadths), and the distance from the hyoid to the thyroid cartilage (2 fingerbreadths). A reduced hyoid-to-thyroid distance indicates a more anterior larynx and predicts difficult laryngoscopy.

Question: 3488

Which antiplatelet agent produces irreversible inhibition of the platelet P2Y₁₂ receptor after hepatic bioactivation and therefore requires several days for recovery of normal platelet function after discontinuation?

- A. Cangrelor, an intravenous reversible P2Y₁₂ antagonist
- B. Clopidogrel, a thienopyridine prodrug generating an active thiol metabolite
- C. Ticagrelor, a direct-acting reversible P2Y₁₂ antagonist
- D. Vorapaxar, a protease-activated-receptor-1 antagonist

Answer: B

Explanation: Clopidogrel is converted by CYP2C19 to an active metabolite that covalently binds the P2Y₁₂ receptor. Because the inhibition is irreversible, platelet function recovers only as new platelets are generated (approximately 5–7 days), necessitating careful timing of elective surgery.



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