NEET PG Pharmacology Sample Paper-1

Duration: 15 Minutes **Maximum Marks: 80**

Instructions

- This paper contains **20** Multiple Choice Questions.
- Each correct answer carries **+4** mark. Incorrect answer: **−1** marks. Only **one** correct option.
- Unattempted questions carry **0** marks.
- Use of mobile phones, smartwatches, or any electronic gadgets is strictly prohibited.

Q1. A novel tyrosine kinase inhibitor exhibits a volume of distribution (V_d) of 25 L/kg and is highly bound to tissue proteins. In an acute overdose scenario, a resident suggests attempting hemodialysis to clear the drug rapidly. Which parameter best explains why hemodialysis will be ineffective?

(A) Low plasma protein binding clearance

(B) High apparent volume of distribution

(C) Zero-order elimination kinetics profile

(D) High hepatic extraction ratio

Q2. A patient with a genetic polymorphism resulting in ultra-rapid CYP2D6 metabolism is prescribed a standard analgesic regimen following major orthopedic surgery. Which of the following therapeutic scenarios is most likely to occur?

(A) Toxic accumulation of Codeine due to lack of clearance

(B) High efficacy and potential toxicity from Losartan

(C) Therapeutic failure of Tramadol due to poor active metabolite conversion

(D) Profound respiratory depression following normal doses of Codeine

Q3. During a clinical trial, Drug X is found to shift the log-dose response curve of Norepinephrine to the right without reducing its maximal therapeutic efficacy (E_{max}). However, when the concentration of Drug X is increased tenfold, the E_{max} of Norepinephrine begins to decline significantly. This drug is best characterized as a:

(A) Pure competitive antagonist

(B) Non-competitive allosteric antagonist

(C) Competitive antagonist with low-affinity non-competitive properties

(D) Irreversible covalent antagonist

Q4. An investigative agent undergoes phase II biotransformation via glucuronidation. A patient with a congenital deficiency in UDP-glucuronosyltransferase 1A1 (UGT1A1) is enrolled in the safety trial. This patient is at a significantly elevated risk for severe systemic toxicity if administered which active drug class?

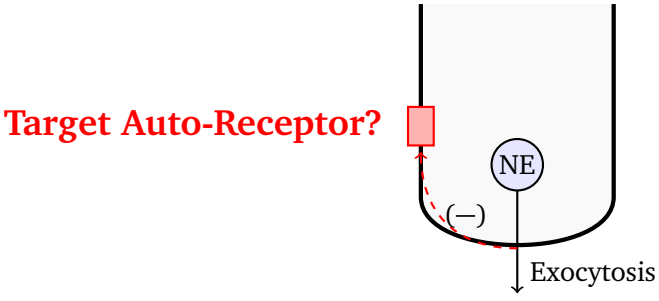
(A) Irinotecan active metabolite (SN-38)

(B) N-acetyl-p-benzoquinone imine (NAPQI)

(C) Sulfamethoxazole metabolites

(D) Azathioprine active intermediate (6-MP)

Q5. An experimental model maps out the auto-regulatory feedback loops operating on a sympathetic adrenergic nerve terminal. Identify the specific receptor type denoted by the highlighted molecular block layout that provides negative feedback inhibition on endogenous norepinephrine release:



(A) α_1-Adrenergic receptor

(B) α_2-Adrenergic receptor

(C) β_1-Adrenergic receptor

(D) β_2-Adrenergic receptor

Q6. A 62-year-old patient with severe open-angle glaucoma is prescribed a topical ophthalmic medication that lowers intraocular pressure by increasing uveoscleral outflow rather than acting via the trabecular meshwork. Which of the following drugs corresponds to this mechanism?

(A) Timolol maleate

(B) Brimonidine tartrate

(C) Latanoprost

(D) Pilocarpine hydrochloride

Q7. A patient experiencing severe bradycardia following an acute toxic ingestion is treated with high-dose atropine. Shortly after, the patient develops central anticholinergic syndrome presenting with delirium and hyperthermia. Which agent should be selected to reverse both the central and peripheral manifestations?

(A) Neostigmine methylsulfate

(B) Pyridostigmine bromide

(C) Edrophonium chloride

(D) Physostigmine salicylate

Q8. A patient undergoing an elective surgical procedure is given an intravenous bolus of a neuromuscular blocking agent. Within two minutes, the patient exhibits profound muscle relaxation accompanied by transient facial flushing and systemic hypotension due to rapid histamine release. The drug is metabolized via spontaneous Hofmann elimination. Identify the agent:

(A) Vecuronium bromide

(B) Cisatracurium besylate

(C) Succinylcholine chloride

(D) Atracurium besylate

Q9. A 29-year-old patient with refractory focal epilepsy is initiated on an adjunctive antiepileptic drug that acts primarily as a structural analog of GABA but does not bind to GABA receptors; instead, it selectively inhibits $\alpha_2\delta$ subunits of voltage-gated calcium channels. Which drug is this?

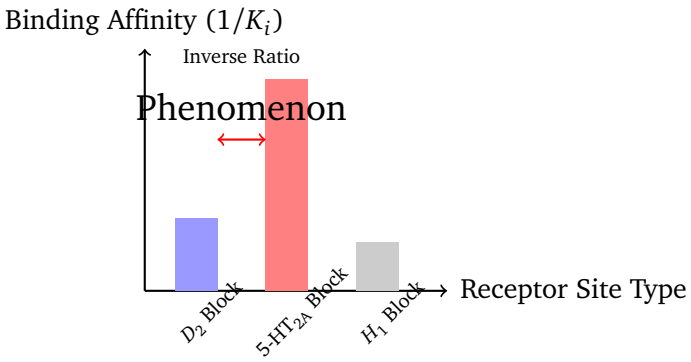
(A) Vigabatrin

(B) Tiagabine

(C) Gabapentin

(D) Topiramate

Q10. A functional pharmacodynamic profile compares the intracellular signaling cascade of atypical antipsychotics. Identify the receptor-binding signature profile highlighted below that distinguishes atypical antipsychotics from typical first-generation low-potency neuroleptics:



(A) High D_2 receptor affinity coupled with weak D_1 activation

(B) High 5-HT_{2A} receptor antagonism relative to weak D_2 affinity

(C) High M_1 muscarinic blockage with zero 5-HT_1 affinity

(D) Selective D_4 receptor agonism without peripheral clear zone

Q11. A patient undergoing long-term maintenance therapy for parkinsonism with Levodopa-Carbidopa starts experiencing disabling "on-off" motor fluctuations.

The neurologist decides to introduce a drug that selective blocks Catechol-O-methyltransferase (COMT) both peripherally and centrally. Which agent matches this requirement?

(A) Entacapone

(B) Tolcapone

(C) Selegiline

(D) Pramipexole

Q12. A 45-year-old male presenting with severe treatment-resistant chronic depression is initiated on an antidepressant regimen. After a week, he presents to the emergency room with severe throbbing headache, palpitations, neck stiffness, and a blood pressure reading of 210/130 mmHg after consuming aged cheese. Which drug did he take?

(A) Tranylcypromine

(B) Duloxetine

(C) Mirtazapine

(D) Sertraline

Q13. A critical patient grows a strain of Klebsiella pneumoniae producing extended-spectrum beta-lactamases (ESBL). The strain is found to be highly resistant to Ceftriaxone and Aztreonam. Which genetic resistance mechanism is most commonly responsible for this specific phenotype?

(A) Plasmid-mediated TEM-1 or SHV-1 mutations expression

(B) Chromosomal mutation in DNA gyrase encoding genes

(C) Porin channel loss combined with normal PBP modification

(D) Methylation of 23S rRNA ribosomal binding subunit

Q14. An intensive care patient is treated with high-dose intravenous Daptomycin for vancomycin-resistant Enterococcus (VRE) endocarditis. Which laboratory parameter must be closely monitored at regular weekly intervals during this therapeutic course?

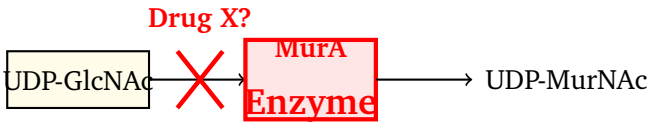
(A) Serum creatinine phosphokinase (CPK) levels

(B) Absolute neutrophil count (ANC)

(C) Serum uric acid concentrations

(D) Methemoglobin percentage profile

Q15. A molecular biological screen demonstrates the step-wise assembly of the bacterial peptidoglycan cell wall structure. Identify the specific phase or enzyme block target where the antimicrobial agent Fosfomycin exerts its therapeutic disruption:



(A) Alanine racemase inactivation step

(B) D-Alanyl-D-Alanine ligase sequence binding

(C) Enolpyruvyl transferase (MurA) condensation reaction

(D) Bactoprenol pyrophosphate dephosphorylation sequence

Q16. A 54-year-old patient treated for a severe anaerobic intra-abdominal infection develops profound pseudomembranous colitis. After failing oral Vancomycin therapy, the clinician decides to switch to a macrocyclic antibiotic that acts via inhibiting the sigma subunit of bacterial RNA polymerase. What is this drug?

(A) Linezolid

(B) Fidaxomicin

(C) Rifaximin

(D) Tedizolid

Q17. A patient on highly active antiretroviral therapy (HAART) is diagnosed with pulmonary tuberculosis. The infectious disease specialist notes that the

standard antitubercular regimen must be altered to prevent profound induction of hepatic microsomal enzymes, which would otherwise accelerate the clearance of Protease Inhibitors. Which agent should replace Rifampin?

(A) Rifabutin

(B) Rifapentine

(C) Ethionamide

(D) Streptomycin

Q18. A patient presenting with acute decompensated heart failure requires an inotropic agent that enhances myocardial contractility through a unique dual mechanism: inhibiting phosphodiesterase 3 (PDE3) while simultaneously acting as a calcium sensitizer without increasing myocardial oxygen demand excessively. Identify this agent:

(A) Milrinone

(B) Dobutamine

(C) Levosimendan

(D) Nesiritide

Q19. A 58-year-old patient with type 2 diabetes and stable chronic kidney disease ($eGFR = 42\,\text{mL/min/1.73m}^2$) requires optimization of glycemic control. The drug selected acts by inhibiting sodium-glucose cotransporter 2 (SGLT2) in the proximal convoluted tubule. Aside from glycemic control, which primary renal benefit is associated with this class?

(A) Reversal of proximal tubular casts formation

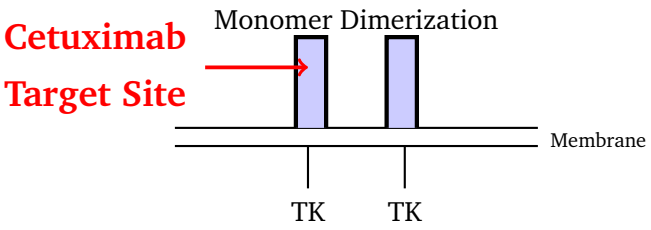
(B) Reduction in intraglomerular pressure via afferent arteriole constriction

(C) Direct blockade of aldosterone receptors on principal cells

(D) Direct chemical inhibition of the loop of Henle symporters

Q20. The cellular signaling diagram outlines the targeted entry profile of a major class of biological therapies used in oncology. Identify the specific targeted

receptor or ligand block disrupted by the monoclonal antibody Cetuximab within this pathway cascade:



(A) Vascular Endothelial Growth Factor (VEGF-A) ligand

(B) Epidermal Growth Factor Receptor (EGFR) extracellular domain

(C) Human Epidermal Growth Factor Receptor 2 (HER2) transmembrane locus

(D) Anaplastic Lymphoma Kinase (ALK) intracellular core

Detailed Solutions

Q1.

Solution

Concept: Hemodialysis is highly effective for clearing drugs that are primarily confined to the intravascular compartment, characterized by a low apparent volume of distribution ($V_d < 1\,\text{L/kg}$) and low tissue protein binding.

Solution:

Let's analyze the pharmacokinetic parameters described in the scenario:

(a) The novel tyrosine kinase inhibitor has an exceptionally large **volume of distribution ($V_d = 25\,\text{L/kg}$)**, indicating that the vast majority of the drug resides outside the plasma compartment and is sequestered deeply within peripheral tissues.

(b) Hemodialysis can only filter drug molecules present in the circulating plasma water. Since only a tiny fraction of the total body burden of this drug is circulating in the blood at any given time, dialysis will fail to remove a clinically significant amount of the agent.

(c) Let's evaluate why the alternative choices do not explain this outcome:

- Low plasma protein binding generally *increases* dialyzability because free drug passes through the dialyzer membrane easily, but this is completely negated here by the massive tissue sequestration.
- Zero-order elimination or a high hepatic extraction ratio dictate biological clearance pathways but do not directly influence the physical limitations of hemodialysis extraction from the central compartment.

Final Answer: High apparent volume of distribution

Answer: (B)

Go Back to Question 1

Q2.

Solution

Concept: Cytochrome P450 2D6 (CYP2D6) is a highly polymorphic enzyme responsible for the bioactivation of prodrug opioids. Ultra-rapid metabolizers possess multiple functional copies of the *CYP2D6* gene, leading to accelerated conversion of a prodrug into its active metabolite.

Solution:

Let's evaluate the pharmacogenomic outcomes for the options provided:

(a) Codeine is a prodrug that must undergo *O*-demethylation via **CYP2D6** to be converted into its highly active metabolite, **morphine**.

(b) In an **ultra-rapid CYP2D6 metabolizer**, standard therapeutic doses of codeine are metabolized at an exceptionally high rate, resulting in rapid, high-concentration spikes of morphine in the blood. This can lead to severe opioid toxicity, manifesting as **profound respiratory depression**, CNS depression, and potential death.

(c) Let's look at why the other options are incorrect:

- Accumulation of codeine itself does not occur; instead, it is cleared too quickly into morphine.
- Tramadol also requires CYP2D6 bioactivation to its active *O*-desmethyltramadol (*M*1) metabolite; ultra-rapid metabolizers experience *increased* efficacy/toxicity, not therapeutic failure.
- Losartan is metabolized by CYP2C9 and CYP3A4, not CYP2D6.

Final Answer: Profound respiratory depression following normal doses of Codeine

Answer: (D)

Go Back to Question 2

Q3.

Solution

Concept: Antagonist behavior can display concentration-dependent variations in receptor selectivity and binding dynamics. While a pure competitive antagonist can always be overcome by increasing agonist concentration, high concentrations may cause off-target or low-affinity allosteric/non-competitive blockade.

Solution:

Let's analyze the pharmacodynamic shifts described in the curve profile:

(a) Initially, Drug X shifts the log-dose response curve of Norepinephrine to the right **without reducing its maximal therapeutic efficacy (E_{max})**. This parallel rightward shift is the classic signature of a **reversible competitive antagonist**, where the agonist can outcompete the blocker if given at a high enough dose.

(b) However, when the concentration of Drug X is increased tenfold, the E_{max} begins to drop significantly. This loss of maximum response indicates that at high concentrations, the drug interacts with an additional low-affinity non-competitive/allosteric site or binds irreversibly, preventing full receptor activation regardless of Norepinephrine levels.

(c) Therefore, Drug X is best characterized as a **competitive antagonist with low-affinity non-competitive properties**.

Final Answer: Competitive antagonist with low-affinity non-competitive properties

Answer: (C)

Go Back to Question 3

Q4.

Solution

Concept: UDP-glucuronosyltransferase 1A1 (UGT1A1) is the primary enzyme responsible for the glucuronidation of bilirubin as well as specific active drug metabolites, rendering them water-soluble for biliary and renal excretion.

Solution:

Let's evaluate the metabolic pathways of the listed drug classes:

(a) **Irinotecan** is a camptothecin topoisomerase I inhibitor prodrug used in colorectal cancer. It is converted by endogenous carboxylesterases into its highly active, toxic metabolite, **SN-38**.

(b) Inactivation and clearance of SN-38 rely almost exclusively on **glucuronidation by UGT1A1**.

(c) A patient with a congenital deficiency in UGT1A1 (such as in Gilbert syndrome or Crigler-Najjar syndrome) cannot adequately clear SN-38, leading to toxic accumulation that causes life-threatening neutropenia and severe, refractory diarrhea.

(d) Let's review the alternative pathways: NAPQI is conjugated by glutathione; sulfamethoxazole metabolites undergo acetylation/glucuronidation via other enzymes; and 6-MP is inactivated by xanthine oxidase and thiopurine methyltransferase (TPMT).

Final Answer: Irinotecan active metabolite (SN-38)

Answer: (A)

Go Back to Question 4

Q5.

Solution

Concept: Presynaptic auto-receptors serve as homeostatic feedback regulators that modulate neurotransmitter release into the synaptic cleft.

Solution:

Let's interpret the presynaptic feedback loop illustrated in the molecular block diagram:

(a) The diagram depicts an adrenergic nerve terminal releasing Norepinephrine (NE) via exocytosis. A fraction of the released NE diffuses backward to engage a specific presynaptic auto-receptor, sending an inhibitory signal (—) to arrest further vesicle fusion.

(b) This specific inhibitory presynaptic auto-receptor is the **α_2-adrenergic receptor**. It is coupled to a G_i protein-coupled signaling pathway that decreases intracellular cyclic AMP (cAMP), inhibits voltage-gated calcium channels, and opens potassium channels, hyperpolarizing the terminal to suppress further neurotransmitter release.

(c) In contrast, α_1 and β_1 receptors are primarily postsynaptic targets that drive excitation, while presynaptic β_2 receptors typically facilitate positive feedback (enhancing neurotransmitter release), rather than negative inhibition.

Final Answer: α_2-Adrenergic receptor

Answer: (B)

Go Back to Question 5

Q6.

Solution

Concept: Intraocular pressure (IOP) can be pharmacologically managed by either reducing aqueous humor production or enhancing its clearance via two separate anatomical pathways: the trabecular meshwork or the uveoscleral outflow tract.

Solution:

Let's categorize the mechanisms of action for the primary antiglaucoma medications listed:

(a) **Latanoprost** is a synthetic prostaglandin $F_{2\alpha}$ analog. It lowers IOP by remodeling the extracellular matrix within the ciliary muscle, significantly **increasing aqueous humor drainage via the uveoscleral pathway**.

(b) Let's verify why the other choices are incorrect for this specific route:

- Timolol is a β-blocker that lowers IOP by decreasing aqueous humor *production* at the ciliary epithelium.
- Brimonidine is an α_2-agonist that acts via a dual mechanism (decreasing production and slightly increasing uveoscleral flow), but latanoprost is the prototypical agent chosen specifically for pure uveoscleral outflow enhancement.
- Pilocarpine is a muscarinic agonist that contracts the ciliary muscle, pulling the scleral spur to open the **trabecular meshwork**, which decreases uveoscleral outflow while heavily increasing trabecular drainage.

Final Answer: Latanoprost

Answer: (C)

Go Back to Question 6

Q7.

Solution

Concept: Acetylcholinesterase inhibitors increase synaptic acetylcholine concentrations. To reverse toxic effects in the central nervous system, an agent must possess lipid solubility to cross the blood-brain barrier (BBB).

Solution:

Let's analyze the chemical structures and distribution properties of the options:

(a) The patient has central anticholinergic syndrome (delirium, hyperthermia) brought on by high-dose atropine administration. To resolve both the central neurological deficits and peripheral toxicities, the antidote must readily penetrate the central nervous system.

(b) **Physostigmine salicylate** is a **tertiary amine**. Because it lacks a permanent positive charge, it is lipophilic and successfully **crosses the blood-brain barrier** to restore cholinergic transmission in the brain.

(c) Conversely, Neostigmine, Pyridostigmine, and Edrophonium contain **quaternary ammonium groups**. Their permanent positive charge makes them highly polar, preventing them from crossing the BBB. As a result, they can only reverse peripheral anticholinergic effects.

Final Answer: Physostigmine salicylate

Answer: (D)

Go Back to Question 7

Q8.

Solution

Concept: Neuromuscular blocking drugs of the benzylisoquinolinium class can undergo spontaneous chemodegradation independent of renal or hepatic clearance.

Solution:

Let's distinguish between the two benzylisoquinolinium options that undergo Hofmann elimination:

(a) Both atracurium and cisatracurium undergo spontaneous molecular degradation via **Hofmann elimination** (a non-enzymatic chemical breakdown triggered by physiological pH and temperature).

(b) However, **Atracurium besylate** consists of a mixture of ten stereoisomers and is well-known for triggering **significant, rapid histamine release** from mast cells when delivered as an intravenous bolus. This histamine release accounts for the transient facial flushing and systemic hypotension described in the vignette.

(c) Cisatracurium, a purified single isomer of atracurium, is much more potent, which allows for lower clinical dosing. Consequently, it causes negligible histamine release and does not typically provoke flushing or hemodynamic drops, making Atracurium the correct clinical match here.

Final Answer: Atracurium besylate

Answer: (D)

Go Back to Question 8

Q9.

Solution

Concept: Certain antiepileptic drugs are structural derivatives of neurotransmitters but function through entirely independent molecular pathways.

Solution:

Let's analyze the specific mechanism of action described:

(a) The drug described is a structural analog of Gamma-Aminobutyric Acid (GABA) but has no direct binding affinity or activity at $GABA_A$ or $GABA_B$ receptors, nor does it alter GABA metabolism or uptake.

(b) Instead, its therapeutic efficacy stems from binding to the **$\alpha_2\delta$ auxiliary subunit of voltage-gated calcium channels** in the central nervous system. This binding reduces calcium influx into presynaptic terminals, suppressing the release of excitatory neurotransmitters like glutamate.

(c) This mechanism defines **Gabapentin** (and its relative pregabalin).

(d) Let's verify why the other choices are incorrect: Vigabatrin irreversibly inhibits GABA transaminase; Tiagabine blocks the GAT-1 GABA transporter; and Topiramate acts primarily on sodium channels, AMPA receptors, and carbonic anhydrase.

Final Answer: Gabapentin

Answer: (C)

Go Back to Question 9

Q10.

Solution

Concept: Atypical (second-generation) antipsychotics are distinguished from classic typical (first-generation) antipsychotics by their specific multi-receptor binding profiles, which reduce the risk of extrapyramidal side effects (EPS).

Solution:

Let's interpret the binding affinity bar graph:

(a) The diagram highlights an "Inverse Ratio Phenomenon" where the drug demonstrates a substantially higher affinity for blocking **5-HT_{2A} serotonin receptors** compared to its weaker binding affinity at the **D_2 dopamine receptor** site.

(b) This classic pharmacodynamic signature—**high 5-HT_{2A} receptor antagonism relative to weak D_2 affinity**—is the defining feature of atypical antipsychotics (such as olanzapine, risperidone, and quetiapine).

(c) This high ratio allows for effective control of psychotic symptoms with a significantly lower risk of inducing extrapyramidal side effects or hyperprolactinemia compared to typical high-potency neuroleptics (like haloperidol), which cause intense, prolonged D_2 receptor blockade.

Final Answer: High 5-HT_{2A} receptor antagonism relative to weak D_2 affinity

Answer: (B)

Go Back to Question 10

Q11.

Solution

Concept: Catechol-O-methyltransferase (COMT) inhibitors prevent the breakdown of levodopa, expanding its availability for central nervous system entry. These agents differ fundamentally in their tissue distribution and site of action.

Solution:

Let's evaluate the compartment activity of the COMT inhibitors:

(a) Levodopa is combined with carbidopa (a peripheral DOPA decarboxylase inhibitor). When DOPA decarboxylase is blocked, the body increases its reliance on COMT to metabolize levodopa into 3-O-methyldopa (3-OMD) in the periphery.

(b) To counter this, a COMT inhibitor is added. **Tolcapone** is an agent that crosses the blood-brain barrier, allowing it to inhibit COMT **both peripherally and centrally**. This dual action maintains stable levodopa levels in both the plasma and the brain.

(c) In contrast, **Entacapone** acts **only in the periphery** because it cannot cross the blood-brain barrier.

(d) Selegiline is a selective MAO-B inhibitor, and Pramipexole is a direct dopamine receptor agonist.

Final Answer: Tolcapone

Answer: (B)

Go Back to Question 11

Q12.

Solution

Concept: Inhibition of Monoamine Oxidase A (MAO-A) prevents the normal breakdown of dietary tyramine in the gastrointestinal tract, predisposing patients to severe hyperadrenergic crises upon consumption of specific foods.

Solution:

Let's break down the clinical presentation and identify the underlying cause:

(a) The patient presented with a hypertensive crisis (210/130 mmHg), severe headache, and palpitations triggered by eating aged cheese. This describes the classic **"cheese reaction."**

(b) Aged cheese contains high levels of **tyramine**, an indirect sympathomimetic amine. Normally, dietary tyramine is safely degraded in the gut wall and liver by the enzyme MAO-A.

(c) **Tranylcypromine** is a potent, non-selective, irreversible Monoamine Oxidase Inhibitor (MAOI). By blocking MAO-A, it allows intact tyramine to enter the systemic circulation. This systemic tyramine enters sympathetic nerve terminals via the NET transporter and displaces large amounts of stored norepinephrine into the synaptic cleft, causing widespread vasoconstriction and dangerous spikes in blood pressure.

(d) The other choices (duloxetine, mirtazapine, sertraline) do not inhibit MAO-A and are not associated with tyramine-induced hypertensive crises.

Final Answer: Tranylcypromine

Answer: (A)

Go Back to Question 12

Q13.

Solution

Concept: Extended-Spectrum Beta-Lactamases (ESBLs) are bacterial enzymes that hydrolyze penicillins, cephalosporins (including third- and fourth-generation agents like ceftriaxone), and monobactams (such as aztreonam), but remain susceptible to carbapenems.

Solution:

Let's analyze the molecular genetics of ESBL resistance in Enterobacteriaceae:

(a) The vignette describes an infection with an ESBL-producing strain of *Klebsiella pneumoniae* that is resistant to ceftriaxone and aztreonam.

(b) This phenotype is most commonly caused by **plasmid-mediated mutations in the structural genes for TEM-1, TEM-2, or SHV-1** β-lactamases (as well as the acquisition of CTX-M type enzymes). These point mutations alter the configuration of the enzyme's catalytic site, expanding its substrate specificity to include advanced-generation cephalosporins and monobactams.

(c) Let's verify why the other choices are incorrect: mutations in DNA gyrase cause fluoroquinolone resistance; porin alterations can contribute to resistance but do not define the production of ESBLs; and 23S rRNA methylation leads to macrolide/clindamycin/linezolid resistance.

Final Answer: Plasmid-mediated TEM-1 or SHV-1 mutations expression

Answer: (A)

Go Back to Question 13

Q14.

Solution

Concept: Daptomycin is a lipopeptide antibiotic that disrupts the bacterial cytoplasmic membrane in a calcium-dependent manner. Its clinical use requires routine monitoring due to its well-documented skeletal muscle toxicity.

Solution:

Let's identify the primary toxicological tracking parameter for Daptomycin:

(a) A key adverse effect of high-dose or prolonged daptomycin therapy is **myopathy**, which can progress to clinical rhabdomyolysis.

(b) To ensure patient safety, clinician guidelines mandate regular weekly monitoring of **serum creatinine phosphokinase (CPK) levels**. Treatment should be paused if patients develop unexplained muscle pain accompanied by significant elevations in CPK.

(c) Let's look at the alternative parameters: absolute neutrophil count is tracked for linezolid or ganciclovir; serum uric acid is monitored during pyrazinamide or tumor lysis monitoring; and methemoglobin profiles are checked during dapsone or local anesthetic therapies.

Final Answer: Serum creatinine phosphokinase (CPK) levels

Answer: (A)

Go Back to Question 14

Q15.

Solution

Concept: Bacterial cell wall synthesis begins in the cytoplasm with the conversion of UDP-N-acetylglucosamine (UDP-GlcNAc) into UDP-N-acetylmuramic acid (UDP-MurNAc).

Solution:

Let's analyze the enzymatic pathway targeted in the diagram:

(a) The diagram illustrates the initial step of peptidoglycan monomer synthesis, where an enzyme catalyzes the condensation of UDP-GlcNAc and phosphoenolpyruvate (PEP). This step is interrupted by "Drug X."

(b) The enzyme responsible for this specific step is UDP-N-acetylglucosamine enolpyruvyl transferase, commonly known as **MurA**.

(c) **Fosfomycin** acts as a structural analog of phosphoenolpyruvate. It binds covalently to a cysteine residue in the active site of **MurA (enolpyruvyl transferase)**, irreversibly inactivating the enzyme. This blocks the synthesis of UDP-MurNAc, halting cell wall construction at its earliest stage.

(d) The alternative pathways—alanine racemase and D-Ala-D-Ala ligase—are targeted by cycloserine, while bactoprenol dephosphorylation is blocked by bacitracin.

Final Answer: Enolpyruvyl transferase (MurA) condensation reaction

Answer: (C)

Go Back to Question 15

Q16.

Solution

Concept: Severe, refractory *Clostridioides difficile* infection (pseudomembranous colitis) can be treated with targeted narrow-spectrum macrocyclic antibiotics that exhibit minimal systemic absorption.

Solution:

Let's identify the correct antibiotic based on its molecular target:

(a) The patient has severe pseudomembranous colitis and failed standard oral vancomycin therapy.

(b) **Fidaxomicin** is a narrow-spectrum macrocyclic antibiotic that is minimally absorbed when taken orally, allowing it to concentrate within the gastrointestinal tract.

(c) It exerts its bactericidal effect by binding to and **inhibiting the sigma (σ) subunit of bacterial RNA polymerase**. This action blocks transcription initiation, arresting protein synthesis specifically in clostridia while sparing much of the surrounding normal anaerobic gut microbiota.

(d) Let's review the alternatives: Linezolid and tedizolid are oxazolidinones that inhibit the 50S ribosomal subunit; Rifaximin is a rifamycin derivative that binds to the β-subunit of RNA polymerase rather than the sigma factor.

Final Answer: Fidaxomicin

Answer: (B)

Go Back to Question 16

Q17.

Solution

Concept: Rifamycins are key components of antitubercular regimens but are potent inducers of the hepatic cytochrome P450 enzyme system, which can complicate drug regimens for patients with co-infections.

Solution:

Let's analyze the drug interactions in a patient undergoing HAART:

(a) Rifampin is a powerful inducer of CYP3A4 and other microsomal enzymes. In a patient on highly active antiretroviral therapy (HAART) containing Protease Inhibitors (or Non-Nucleoside Reverse Transcriptase Inhibitors), rifampin accelerates the clearance of these antiviral agents, dropping their plasma concentrations below therapeutic levels and risking HIV treatment failure.

(b) To avoid this interaction, **Rifabutin** is substituted for rifampin. Rifabutin is a related rifamycin that maintains excellent bactericidal efficacy against *Mycobacterium tuberculosis* but has a **significantly lower capacity for cytochrome P450 induction**, making it safer to co-administer with protease inhibitors.

(c) Rifapentine is an even longer-acting rifamycin that still causes substantial enzyme induction. Ethionamide and Streptomycin belong to entirely different chemical classes and do not serve as direct substitutes for the rifamycin core of first-line TB therapy.

Final Answer: Rifabutin

Answer: (A)

Go Back to Question 17

Q18.

Solution

Concept: Advanced inotropic agents can enhance myocardial contraction without excessively increasing myocardial oxygen consumption by altering the sensitivity of contractile proteins to existing calcium levels.

Solution:

Let's evaluate the mechanical properties of the listed inotropic agents:

(a) The agent specified operates via a unique dual mechanism: it inhibits **phosphodiesterase 3 (PDE3)** (which increases intracellular cAMP and supports contractility) and acts as a **calcium sensitizer**.

(b) This dual profile defines **Levosimendan**. By binding to cardiac troponin C in a calcium-dependent manner, it stabilizes the calcium-induced conformational change without increasing total intracellular calcium concentrations during systole. This enhances contractility without significantly increasing myocardial oxygen demand or predisposing the heart to dangerous arrhythmias.

(c) Let's cross-check the alternatives: Milrinone is a pure PDE3 inhibitor without calcium-sensitizing properties; Dobutamine is a β_1-adrenergic receptor agonist; and Nesiritide is a synthetic recombinant B-type natriuretic peptide (BNP) that acts as a vasodilator rather than a direct positive inotrope.

Final Answer: Levosimendan

Answer: (C)

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Q19.

Solution

Concept: Sodium-glucose cotransporter 2 (SGLT2) inhibitors (gliflozins) alter hemodynamics within the nephron, providing cardiorenal protection independent of their glucose-lowering effects.

Solution:

Let's evaluate the physiological mechanics of SGLT2 inhibition at the juxtaglomerular apparatus:

(a) SGLT2 inhibitors block glucose and sodium reabsorption in the early proximal convoluted tubule, which increases delivery of both solutes to the distal nephron.

(b) When this excess sodium reaches the **macula densa** in the distal tubule, it activates the **tubuloglomerular feedback** mechanism. The macula densa senses the high sodium load and releases adenosine, which triggers **vasoconstriction of the adjacent afferent arteriole**.

(c) Constricting the afferent arteriole limits blood flow into the glomerulus, **reducing elevated intraglomerular pressure**. This reduction in hyperfiltration relieves mechanical stress on the filtration barrier, helping to preserve long-term kidney function and delay the progression of diabetic nephropathy.

Final Answer: Reduction in intraglomerular pressure via afferent arteriole constriction

Answer: (B)

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Q20.

Solution

Concept: Monoclonal antibodies used in targeted cancer therapies are designed to block specific extracellular receptors or circulating ligands, interrupting downstream intracellular proliferative pathways.

Solution:

Let's trace the molecular target site demonstrated in the cell signaling diagram:

(a) The diagram depicts a transmembrane tyrosine kinase receptor that undergoes ligand-induced monomer dimerization, which then activates its intracellular tyrosine kinase (TK) domains. Cetuximab acts on the outside of the cell, blocking this process.

(b) **Cetuximab** is a recombinant human/mouse chimeric monoclonal antibody that binds specifically to the **extracellular domain of the Epidermal Growth Factor Receptor (EGFR / HER1)**.

(c) By binding to the extracellular domain, Cetuximab sterically blocks endogenous ligands (such as EGF and TGF-α) from binding. This prevents receptor dimerization and halts downstream signaling cascades (like the KRAS-BRAF-MAPK pathway), inhibiting tumor cell proliferation and angiogenesis.

(d) Let's review the alternative options: Bevacizumab targets VEGF-A ligand; Trastuzumab targets the HER2 transmembrane receptor; and Crizotinib inhibits the intracellular core of the ALK kinase receptor.

Final Answer: Epidermal Growth Factor Receptor (EGFR) extracellular domain

Answer: (B)

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Answer Key

Q	Ans	Q	Ans	Q	Ans	Q	Ans	Q	Ans
1	B	2	D	3	C	4	A	5	B
6	C	7	D	8	D	9	C	10	B
11	B	12	A	13	A	14	A	15	C
16	B	17	A	18	C	19	B	20	B