PREP XI RR

STUDY NOTES

PHARMACOLOGY

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PREMIUM STUDY MATERIAL

PREP XI RR

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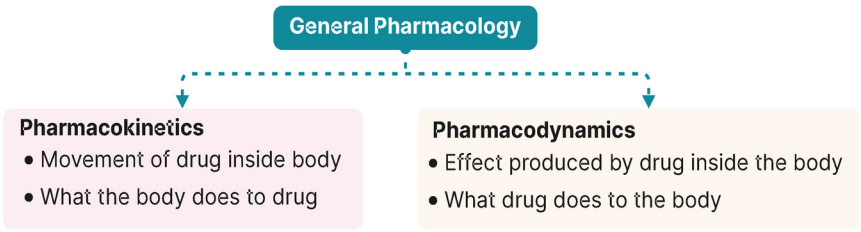
Pharmacology

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1. GENERAL PHARMACOLOGY

BIG QUESTION 1: Differentiate between Pharmacokinetics and Pharmacodynamics

Broad Answer: Pharmacokinetics encompasses the processes by which the body influences the drug. Conversely, pharmacodynamics elucidates the physiological and biochemical effects exerted by the drug on the body



DETAILED QUESTIONS

Q1.1: Define pharmacokinetics and outline its constituent processes

Answer:

- Pharmacokinetics: The study of drug movement within the body; it describes the processes that the body exerts on the drug
- Constituent Processes (ADME):
  - o Absorption
  - o Distribution
  - o Metabolism
  - o Excretion

Q1.2: Specify the primary pharmacokinetic parameters associated with absorption, distribution, and elimination

Answer:

- In absorption: BA (bioavailability)
- In distribution: Vd (volume of distribution)
- In elimination (inclusive of metabolism and excretion): Cl (clearance)

Q1.3: Which additional pharmacokinetic parameters are derived from bioavailability (BA), volume of distribution (Vd), and clearance (Cl)?

Answer:

- Loading dose = (Vd × Target concentration) / F
- Maintenance dose = (Cl × Target concentration) / F
- Half-life ($t_{1/2}$) = (0.693 × Vd) / Cl

BIG QUESTION 2: Describe the primary pathways and factors influencing drug absorption across cell membranes

Broad Answer: The most common pathway for drug absorption across cell membranes into the bloodstream is simple/passive diffusion, which primarily accommodates lipid-soluble compounds due to the phospholipid nature of cell membranes The ionization state of weak acidic or basic drugs, governed by their pK value and the pH of the surrounding medium (as described by the Henderson-Hasselbalch equation), determines their lipid solubility and thus their ability to traverse biological membranes

DETAILED QUESTIONS

Q2.1: What is the most common pathway by which drugs traverse cell membranes to enter the bloodstream, and what characteristic of the drug is essential for this pathway?

Answer:

- M/c Pathway: Simple/passive diffusion
- Essential Characteristic: Only lipid-soluble drugs can cross the cell membrane (due to its phospholipid composition) by simple/passive diffusion

Q2.2 Categorize drugs based on their ability to cross cell membranes

Non-ionized / lipid soluble / non-polar drugs	Strong ions/water soluble/polar drugs	Weak ionic drugs
• Cross cell membrane • Enters the cell by simple/passive diffusion	• **Cannot cross cell membrane** • Not absorbed into blood • Not given orally o Aminoglycosides o Heparin	• Weak acidic or weak basic drugs • Depending on **pK value** o These drugs cross the cell membrane

Q2.3: Define the pK value of a drug and explain how it is determined using the Henderson-Hasselbalch equation

Answer:

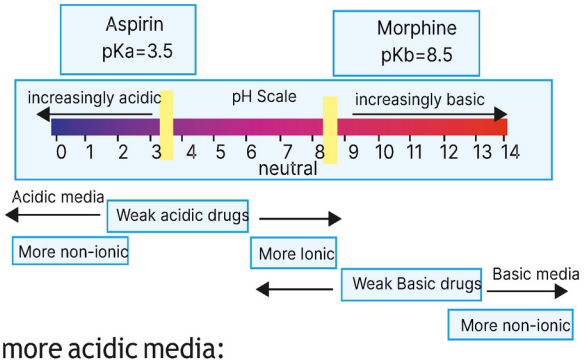
- pK value: The pH at which a drug is 50% ionized and 50% non-ionized
- Determination (Henderson-Hasselbalch equation):
  - o $pH = pK_{\alpha} + \text{Log}_{10}\left(\frac{[A^-]}{[HA]}\right)$
  - o Where:
    - → A^- = ionic concentration of drug
    - → HA = non-ionic concentration of the drug
  - o When A^- and HA are 50% (ie, $[A^-]/[HA] = 1$), then $\text{Log}_{10}(1) = 0$, and thus pH = pKa

Q2.4: If the pH of a media is changed to 1, by how much does the ionization of a drug change?

Answer: If the pH of the media changes to 1 unit, the degree of ionization changes by a factor of 10

Q2.5: How does the pH of the medium influences the ionization and lipid solubility of weak acidic and weak basic drugs

Answer:



- Influence of pH on Weak Ionic Drugs:
  - o Weak acidic drug in a more acidic media OR Weak basic drug in a more basic media:
    - → Drug becomes more non-ionic
    - → Drug becomes more lipid soluble (and thus can cross cell membrane by simple/passive diffusion)
  - o Weak acidic drug in more basic media OR Weak basic drug in a more acidic media:
    - → More ionic forms
    - → Drug becomes more water soluble (and thus cannot readily cross the cell membrane)

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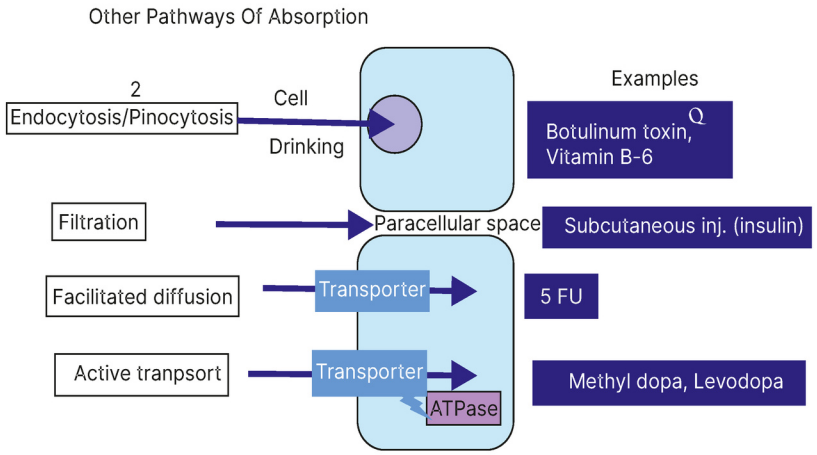
Q2.6: How is Aspirin (pKa 3.5) absorbed in the stomach, and what are the potential side effects?

Answer: **Oral aspirin (pKa 3.5) entering the stomach:**

Oral aspirin - enter stomach (pH 0-1)	Inside stomach cell (pH - 7.4)
• Becomes **non ionized** • Crosses cell membrane of the stomach • Enters into **the stomach cell**	• Ionized Aspirin shows **ion trapping** inside the stomach cell so that it can enter into the blood. • **S/E:** Gastric ulcers

Q2.7 What are the other pathways of absorption?

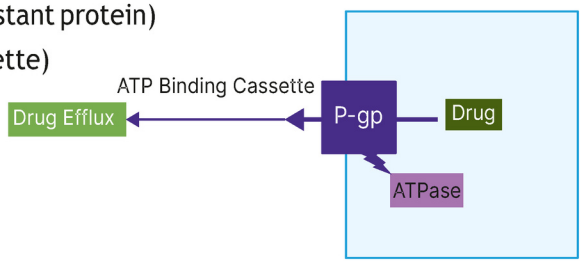
Answer:



Q2.8: What is P-glycoprotein, and what is its mechanism of action and effect?

Answer:

- Active transporter
- Also known as efflux transporter/MRP-2 protein (Multi-drug resistant protein)
- Requires ATP and thus is known as ABC protein (ATP binding cassette)
- If P-gp identifies a drug:
  - **GIT:** Reduces systemic absorption and bioavailability
  - **Kidney:** Enhances renal excretion of the drug
  - **Liver:** Augments biliary excretion
  - **BBB, Placenta:** Diminishes drug entry into these compartments



Q2.9: Identify a known pharmaceutical substrate of P-glycoprotein

Answer: Digoxin

Q2.10: What are the clinical implications of P-glycoprotein (P-gp) inhibition with Cyclosporine?

Answer:

- Cyclosporine: An immunosuppressive agent administered in organ transplantation
- MOA: It inhibits P-gp
- Clinical Consequence: As P-gp is instrumental in bile excretion, its inhibition by Cyclosporine leads to reduced biliary excretion, clinically manifesting as cholestatic jaundice

Q2.11: What is the difference between P-gp inducers and inhibitors?

Answer:

P-gp inducers	P-gp inhibitors

• Drugs increases the activity of p-gp
• Example: Rifampicin
• If Rifampicin combined with Digoxin
  o **Increase urinary excretion of Digoxin**
  o Reduce plasma concentration
  o Loss of effect of Digoxin
	• Reduces the activity of p-gp
	• Drugs - **mnemonic: QVACK**
	  o **Q**uinidine
	  o **V**erapamil
	  o **A**miodarone
	  o **C**larithromycin/erythromycin
	  o **K**etoconazole
	• When these drugs combined with Digoxin
	  o **Reduce the urinary excretion of Digoxin**
	  o Increases plasma concentration
	  o Leads to toxicity

Q2.12: Which transporter is responsible for the excretion of Digoxin in urine?

Answer:

- P-glycoprotein

BIG QUESTION 3: What are the various routes of drug administration?

Broad answer

- Oral route
- Sublingual/Buccal
- Rectal
- Intramuscular
- Transdermal

DETAILED QUESTIONS

Q3.1: Which route is predominantly utilized for systemic drug administration?

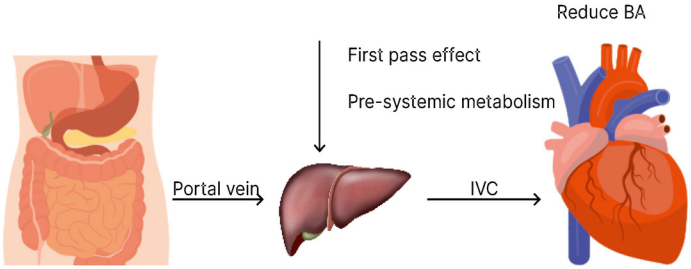
Answer:

- Most common route of administration: Oral route

Q3.2: Describe the main site and pathway of oral drug absorption to the liver

Answer:

- Most oral drugs are absorbed in the small intestine (especially the duodenum) due to its large surface area. From there, they enter the portal vein and reach the liver via the portal circulation



Q3.3: Explain the hepatic metabolism (first-pass effect) of oral drugs and its impact on bioavailability

Answer:

- The first-pass effect (also called pre-systemic metabolism) refers to the metabolism of a drug in the liver before it reaches systemic circulation
- Drugs absorbed from the gastrointestinal tract first pass through the liver via the portal vein
- This reduces the bioavailability of the drug, as a significant portion is metabolized before reaching the heart via the inferior vena cava (IVC)
- Clinical significance: Oral drugs with high first-pass metabolism may require higher doses or alternative routes (e.g., sublingual, IV) to achieve therapeutic levels

Q3.4: What are the implications for oral administration of drugs exhibiting a high first-pass metabolism effect?

Answer:

- Drugs exhibiting a high first-pass metabolism effect are not given orally
- If given, then taken in a high oral dose

Drugs not given orally	Drugs given in high oral dose

• Lignocaine
• Fentanyl
• Natural steroids
  o Hydrocortisone
  o Aldosterone
  o Oestrogen
  → Hence synthetic oestrogen is given orally in OCP
  o Testosterone
	• Propranolol
	• Morphine
	• Nitrates

Q3.5: How to bypass the FPM of the liver?

Answer:

- By giving the drug by all other systemic routes except the oral route

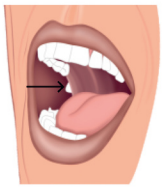
Q3.6: Describe the systemic absorption pathway for drugs administered via the sublingual/buccal route

Answer:

- Drugs administered via the sublingual or buccal route are absorbed directly into the systemic circulation through the oral mucosa.
  - They enter the superior vena cava, reach the heart, and bypass hepatic first-pass metabolism
- Sublingual nitrates are the drug of choice (DOC) in acute angina because they act rapidly and avoid first-pass degradation



Sublingual Route

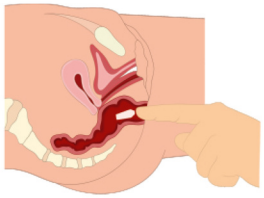


Buccal Route

Q3.7: Describe the systemic absorption pathway for drugs administered via the rectal route

Answer:

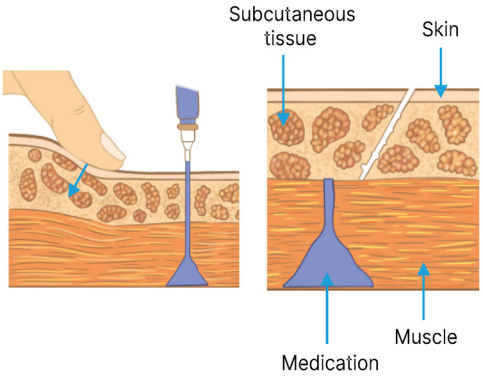
- The drug enters the External hemorrhoidal vein and drains into the Inferior vena cava, thereby bypassing first-pass metabolism
- Example: Rectal diazepam- DOC in febrile seizures in children



Rectal Route

Q3.8: What is a potential issue associated with intramuscular drug administration, and how can it be prevented? List common pharmaceutical agents administered via this route.

Answer:



- When a drug is given intramuscularly (IM), it may leak back from the muscle and stain the subcutaneous tissue, leading to discoloration or irritation.
- To prevent this, the Z-track technique is used, which involves:
  - Pulling the skin and subcutaneous tissue laterally before injecting the drug.
  - This creates a zig-zag path that seals the drug in the muscle once the needle is withdrawn.
- Drugs commonly given by the Z-track technique:
  - Iron dextran (to prevent skin staining)
  - Antipsychotics (e.g., Haloperidol decanoate)

Q3.9: Describe the transdermal/topical route of administration, identify the anatomical sites of maximum and least drug absorption, and indications

Answer:



- Transdermal patches:
  - Long-acting route
  - Drug absorbed continuously and sustained plasma levels achieved
  - Usually given for long-term chronic diseases
- Site of maximum absorption:
  - Post auricular area > Scrotum > face and neck
- Site of least absorption: Where the skin is thick - due to heavy keratinization
  - Palms
  - Soles

Patch	Indication
Nicotine patch	Smoking cessation
Hyoscine (scopolamine), Diphenhydramine	Motion sickness
Nitrates	Chronic Angina
Clonidine	Hypertension
Selegiline	Depression
Rivastigmine	Alzheimer's
Rotigotine	Parkinson's disease
Oestrogen, progesterone	HRT (Hormone Replacement Therapy)

BIG QUESTION 4: What is the definition of bioavailability, how does it vary by route of administration, and what is the standard method for its calculation?

Broad Answer: Bioavailability is the fraction of an administered drug that reaches the systemic circulation in an unchanged form over time, without being degraded by the liver. Intravenous drugs exhibit 100% bioavailability as they bypass absorption barriers, whereas other routes have less than 100%. It is calculated by comparing the Area Under the Curve (AUC) of oral administration to that of intravenous administration

YOURWISH

DETAILED QUESTIONS

Q4.1: Define bioavailability in the context of drug disposition

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Answer:

- Fraction of drug that reaches systemic circulation in unchanged form with time and is not degraded by liver

Q4.2: Why is the bioavailability of intravenously administered drugs 100%?

Answer:

- BA of IV drugs: 100%
- The drug is directly administered into the systemic circulation, with no cellular barriers or absorption involved

Q4.3: How is bioavailability (F) calculated using Area Under the Curve (AUC)?

Answer:

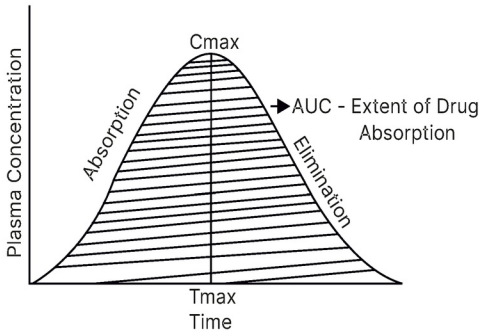
- BA calculation:
  - The bioavailability is calculated from the AUC of oral drug and AUC of the IV drug
  - Bioavailability (F) = $\frac{AUC_{po}}{AUC_{iv}}$
- BA has no units as it is a fraction
- Symbol: F

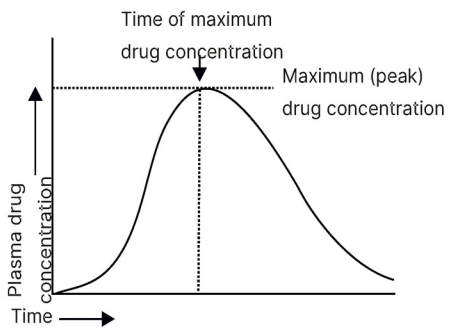
Q4.4: How is Area Under the Curve (AUC) calculated, and what do C_{max} and T_{max} represent in pharmacokinetics, defining the rate and extent of drug absorption?

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Answer:

- Area under the curve (AUC): Calculated by Trapezoidal rule
- The maximum (peak) drug concentration corresponds to C_{max}
- Time at which C_{max} achieved - T_{max}
  - Defines rate of absorption (how fast the drug is getting absorbed)
- If T_{max}:
  - Small - Drug get rapidly absorbed
  - Large - Drug get slowly absorbed into blood
- C_{max} - Maximum plasma concentration achieved in the blood max
- AUC - Total extent of absorption of a drug





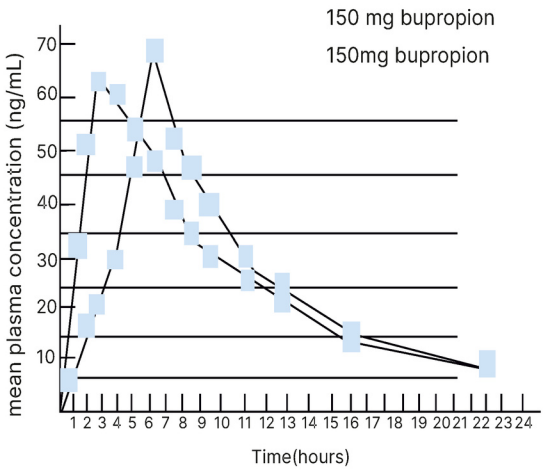
Q4.5: What is the purpose of assessing bioequivalence, and what is the acceptable range of bioavailability variation for drugs to be considered bioequivalent?

Answer:

- Bioequivalence: Compare the bioavailability of different brands of same drug (generic drugs)

- Acceptable variation in BA : 80% - 125%
- Drugs having equal variation are known as bioequivalent drugs
- Can interchange the brands

Q4.6: Identify a notable exception to the acceptable bioavailability variation for bioequivalence, and explain why different brands of this drug are considered bio-inequivalent



Answer:

- Exception: Phenytoin
- For most drugs, a bioavailability variation of 80-125% is considered acceptable for bioequivalence
- However, Phenytoin is a narrow therapeutic index drug and follows non-linear (zero-order) kinetics
- Even small variations in bioavailability can lead to toxicity or subtherapeutic levels
- Therefore, no two brands of Phenytoin are bioequivalent, and they should not be interchanged

BIG QUESTION 5: What is the concept of Volume of Distribution

Broad Answer: The volume of distribution represents the apparent volume required to contain the total drug in the body at the same concentration as in the plasma, reflecting its extravascular movement into tissues. Factors like protein binding significantly influence it, and high Vd can have implications for drug toxicity and removal methods

DETAILED QUESTIONS

Q5.1: What is the definition of the Volume of distribution (Vd)

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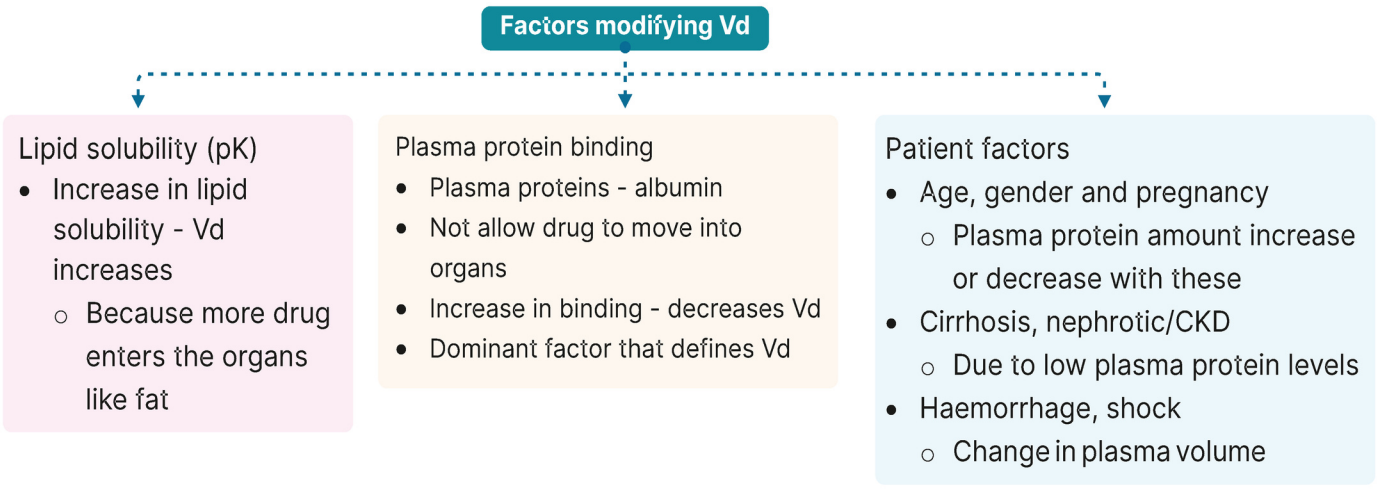
Answer:

- Volume of plasma (liters) required to contain a drug in equal concentration as that of the plasma
  - More amount of drug enters the organ, more Vd

Q5.2.What are the factors that modify the Volume of Distribution (Vd) of a drug?

Answer:

- The **Volume of Distribution (Vd)** is influenced by several physiological and pathological factors:



Q5.3: Explain why Warfarin, despite its lipid solubility, exhibits a low volume of distribution

Answer:

- Warfarin has low Vd due to high protein binding (Predominant factor)

Q5.4.Do antiepileptic drugs increase each other's toxicity? What is the mechanism?

Answer:

- Yes, they displace each other from albumin, increasing the free (active) drug fraction, which raises the volume of distribution (Vd) and enhances tissue penetration, leading to increased toxicity

Q5.5: Why is Sulfonamide (Cotrimoxazole) contraindicated in neonates and during the third trimester of pregnancy?

Answer:

- Sulfonamides cause the displacement of bilirubin (endogenous toxin) from albumin
- Displacement of bilirubin by sulfonamides increases free bilirubin, which can cross the immature blood-brain barrier (BBB) in neonates, leading to brain toxicity and **kernicterus (bilirubin-induced encephalopathy)**

Q5.6: Why is hemodialysis ineffective in poisoning with certain drugs

Answer:

- Hemodialysis is ineffective for drugs with a high volume of distribution (Vd) because these drugs are stored in tissues rather than circulating in the blood As a result, they cannot be effectively removed from the body via dialysis

Q5.7: How are drugs categorized in poisoning based on the effectiveness of hemodialysis, and which drugs are not suitable for dialysis?

Do hemodialysis Mnemonic: **BLAST**	No role Mnemonic: **AVOID ABC**
• **B**arbiturates • **L**ithium • **A**lcohols • **A**spirin • **S**alicylates • **T**heophylline	• **A**mphetamin • **V**erapamil/warfarin • **O**rganophosphate • **I**mipramine • **D**igoxin (Vd- 450 litres) • **A**miodarone • **B**enzodiazepines • **C**hloroquine

Q5.8: What is the approximate volume of distribution for Chloroquine, and where does it extensively deposit in the body?

Answer:

- Chloroquine has highest volume of distribution - around 15000 litres
- Deposits in all organs

Q5.9: What specific ocular adverse effect is associated with Chloroquine deposition, and what is its prognosis?

Answer:

- It get deposited in retina

- Cause Bull's eye maculopathy - permanent blindness



Q5.10: Which class of drugs exhibit redistribution?

Answer:

- Seen with highly lipid-soluble drugs like:
  - Thiopentone
  - Fentanyl

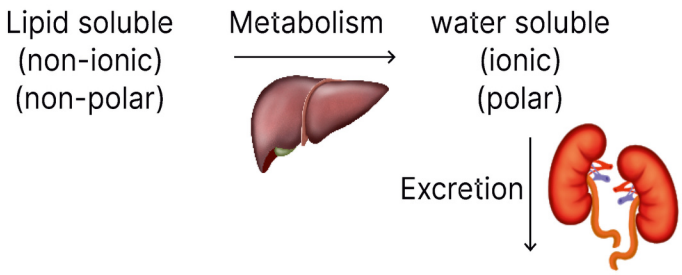
Q5.11: By what primary mechanism is the action of Thiopentone terminated?

Answer:

- Redistribution into fats not by elimination in urine

BIG QUESTION 6: What are the primary objectives of drug metabolism and the principal organ involved, and how does this process facilitate drug excretion?

Broad Answer: Drug metabolism primarily involves converting lipid-soluble/non-ionic compounds into water-soluble, ionic forms. The liver is the most common organ where this transformation occurs, which is crucial as water-soluble forms are then readily excreted from the body, predominantly via the kidneys through urine



DETAILED QUESTIONS

Q6.1: What is the main objective of drug metabolism, and which organ is most commonly involved in this process?

Answer:

- Converting lipid soluble/non-ionic/non-polar drug into water-soluble/ionic/polar form
- Liver is the most common organ of metabolism

Q6.2: How do water-soluble drug forms facilitate elimination from the body, and what is the most common route of drug excretion?

Answer:

- Water soluble forms are easily excreted out of the body through saliva/urine/sweat
- Most common route of Excretion - Urine by kidneys

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Q6.3 Describe the Activity of drug after metabolism with examples

Active drug to active form	Active drug to inactive metabolite	Inactive forms (prodrug) to active metabolite
• Most drugs converted to inactive forms after metabolism • Example; **mnemonic - FADS CP** o **F**luoxetine o **A**llopurinol o **D**iazepam o **S**pironolactone o **C**odeine o **P**rimidone	• Most drugs undergo this process	• Examples of prodrugs; **mnemonic - PLASMA CCD** o **P**rednisone o **L**evodopa o **A**CE inhibitors (pril) o **S**ulfasalazine o **M**ycophenolate mofetil o **A**cyclovir/Ganciclovir o **C**arbimazole o **C**lopidogrel/Prasugrel o **D**ipivefrin

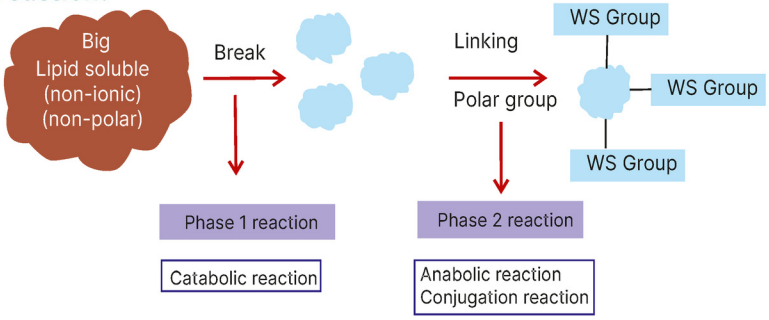
Q6.4: Which ACE inhibitors are not prodrugs?

Answer:

- Captopril
- Lisinopril

Q6.5: Describe hepatic drug metabolism and phase reaction?

Answer: Hepatic (liver) metabolism transforms drugs into more water-soluble forms for excretion, mainly via urine or bile It occurs in two phases:
2 chemical reactions are carried out



Phase 1 reaction	Phase 2 reaction
• Catabolic reaction	• Anabolic reaction/conjugation reaction • Linking or **conjugation of polar group** to each small fragment • Drug become water soluble
• Drug becomes active or inactive • Prodrug converted to active form	• Drug becomes inactive only • Except for morphine and minoxidil - they become active
Reactions • Oxidation o Carried out by CYP450 enzymes in liver • Reduction o Carried out by CYP450 enzymes in liver • Dehydrogenation • Deamination • Cyclization • Decyclization	**Reactions** PYQ: FMGE 2021 • Glucuronide conjugation (Most common) o Carried out by UDP-GT enzyme in liver • Glycination • Sulfation • Methylation • Acetylation • Glutathione conjugation
• All phase 1 reactions - Microsomal reaction (inside smooth endoplasmic reticulum)	• All phase 2 reactions - Non Microsomal reaction o Occur outside smooth endoplasmic reticulum o Except glucuronide conjugation → Microsomal reaction

Q6.6: What are the key characteristics of Cytochrome P450 enzymes?

Answer:

- Contains heme pigment
- Shows genetic variation/polymorphism in high/ low amount

Q6.7: What are CYP enzyme inducers and inhibitors?

Answer:

Category	Mnemonic	Drugs
CYP Enzyme Inducers	GRASS	• **G**riseofulvin • **R**ifampicin • **A**lcohol (chronic) • **A**ll antiepileptics (except valproate): o Phenobarbitone o Phenytoin o Carbamazepine • **S**moking • **S**t John's Wort (plant product)
CYP Enzyme Inhibitors	COKE IVC GAR	• **C**imetidine • **O**meprazole • **K**etoconazole • **E**rythromycin • **I**soniazid : Inhibits all CYP types, Except CYP2E1 which it induces • **V**alproate • **C**iprofloxacin • **G**rape-fruit juice • **A**lcohol (acute) • **R**itonavir (HIV

Q6.8: Describe the Types of CYP and their substrates

Answer:

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CYP type	Substrate (drugs that gets metabolised)
• CYP1A2	• Theophylline, Clozapine
• CYP2C9 (least quantity)	• Phenytoin, Warfarin
• CYP2C19	• Clopidogrel, Azoles, PPI
• CYP2D6	• Mnemonic: **PATTSON** • **P**ropranolol, **A**ntiarrhythmics (quinidine), **T**CA (tricyclic antidepressants), **T**amoxifen, Codeine, Antipsychotic, SSRI
• CYP2E1	• Paracetamol
• CYP3A4 (maximum quantity)	• >50% drugs are metabolised

Q6.9: What component of grape-fruit juice acts as a CYP inhibitor?

Answer:

- Grape-fruit juice contains furanocoumarins which act as CYP inhibitor

Q6.10: Which CYP is induced by Isoniazid?

Answer:

- Isoniazid inhibits all CYP types, except CYP2E1 which it induces

Q6.11: Which is the only antiepileptic which is a CYP inhibitor?

Answer:

- Valproate is the only antiepileptic which is a CYP inhibitor
- All other antiepileptics are CYP inducers

Q6.12: How does chronic versus acute alcoholism affect cytochrome P450 enzyme?

Answer:

- Chronic alcohoism will act as CYP inducer (increases metabolism of other drugs)
- Acute alcoholism acts as a CYP inhibitor

Q6.13: What is the effect of combining CYP inducers or inhibitors with a CYP substrate , give examples of such drug interactions?

Answer:

- CYP inducers or inhibitors when combined with a substrate of CYP, it may increase or reduce plasma levels of substrate
  - Shows drug interactions
- They are:

I. **Oestrogen (oral contraceptive pill)**	II. **Cisapride (for constipation), Astemizole and Terfenadine (antihistaminic)**	III. **Clopidogrel (prodrug)**
o Metabolised by CYP3A4 o If given with Rifampicin → CYP inducer o Oestrogen gets rapidly metabolized o **Causing Contraceptive failure**	o Metabolised by CYP3A4 o When combined with Erythromycin/ketoconazole → CYP inhibitors o Plasma levels of substrates increase o Lead to toxicity - **Torsades de pointes** → QTc increases o Hence these are banned	o Converted to active form - by CYP2C19 o Antiplatelet drugs can cause stomach bleeding o Omeprazole is given (CYP inhibitor) o Clopidogrel not converted to active form o Leads to **increased risk of MI/Stroke**

Q6.14: Which drugs undergo metabolism via acetylation, and differentiate between fast and slow acetylators?

Answer: Mnemonic: **SHIP-DP**

- Sulfonamide
- Hydralazine
- Isoniazid
- Procainamide

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- Dapsone
  - First drug for leprosy
  - Sulphonamide
- PAS : First drug for TB

Fast acetylators	Slow acetylators
• Individuals with high NAT level	• Individuals with poor NAT level • SHIP drugs accumulate in the plasma leading to toxicity • Causes DLE (drug induced lupus erythematosus)

Q6.15: What is the specific enzyme responsible for the acetylation process in drug metabolism?

Answer:

- N-acetyl Transferase enzyme

BIG QUESTION 7: Explain the process of drug elimination and its various routes

Broad Answer:

- Elimination - metabolism + excretion
  - Drug moving out of body with time
  - Rate of removal of drug (mg/min)
- M/c site of metabolism - liver
- M/c route of Excretion - urine (kidney)
- Other routes of excretion include bile, sweat, saliva, tears, and milk

DETAILED QUESTIONS

Q7.1: Describe the enterohepatic reabsorption of Oral Contraceptive Pills (OCPs) via bile, and explain how antibiotics can lead to contraceptive failure

Answer:

- Oral Contraceptive Pills (OCPs) are excreted into bile and reach the intestine
- Intestinal bacteria hydrolyze the conjugated forms, allowing the active drug to be reabsorbed—this is called enterohepatic circulation
- Antibiotics like Doxycycline and Ampicillin kill gut flora, disrupting this reabsorption process
- This reduces OCP plasma levels, potentially causing contraceptive failure

Q7.2: What drugs are avoided in breastfeeding?

Answer:

- **Drugs avoided in breastfeeding:**Mnemonic: SMALL

→ **S**ulfonamides
  - Cause kernicterus

→ **M**ethotrexate
  - Hepatotoxic

→ **A**spirin
  - Reye's syndrome (liver disease)

→ **L**ithium
  - Seizures
  - Metabolic abnormalities

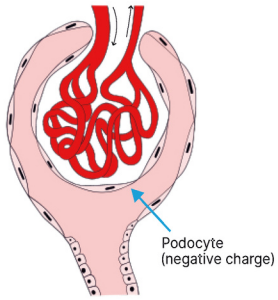
→ **L**evetiracetam
  - Anti-epileptic drug to be secreted maximum in the breast milk.

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Q7.3 What are the 2 methods of urinary? Explain briefly about those methods

Glomerular filtration	Active tubular secretion
• Passive process • Occurs through **Paracellular spaces** o Spaces between podocytes • Protein binding **reduces GFR** • Podocytes contain negative charge o Repels negative charge of basic drug o **Basic drugs filtered less** than acidic drugs	• Active process o Require ATP • Drug excreted into urine - **by transporters** through **pumps** • Protein binding increases secretion rate • OATP transporter o Organic anion transport protein o Excretes acidic drugs: **Penicillins** o Probenecid inhibits OATP • OCTP transporter o Organic cation transport protein o Excretes basic drugs: **Tubocurare** • P-gp o P-glycoprotein o Excretes neutral drugs: **Digoxin**



Q7.4 What transporter does Probenecid inhibit, and what is its clinical effect when given with Penicillins?

Answer: Probenecid inhibits the OATP transporter, which reduces the renal excretion of Penicillins, thereby prolonging their duration of action in the body

Q7.5 Which type of drugs facilitates their reabsorption via passive tubular reabsorption in the kidneys?

Answer: Lipid soluble drugs get reabsorbed

Q7.6 Explain the types of weak drug poisoning, the therapeutic strategy, and examples

In weak acidic drug poisoning	In weak basic drug poisoning
• To convert this weak acidic drug to **more water soluble form** to be excreted out in urine • Change the pH of urine to alkaline • **Forced Alkaline Diuresis** o By Sodium bicarbonate • Drugs; **Mnemonic: AMB** o Aspirin, acetaminophen o Methotrexate o Barbiturates	• Convert weak basic drug to water soluble form • Change pH of urine to acidic • **Forced Acid Diuresis** o By Ammonium chloride • Drugs; **mnemonic: ASMAQ** o Amfetamine o Strychnine o Morphine o Atropine o Quinine

Q7.7: What agent is used as the antidote for Aspirin poisoning?

Answer: Sodium bicarbonate

Q7.8: What agent is used as the antidote for Amphetamine poisoning?

Answer:

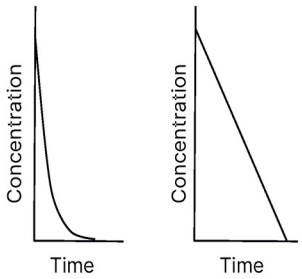
- Ammonium chloride

Q7.9: What is the order of kinetics of drug elimination, and how do first-order and zero-order kinetics differ?

Answer:

- The order of kinetics of elimination refers to the rate at which a drug is removed from the body
- First-order kinetics: Capacity to remove or eliminate a drug is very high (constant)
- Zero-order kinetics: Clearance capacity is very low (saturation kinetics)

First order kinetics	Zero order kinetics
Elimination - directly proportional to plasma concentration	Elimination is **constant**
Constant fraction eliminated	Constant amount eliminated
Half life **constant**	Half life - directly proportional to plasma concentration
Most drugs	Few drugs



Q7.10: List the drugs that typically exhibit zero-order kinetics?

Answer:

PYQ: FMGE 2021

- Mnemonic: **WHATS App**
  - **W**arfarin
  - **H**eparin
  - **A**lcohol
  - **T**heophylline
  - **S**alicylates
  - **A**spirin
  - **P**henytoin

Q7.11: How does the administered dose of a drug generally influence whether it follows first-order or zero-order kinetics and what are the exceptions?

Answer:

- Any drug in a low dose, that is dose below clearance capacity shows first-order kinetics
- Any drug in a high dose, that is above clearance capacity shows zero order kinetics
- Exceptions
  - Alcohol: At all doses shows zero order kinetics
  - Phenytoin: In normal dose shows zero as well as pseudo zero order kinetics

Q7.12: What is the formula used to calculate bioavailability (F) based on Area Under the Curve (AUC) from oral and intravenous administration, and also based on the administered doses?

Answer: Bioavailability (F)= AUC /AUC = Dose (iv)/Dose (oral) po iv

Q7.13: What is the formula for calculating the Volume of Distribution (Vd)?

Answer: $Vd = \frac{\text{Dose administered IV}}{\text{Plasma concentration}}$

Q7.14: What is the formula to calculate Elimination in terms of Clearance and Concentration?

Answer: Elimination= Clearance × Concentration

Q7.15: What are the derived formulas for calculating Loading Dose, Maintenance Dose, Half-life (t1/2), and Elimination Rate Constant (K)?

Answer:

- Loading dose= Vd × Target Conc
- Maintenance dose = Clearance × Target Conc
- $t_{1/2} = \frac{0.693 \times V_d}{Cl} = \frac{0.693}{K}$
- Elimination rate constant (K)= $\frac{\text{Clearance}}{V_d}$

Q7.16: Define the half-life of a drug

Answer: Time required to reduce plasma concentration by 50% after the drug is completely absorbed

Q7.17: Upon what pharmacokinetic parameter does the half-life of a drug *not* depend?

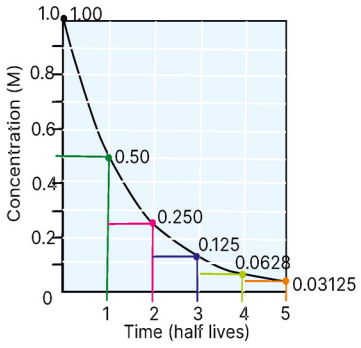
Answer: Absorption

Q7.18: What percentage of drug elimination occurs within 3.3 half-lives, and what percentage signifies "complete elimination" of a drug, along with the theoretical duration for 100% elimination?

Answer:

- 90% elimination occurs in 3.3 Half lives
- 95% elimination of drug occurs in 4 to 5 half lives this is known as complete elimination of a drug
- 100% elimination takes infinite half lives which never occurs

Half life	Plasma conc.	Elimination
0	100	0
1	50	50
2	25	75
3	12.5	87.5
4	6.25	93.125
5	3.125	96.875



Q7.19: What assumption is made regarding the action of a drug once more than 95% of it has been eliminated from plasma (ie, after 4-5 half-lives)?

Answer:

- If >95% of drug is eliminated from plasma (4-5 half-lives)
- Complete elimination of the drug
- Action of a drug is over

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Q7.20: Using the example of Lithium (half-life: 1 day) cessation, predict the approximate time after which its effect will cease

Answer:

- Patient stopped taking Lithium after 6 months (Half-life: 1 day)
- Effect of Lithium will be over after 4-5 days

Q7.21: What are "hit and run" drugs?

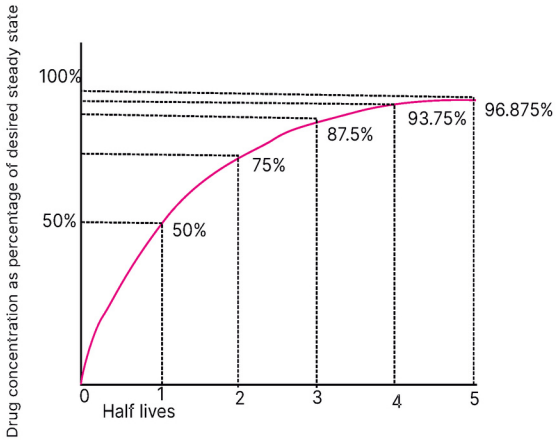
Answer:

- Hit and run drugs: Continue to produce action even after the complete elimination of the drug
- Reason for exception: They irreversibly attached to the organ
  - In plasma drug is removed
- These drugs are also known as Suicide inhibitors
- Mnemonic: **MOOGRA**
  - **M**AO inhibitors
  - **O**meprazole: All PPI inhibit H+ / K+ ATPase irreversibly
  - **O**rganophosphate
  - **G**uanethidine
  - **R**eserpine/Ritonavir
  - **A**spirin inhibit COX enzyme irreversibly

Q7.22: What is the Plateau Principle in pharmacokinetics, and how are loading and maintenance doses related to it?

Answer:

- The Plateau principle states that when a drug is administered at a constant rate, it reaches 95% of its steady-state concentration (Css) in 4-5 half-lives At this point, the rate of drug administration equals the rate of elimination
- To achieve Css quickly, a loading dose is given:
  Loading dose = Vd × Css
- To maintain Css, a maintenance dose is given:
  Maintenance dose = CL × Css



Q7.23: How is a child's drug dose calculated, and what are the commonly used methods?

Answer:

- The best method to calculate a child's drug dose is based on Body Surface Area (BSA), e.g., using the DuBois formula
- A commonly used approximate method from adult dosing is Young's Formula
  - $\text{Child dose} = \left(\frac{\text{Age in years}}{\text{Age in years} + 12}\right) \times \text{Adult dose}$
  - This helps estimate pediatric doses when exact BSA data is unavailable

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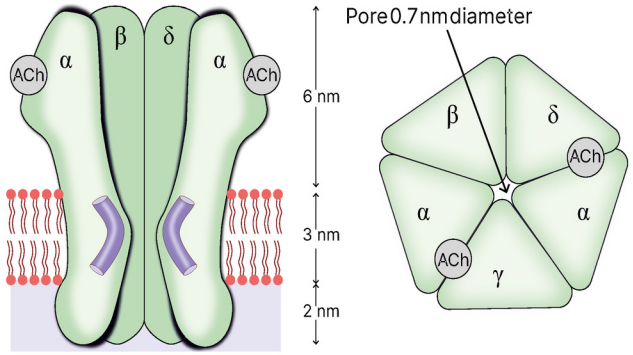
BIG QUESTION 8: Define pharmacodynamics and describe the major types of drug receptors, including their structural characteristics, signaling mechanisms, and key examples

Broad Answer: Pharmacodynamics is the study of the effects drugs produce in the body, typically involving a drug (ligand) binding to a receptor (target) to elicit a biological response Receptors are broadly classified into ionotropic, G-protein coupled receptors (GPCRs), protein kinase receptors, and intracellular receptors, each possessing distinct structural features and mechanisms for signal transduction, often involving secondary messengers.

DETAILED QUESTIONS

Q8.1: Describe the characteristics and examples of Ionotropic receptors

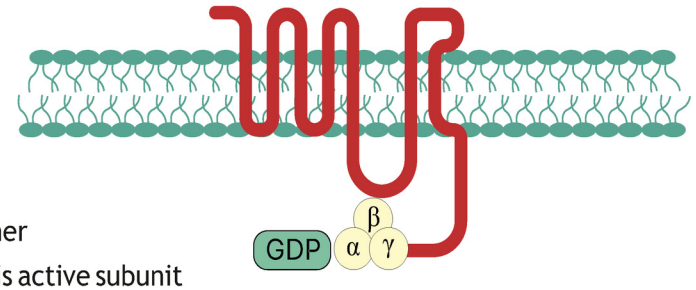
Answer:



- Pentameric rosette shape
- Ions get exchanged
- Examples:
  - Sodium channel opening, entry makes cell excitable:
    - → Nicotinic: Acetylcholine
    - → 5-HT3: Serotonin
    - → Glutamate (NMDA): Glutamate
  - Chloride entry, Hyperpolarization, inhibitory receptor:
    - → GABA-A
    - → Glycine

Q8.2: Describe the structural features and signaling mechanism of G-protein coupled receptors (GPCRs), including their subunits and common secondary messengers

Answer:



- Structural Features:
  - Snake shape: Serpentine/Helical
  - 7 transmembrane serpentine shape
  - Subunits: Alpha (α), beta (β), gamma (γ) heterotrimer
  - Alpha (α) subunit is attached to GDP protein: Alpha is active subunit
- Signaling Mechanism: Also known as Metabotropic receptors
  - These receptors work with the help of secondary messengers
- Secondary Messengers: Molecules increased/decreased inside the cell are known as Secondary messengers:
  - cAMP
  - Ip3
  - DAG

Q8.3: List examples of ligands that act on G-protein coupled receptors, and exceptions

Answer:

- Largest family of receptors, examples:
  - Muscarinic: Acetylcholine
  - 5-HT 1-7: Serotonin (Except 5-HT3: Ionotropic)
  - Alpha (α) / Beta (β): Epi/Norepinephrine

- Histamine
- Opioid
- All hypothalamic hormones
- All pituitary hormones (Except GH, Prolactin)
- Angiotensin receptors

Q8.4.What are the types of G-protein

Answer: 3 types, produce effect inside the cell

Gs	Gq	Gi
• Adenylyl cyclase activation • Increase cAMP	• Activates Phospholipase-C • Increase IP3 (Inositol triphosphate), DAG (Diacylglycerol)	• Inhibit Adenylyl cyclase • Decrease cAMP

Q8.5: Regarding GPCRs, which enzyme is activated by Gq type receptors?

Answer:

- Phospholipase-C

Q8.6: Regarding GPCRs, which enzyme is activated by Gs type receptors?

Answer:

- Adenylyl cyclase

Q8.7: Which molecule acts on the Guanylyl cyclase enzyme, and what secondary messenger does it increase?

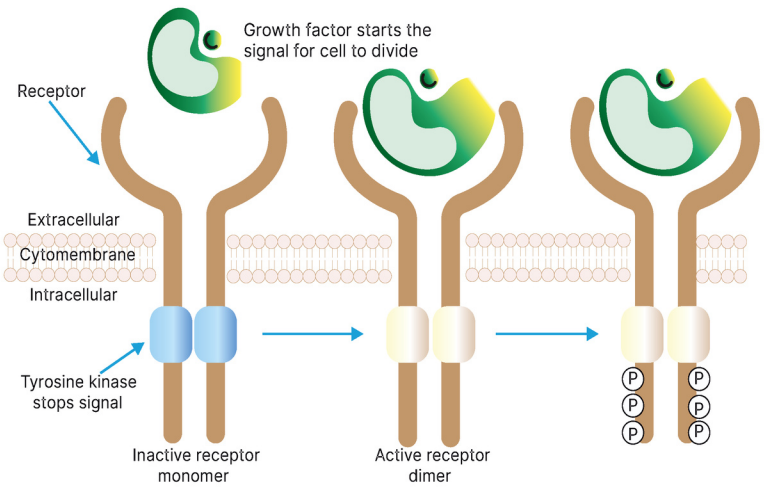
Answer:

- Molecule acting on Guanylyl cyclase enzyme: Nitric Oxide (NO)
- Increases cGMP (secondary messenger)

Q8.8: Describe Protein Kinase Receptors, their function, the type of hormones acting on them, and provide specific examples including subclasses and their associated ligands

Answer:

- Also known as Enzyme linked receptor
- Function: Produce cell division/Growth of cell
- They have Kinase enzyme on their tail
- Anabolic hormones acts on protein kinase receptors
- Examples:
  - Tyrosine kinase receptor:
    - → Insulin
    - → Insulin like growth factor
  - JAK-STAT receptor:
    - → Also known as cytokine receptor
    - → Growth hormone
    - → Prolactin



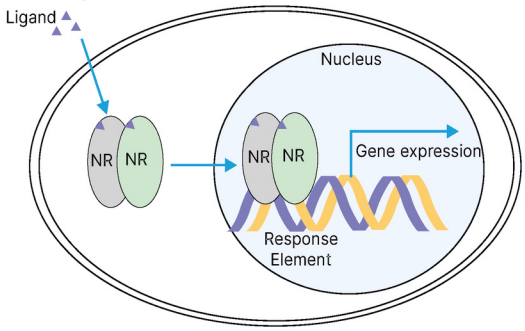
→ Cytokine:
  - Erythropoietin: RBC growth
  - Thrombopoietin: Platelet growth
  - Interleukin, Interferons: WBC growth

→ Leptin: Satiety hormone

Q8.9: Describe Intracellular Receptors, their unique location, mechanism of action and types

Answer:

- Only receptor present inside cell (All other receptors are on cell membrane)
- Also known as Nuclear receptors
  - Causes DNA transcription
  - Activate DNA directly
- Types

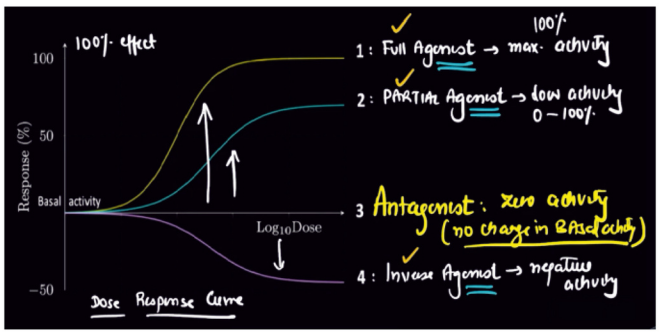


Intracytoplasmic	Intranuclear
• Translocate to DNA • **Steroidal hormones are lipid soluble can cross nuclear membrane** o Vitamin D/Calcitriol o Glucocorticoid o Mineralocorticoids o Testosterone o Progesterone	• Already in DNA • **Mnemonic: TAPE** o **T3/T4** (Thyroid receptors) o **V**itamin A o **P**PAR o **O**estrogen

BIG QUESTION 9: What are the different types of ligands based on their action, and how are they represented on a dose-response curve (DRC)?

Broad Answer:

- Ligands can act as agonists or antagonists, and are classified as follows:
  - Full agonist: Produces maximum activity with 100% effect
  - Partial agonist: Produces a submaximal response (between 0-100%)
  - Inverse agonist: Produces an effect opposite to the agonist (reduces basal activity)
  - Antagonist: Produces no effect but blocks the action of agonists (no change in basal activity)



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DETAILED QUESTIONS

Q9.1 Describe the types of antagonist

PYQ: FMGE 2022

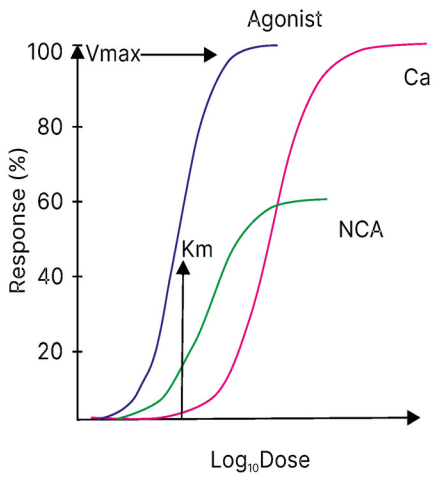
Answer: There are 4 main types of antagonists:

Physical antagonist	Chemical antagonist	Physiological antagonist	Pharmacological antagonist
• Binds physically to agonist • Reduce absorption of agonist from GIT • **Activated charcoal reduce absorption of poison**	• Bind chemically to agonist o Acid vs Base reaction • **Chemical neutralisation** • Examples o Protamine sulphate: HMW Heparin → High basic: Highly acidic o Antacids: Hcl o Chelators: Metals o Sugammadex: Ve/Ri-curonium (Skeletal muscle relaxant)	• **Binds to different receptor** • Produce opposite effect of agonist • Examples o Adrenaline (B2) vs Histamine (H1) → Bronchodilation: Bronchoconstriction o PTH vs Calcitonin → Hyper vs Hypocalcemia o Glucagon vs Beta-blockers → Reduce HR vs increase HR o Insulin Vs Glucagon, Growth hormone → Hypo vs Hyperglycemia o Prostacyclin vs Thromboxane → Inhibit vs induce platelet aggregation	• **AKA: Blockers** • Block the receptor • Divided into o Competitive Antagonist o Non-Competitive Antagonist o Examples → Adrenaline (alpha (a) and Beta (b) receptor) → Phenoxybenzamine (alpha (a) blocker) → Propranolol (beta (b) blocker)

Q9.2 : What is the difference between competitive agonist and non-competitive antagonist?

PYQ: FMGE 2020, 2022

Competitive agonist	Non competitive antagonist
• Block same receptor if agonist	• Antagonist binds to different site
• Antagonist blocks activity	• Reduce affinity of agonist to bind to receptor
• Right shift in DRC o Overcome effect of competitive antagonist by increasing dose of agonist	• Reduce slope of DRC o Downward shift o No change with dose
• V_{max} (efficacy): Unchanged	• V_{max} (efficiency): Reduced
• Km (dose): Increased	• Km (dose): Unchanged



Q9.3: True about competitive antagonism is

A. V_{max} is unchanged, but K_m increases

B. V_{max} is reduced, but K_m increases (NCA)

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C. V_{max} and K_m increase

D. V_{max} and K_m reduced

Answer: A. V_{max} is unchanged, but K_m increases

- In competitive antagonism, the antagonist competes with the agonist at the same receptor binding site. This means:
- K_m (affinity) increases - more agonist is needed to achieve the same effect
- V_{max} (maximum response) remains unchanged - because high enough concentrations of agonist can overcome the antagonist

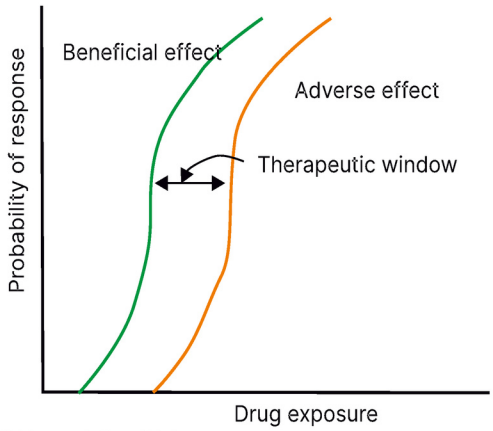
BIG QUESTION 10: Define the Therapeutic Index, its calculation, clinical significance as a safety margin, and list categories of drugs that require therapeutic drug monitoring due to a narrow therapeutic index

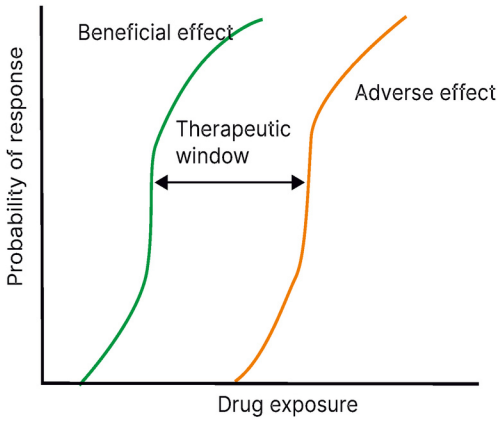
Broad Answer: The Therapeutic Index (TI) quantifies a drug's safety margin by comparing its toxic dose (TD_{50} or LD_{50}) to its effective dose (Ed_{50}). A low TI indicates an unsafe drug requiring careful therapeutic drug monitoring (TDM) of plasma concentrations to prevent toxicity Several drug classes, including digoxin, antiepileptics, aminoglycosides, and immunosuppressants, fall into this category

DETAILED QUESTIONS

Q10.1: What is the formula for calculating the Therapeutic Index (TI), and define its constituent terms (TD_{50}, ED_{50})?

PYQ: NEET PG 2022 PYQ: FMGE 2020





Answer:

- TI = TD_{50} / ED_{50} or LD_{50} / Ed_{50}
- TD_{50}: Toxic dose in 50% of population. Also known as 50 Lethal dose
- ED_{50}: Effective dose which cures a disease in 50% of population
- TI : Therapeutic index

Q10.2: How does the numerical value of the Therapeutic Index relate to the safety margin of a drug, and what is the implication of a small Ti value?

Answer:

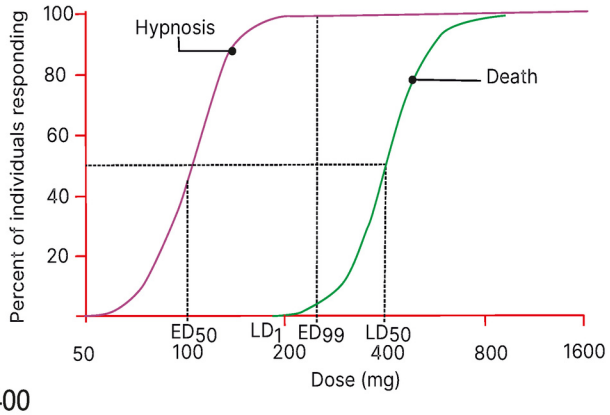
- Therapeutic index is the difference or space between ED_{50} and Td_{50}
  - o If value is small, toxicity occurs easily
- TI gives Safety margin of the drug
  - o Low value: Unsafe drugs
  - o Narrow therapeutic index drugs
    - → Requires monitoring

Q10.3: List the categories and specific examples of drugs that typically require Therapeutic Drug Monitoring (TDM) of their plasma concentrations

Answer:

- Drugs requiring Therapeutic Drug Monitoring, plasma concentration:
- Mnemonic: **DAAT LAAT CC**
  - o **D**igoxin
  - o **A**nti epileptic:
    - → Phenytoin
    - → Valproate
  - o **A**minoglycoside
  - o **T**heophylline (Anti asthmatic)
  - o **L**ithium
  - o **A**nti arrhythmic
  - o **A**ntipsychotic:
    - → Tricyclic antidepressants
  - o **C**yclosporine/Tacrolimus (Immunosuppressants)
  - o **C**ancer drugs (Methotrexate)

Q10.4 Calculate the therapeutic index of a drug whose DRC are plotted as shown below



- TD_{50} (Toxic Dose for 50%) = 400
- ED_{50} (Effective Dose for 50%) = 100
- Therapeutic Index (TI) = $\frac{TD_{50}}{ED_{50}} = \frac{400}{100} = 4$

Q10.5 :Give antidotes for the drug poisoning given below

Answer:

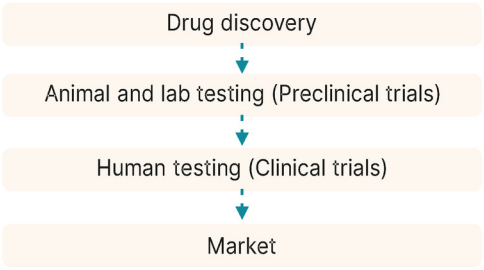
PYQ: FMGE 2020, 2021, 2022, 2023 | PYQ: NEET PG 2021, 2022

Drug poisoning	Antidote
• Digoxin	• DIGIBIND/DIGIFAB o Monoclonal Antibody against digoxin
• Lignocaine/ Bupivacaine (Local anaesthetic)	• 20% intralipid
• Aspirin	• Sodium bicarbonate
• Paracetamol	• N-acetylcysteine
• Morphine (opioids)	• i.v Naloxone
• Amphetamine	• Ammonium chloride

• Tricyclic antidepressant	• Sodium bicarbonate
• Organophosphate	• Atropine with Oxime o Pralidoxime
• Carbamate	• Atropine only o Oximes are contraindicated
• Atropine (Belladonna, Datura)	• Physostigmine o Increase acetylcholine level
• Methanol, Ethylene glycol	• Fomepizole
• Diazepam (Benzodiazepine)	• Flumazenil
• CCB (Verapamil)	• Calcium gluconate
• Propranolol (Beta-blockers) o Cause Bradycardia	• Glucagon hormone o Increase Heart rate

BIG QUESTION 11 : What is drug development and what are the steps involved?

Broad Answer: Drug development is a multi-step scientific process aimed at discovering, testing, and bringing new drugs to market It includes the following major stages:



DETAILED QUESTION

Q11.1: Explain different phases of clinical trials including number and type of volunteers involved, trial design, and main purpose?

Answer:

PYQ: FMGE 2023

Phase	AKA	Number and type volunteers	Design of trail	Purpose
Phase 0 (Not mandatory)	Micro-doing trail	2-5 healthy humans	Unblinded	• 100 micrograms of radiolabeled drug is given • Target binding is checked
Phase 1	Safety and pharmacology trail	20-50 healthy humans	Unblinded	• Safety: Max. Tolerable dose • PK: ADME • Not for efficacy
Phase 2	Therapeutic exploratory trials	200-500 patients	RCT (Randomised control trial) + Blinding	• Efficacy is explored • Dose at which drug is effective
Phase 3	Therapeutic confirmatory trials	2000-5000 patients	RCT + Blinding	• Confirm actual dose
Phase 4 (Market approval after phase 3)	Post-marketing surveillance	Patients	Unblinded	• Safety o Rare or missed ADR

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Q11.2: Which of the following is typically NOT the primary objective of Phase 1 clinical trials?

A. Efficacy

B. Safety

C. Max. tolerable dose

D. Pharmacokinetics

Answer: A. Efficacy

- Efficacy is explored in Phase 2 of clinical trials

Q11:3: Which phase of clinical trials is typically the most costly, involves multi-site trials, and is conducted on a heterogeneous population?

Answer:

- **Phase 3**
  - **Most costly**
  - **Multi-site trial**
  - **Heterogeneous population**

Q11.4: In terms of safety and efficacy data, how do the clinical trial phases generally compare?

Answer:

- Best data on safety: 3>2>1
- Best data on efficacy: 3>2

Q11.5: In which phase of clinical trials does the maximum rate of drug failure typically occur?

Answer: Maximum failure: 2

Q11.6: After which phase of clinical trials does a drug typically receive market approval?

Answer: Drug comes into market after: 3

Q11.7: Which phase of clinical trials is not mandatory?

Answer: Not mandatory: Phase 0

Q11.8: If a drug already approved in Europe needs to be marketed in India, which phase of the clinical trial must be conducted for its approval in India, and what is this type of trial also known as?

Answer:

- Phase 3, AKABridging trials

Q11.9: After market approval of the drug is done after which phase?

Answer: Phase 4

Q11.10: Random control trail along with blinding is done in which phases of clinical trials?

Answer: Phase 2, and 3

Q11.11: Phase 1 clinical trial is performed on whom and what's its main purpose?

Answer:

- Phase 1 is done on healthy humans
- It is done to check max tolerable dose

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BIG QUESTION 12: What are the different classifications of drugs

Broad Answer: Drugs are categorized based on various criteria, including whether they are placebos (inert substances used for blinding in trials), counterfeit drugs (fabricated with intent to deceive, encompassing spurious, misbranded, and adulterated types), or orphan drugs (for rare diseases) Additionally, drugs have brand and generic names, are listed in pharmacopoeias, and have expiry dates Essential drugs are a specific category characterized by affordability, efficacy for prevalent diseases, and availability in various formulations

DETAILED QUESTIONS

Q12.1: What is a Placebo, and its primary use in clinical trials?

Answer:

- AKA: Dummy drug
- Does not contain active drug
- Has inert substance
- Should look exactly similar in looks and taste to active drug
- Used as controlled arm in RCT which helps in blinding
- **Note:** Sham surgery is a fake surgery

Q12.2: What are Counterfeit drugs? Describe the three specific types: Spurious, Misbranded, and Adulterated drugs

Answer:

- Made with intention to cheat/harm
- Spurious drugs:
  - AKA: Falsified drugs
  - No drug in the formulation
- Misbranded drugs:
  - AKA: Substandard drug
  - Dose is incorrect
- Adulterated drugs:
  - Addition of harmful or unwanted excipients

Q12.3: What are Orphan drugs, and what is their prevalence criterion?

Answer:

- Drugs for rare disease
- If prevalence: <1 per 5 lakh population

Q12.4: Name a few rare diseases along with their orphan drug.

Answer:

Rare disease	Orphan drugs
Iron poisoning	Desferioxamine
Digoxin poisoning	DIGIBIND
Methanol & Ethylene glycol poisoning	Fomepizole
Infantile spasm	ACTH hormone

Q12.5: Differentiate between a Brand name and a Generic name of a drug

Answer:

- Brand name: Ecosprin-150
  - o AKA: Proprietary name
  - o Property of a particular company
- Generic name: Aspirin
  - o AKA: Non proprietary name
  - o Not a property of anyone



Q12.6: What does "IP" stand for in the context of pharmacology?

Answer: IP: Indian Pharmacopoeia

Q12.7: What is the significance of expiry dates on drugs regarding manufacturer responsibility?

Answer: After the expiry the manufacturer is not responsible for any adverse effects

Q12.8: Who is legally qualified to open a chemist shop?

Answer: B pharmacy

Q12.9: What are the defining characteristics of Essential drugs, and what is the general recommendation regarding their Fixed Dose Combinations (FDCs)?

Answer:

- Cost effective, affordable
- Highly prevalent disease like Diabetes & Hypertension
- Avoid combining them as FDC (Fixed dose combination)
- Available in all doses and formulation

Q12.10: What are the recommended drug storage temperature ranges and their classifications?

Answer:

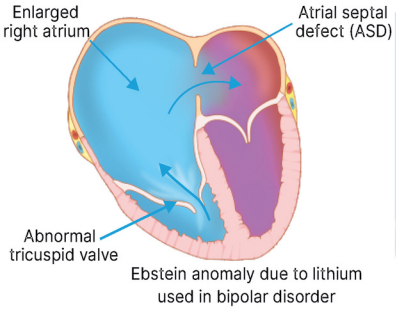
Freeze	-10 to -20°C
Cold	<5°C
Cool and Dry	8-15°C
Warm	30-40°C
Excessive heat	>40°C

Q12.11: What drugs are included in the teratogenic group, and what fetal anomalies are they associated with?

Answer:



Phocomelia



Ebstein Anomaly



Aplasia cutis

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Teratogenic drugs	Fetal Malformations
• Thalidomide	• Phocomelia (Short limbs)
• Lithium • ACE inhibitors (Pril)	• Ebstein anomaly (cardiac anomaly) o Tricuspid valve is not produced properly • Absolutely contraindicated in pregnancy • Renal agenesis
• Warfarin o Contraindicated in first trimester	• Bone and cartilage defect o Saddle nose
• Carbimazole, Methimazole o Contraindicated in first trimester	• Aplasia cutis
• Tetracycline	• Bone and cartilage deformity o Saddle nose
• Valproate, Methotrexate o Antifolate drugs	• Neural tube defects
• Phenytoin o Anti epileptic drug	• Cleft palate, lip

Q12.12: What are the drugs of choice and contraindicated drugs for various diseases during pregnancy?

Answer:

Pregnancy		
Disease in pregnancy	**Drug of choice**	**Contraindicated**
• Epilepsy	• Levetiracetam > Lamotrigine	• Valproate (most teratogenic)
• Bipolar disorder	• Antipsychotic	• Valproate (most teratogenic)
• Hypertension	**Mnemonic: LHMC** • **L**abetalol • **H**ydralazine • **M**ethyldopa • **C**CB (Nifedipine)	• ACE inhibitors • ARBs
• Hyperthyroidism	• 1st trimester: PTU (Propyl thiouracil) • 2 and 3 trimesters: Carbimazole, Methimazole	• 1st trimester: Carbimazole, Methimazole • 2 and 3 trimesters: PTU (Propyl thiouracil)
• Anticoagulant	• LMW/ULMW Heparin	• Warfarin, upto 12 weeks (1st trimester)
• Antibiotics	• Penicillin • Cephalosporin • Macrolide (Azithromycin)	• **F**luoroquinolone: Ciprofloxacin, Ofloxacin • **A**minoglycoside o Streptomicin • **T**etracycline • **S**ulfonamides

BIG QUESTION 13: What are the different categories of scheduled drugs in India?

Broad Answer: Drugs in India are categorized under various schedules that dictate their dispensing and control. Schedule H drugs require a prescription, Schedule X drugs are narcotics/psychotropics with addictive potential, Schedule G drugs necessitate medical supervision, and Schedule Y previously governed clinical trials. These classifications ensure proper regulation and safe use of pharmaceuticals

DETAILED QUESTIONS

Q13.1: Describe the characteristics and dispensing requirements for drugs classified under Schedule H

Answer:

- Prescription drugs
- Only given by physician
- Written by: Rx

Q13.2: Describe the characteristics and dispensing requirements for drugs classified under Schedule X, including their addictive potential and associated prescription notation

Answer:

- Narcotic and psychotropic drugs
- Addictive potential
- Written by: Nrx

Q13.3: What is the primary requirement for drugs classified under Schedule G?

Answer: Given under medical supervision

Q13.4: What was the original purpose of Schedule Y, and what is its current status?

Answer:

- Clinical trials rule in India
- Recently scrapped or replaced with NDCTR-2019 (New Drugs and Clinical Trials Rule)

Q13.5: Which of the following is a Schedule X drug under the Drugs and Cosmetics Act of India?

A Thalidomide
B Enalapril
C Methotrexate
D Ketamine

Answer: D. Ketamine

- Ketamine is classified under Schedule X as it is a narcotic/psychotropic drug with potential for abuse and addiction

Q13.6: What is the primary characteristic of Ketamine in relation to drug scheduling?

Answer: Ketamine is a Narcotic or psychotropic drug

Q13.7: List the drugs mentioned that fall under Category X for pregnancy (teratogenic drugs)

Answer:

- Category X drugs of pregnancy (Teratogenic drugs):

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- Thalidomide
- Enalapril
- Methotrexate

Q13.8: What is Pharmacovigilance, and what is its primary function?

Answer:

- Branch of pharmacology that monitors and reports to higher authorities
  - To Keep Check

Q13.9: What are the types of Adverse Drug Reactions (ADR)?

Answer:

Types of ADR	Name	Example
A	Augmented dose • High dose • **AKA: Toxicity of drug**	• Hypoglycemia to insulin
B	Bizarre • Any dose • **AKA: Idiosyncratic reactions** • Genetically determined	• Allergic reactions
C	Continuous use of drug	• Peptic ulcer to aspirin
D	Delayed onset • Gap between stop of drug and ADR occurrence	• Teratogenic
E	End of treatment • Sudden stoppage of drug	• Withdrawal reactions
F	Failure of effects • No beneficial effects	• Antimicrobial resistance

Q13.10: Clozapine-induced agranulocytosis (bone marrow suppression) is which type of ADR?

A Type A toxicity

B Type B dose-independent idiosyncratic

C Type C chronic use

D Type D delayed onset

Answer: B. Type B dose-independent idiosyncratic

Explanation:

- Type B ADR (Bizarre/Idiosyncratic):
  - Unpredictable
  - Not dose-dependent
  - Often immune-mediated or genetically determined
- Clozapine-induced agranulocytosis is rare, unpredictable, and not related to dosage — making it a classic example of Type B (idiosyncratic) ADR

Q13.11: Describe the drugs that require pharmacogenetic testing, along with the specific genetic test used:

Drug	Pharmacogenetic test
• Warfarin	• VKORC1 + CYP2C9
• Azathioprine, 6- Mercaptopurine	• TPMT (Thiopurine Methyltransferase) o Degrades Thiopurine as azathioprine o Deficient: Azathioprine toxicity
• 5-Fluorouracil	• Degraded by Dihydro pyrimidine dehydrogenase (DHPD)
• Succinylcholine	• Pseudocholinesterase (Dibucaine number)
• Irinotecan, Atazanavir	• Contraindicated in Crigler Najjar syndrome
• Abacavir	• HLAB5701 test o Positive: Severe allergy

Q13.12: Which specific drugs should be avoided in patients with G-6-PD deficiency, and what is the risk associated with them?

Answer:

- Risk: Lead to hemolysis of RBC
- Drugs avoided in G-6-PD deficiency (Mnemonic: **MAD FANS**)
  - o **M**etronidazole
  - o **A**spirin
  - o **D**apsone
  - o **F**luoroquinolone
  - o **A**ntimalarials:
    - → Primaquine
    - → Proguanil
    - → Quinine
  - o **N**itro:
    - → Nitroprusside
    - → Nitrates
  - o **S**ulfa: Sulfonamides

2. AUTONOMIC NERVOUS SYSTEM

BIG QUESTION 1: Explain briefly about the autonomic nervous system.

Broad Answer: The autonomic nervous system (ANS) is a division of the peripheral nervous system that regulates involuntary physiological functions such as heart rate, digestion, respiratory rate, and glandular activity. It is divided into the sympathetic and parasympathetic systems, which generally have opposing effects—sympathetic promotes "fight or flight" responses, while parasympathetic supports "rest and digest" activities. The ANS operates via a two-neuron pathway involving preganglionic and postganglionic neurons

DETAILED QUESTIONS

Q1.1: What is the function of the sympathetic nervous system?

Answer: Function of the Sympathetic nervous system - Fear/emergency

Q1.2: What is the function of the parasympathetic nervous system?

Answer: Function of the Parasympathetic Nervous System - Rest/Digest

Q1.3: Tabulate the difference between the sympathetic and parasympathetic nervous systems.

Answer:

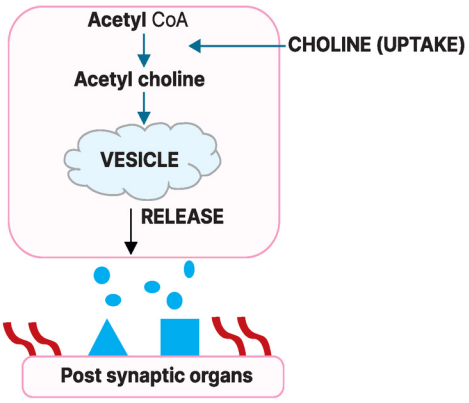
Sympathetic Nervous System	Parasympathetic Nervous System
• Increased HR • Dilated bronchus • Mydriatic pupil • Decreased urination • Decreased HCL production • Decreased peristalsis • Lipolysis • Penile ejaculation	• Decreased HR • Constricted bronchus • Miotic pupil • Increased bladder contraction • Increased HCL • Increased peristalsis • Lipogenesis • Penile erection

Q1.4: What are the key steps and inhibitors involved in the synthesis, storage, release, and degradation of acetylcholine (ACh)?

Answer:

- Choline uptake: Rate-limiting step
  - Blocked by **hemicholinium**
- Vesicle entry is inhibited by vesamicol
- Botulinum toxin: Inhibits the release of Ach
- Acts on postsynaptic organs
  - Nicotinic receptor
  - Muscarinic receptor

- Enzyme attached: Acetylcholinesterase
  - Degrades endogenous Ach
- Similar enzyme: BACHE/ PACHE (butyryl/pseudocholinesterase)
  - Blood/ plasma
  - It degrades exogenous Ach



Q1.5: What is the mechanism of action of botulinum toxin?

Answer:

Inhibits the release of acetylcholine → By blocking calcium channel snare protein (responsible for fusion of vesicles of Ach)

Q1.6: What are the uses of botulinum toxin?

Answer:

- Muscle spasm/ rigidity (Mnemonic: **BATS**)
  - **B**lepharospasm
  - **A**chalasia cardia
  - **T**orticollis
  - **S**quint
- Hyperhidrosis
- Cosmetic use: To reduce wrinkles
  - Botox injection
  - The most commonly used type is Type A toxin

BIG QUESTION 2: Describe the receptors of acetylcholine.

Broad Answer: Acetylcholine acts on two main types of receptors: **nicotinic** and **muscarinic** receptors. Nicotinic receptors are ionotropic and found at neuromuscular junctions, autonomic ganglia, and the adrenal medulla, mediating fast synaptic transmission. Muscarinic receptors are G-protein-coupled and are primarily located in target organs of the parasympathetic nervous system, where they mediate slower, modulatory responses

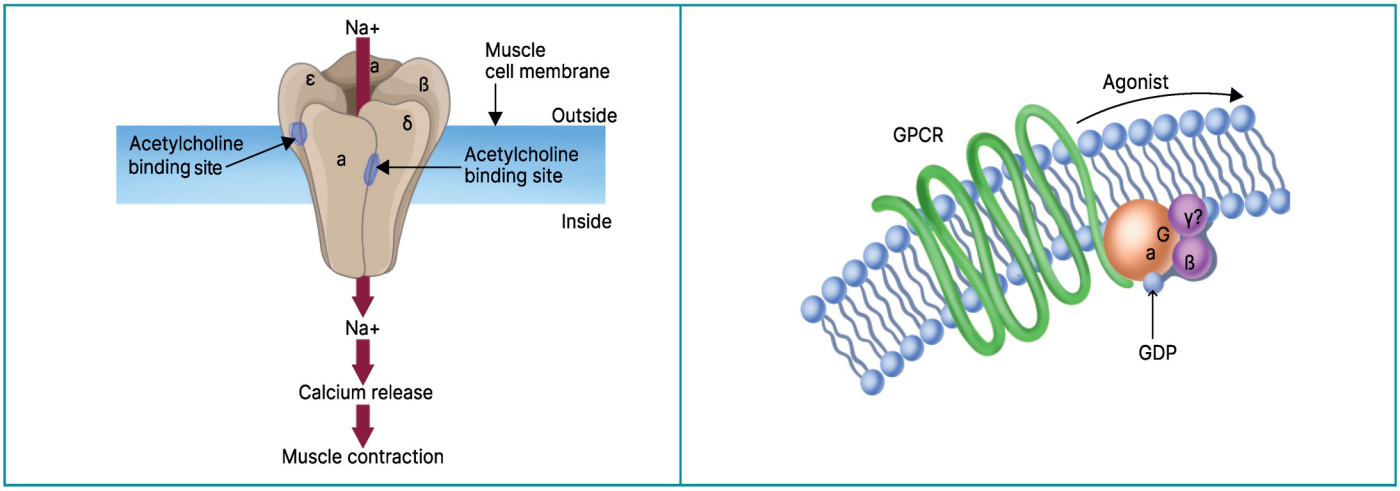
DETAILED QUESTIONS

Q2.1: What are the receptors of acetylcholine?

Answer:

Nicotinic receptors	Muscarinic receptors
• Ionotropic receptor: Conducts Sodium • **Pentameric Rosette shape**	• G protein-coupled receptors • 7 transmembrane serpentine

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Q2.2: Write briefly about the location, types, agonist and antagonist of nicotinic receptors.

Answer:

Nicotinic receptors		
Type	Nn	Nm
Location	Postganglionic neurons • SNS • PSNS	Skeletal muscle: Depolarizes and contracts due to sodium entry
Agonist	Nicotine	Nicotine
Antagonist	• Ganglionic blockers • Drugs o Hexamethonium o Mecamylamine o Trimethaphan: During arterial surgeries	• Nondepolarizing muscle relaxants • Drugs o Tubocurare o Atracurium o Vecuronium

Q2.3: How do muscarinic receptors in the brain influence memory and movement, and what is their role in the treatment of Alzheimer's and Parkinson's disease?

Answer:

- Location: Brain (Mainly M1)
  - o Hippocampus:
    - → Increased Ach
    - → Increased memory
    - → Given in Alzheimer's (Cholinergic drugs are given)
  - o Basal ganglia
    - → Reduced dopamine secretion
    - → Given in Parkinson's (Anti-cholinergic drugs are given)

Q2.4: Which muscarinic receptors are excitatory or inhibitory, and what type of G-protein do they couple with?

Answer:

Muscarinic Receptors → M1, M3, M5 → Gq (excitatory)
Muscarinic Receptors → M2, M4 → Gi (inhibitory)

Q2.5: Explain briefly about M1, M2, and M3 receptors concerning their location, effects, and examples of their agonists and antagonists.

Type	M1	M2	M3
Periphery Location	Stomach	Heart	Rest
Effect	Increased Hcl	Bradycardia	Increased activity
Agonist	-	Methacholine	Bethanechol
Antagonist	• Pirenzepine • Telenzepine o Given in peptic ulcer	-	• Sorifenacin • Darifenacin

BIG QUESTION 3: Write briefly about cholinergic drugs.

Broad Answer: Cholinergic drugs are agents that mimic the action of acetylcholine by stimulating cholinergic receptors. They can be **direct-acting** (e.g., pilocarpine, bethanechol), which activate muscarinic or nicotinic receptors, or **indirect-acting** (e.g., neostigmine, physostigmine), which inhibit acetylcholinesterase, increasing acetylcholine levels. These drugs are used in conditions like glaucoma, myasthenia gravis, and urinary retention

DETAILED QUESTIONS

Q3.1: What are the effects of cholinergic drugs?

Answer:

- Increases all secretions
- Mnemonic: **DUMBBELLS**
  - o **D**iarrhoea: M3
  - o **U**rination: M3
  - o **M**iosis: M3
  - o **B**ronchospasm: M3
  - o **B**radycardia: M2
  - o **E**xcess HCL: M1
  - o **L**acrimation: M3
  - o **S**alivation: M3
  - o **S**weating: M3

Q3.2: Tabulate the directly acting cholinergic drugs.

Answer:

Esters	Alkaloids
• Acetylcholine o Shortest-acting o Rapidly degraded by pseudocholinesterase • Bethanechol o M3 agonist: Contracts bladder and intestine o Given in postoperative bladder atony, paralytic ileus • Carbachol o Same as Bethanechol	• Natural drugs • Pilocarpine o Eye drops: 0.5-4% o DOC to produce miosis → In glaucoma o Also given in Xerostomia and Xerophthalmia → Sjogren Syndrome

• Methacholine o M2 agonist o Inhalational to provoke asthma if susceptible → Methacholine challenge test	→ Cystic fibrosis → Radiotherapy • Nicotine: Used in smoking de-addiction • Muscarine: Used in poisonous mushroom

Q3.3: What are the common pharmacological options and their routes or mechanisms used for smoking de-addiction treatment?

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Answer:

- Nicotine: Given by transdermal route, nasal spray, lozenges/ gums
- Varenicline
  - o A partial agonist at the nicotinic receptor that is given orally
  - o S/E: Depression/suicide
- Bupropion: Antidepressant (NDRI- Norepinephrine-Dopamine Reuptake Inhibitor)

Q3.4: Nicotine, Varenicline, and Bupropion are contraindicated in which conditions?

Answer:

- Nicotine, Varenicline, and Bupropion are contraindicated in:
  - o Heart diseases- HTN, Angina
  - o CNS- Seizures

Q3.5: What is the 2nd drug used in the treatment of smoking addiction?

Answer: Clonidine: Safe for the heart and in CNS disease

Q3.6: What is the most effective treatment and the most effective drug used in smoking de-addiction?

Answer:

- Most effective treatment: Psychological overcoming/quitting
- Most effective drug: Varenicline
  - o Also approved for tobacco chewing addiction

Q3.7: Tabulate the difference between early, late and hallucinogenic mushroom poisoning ?

Answer:

	Early Mushroom Poisoning	Late Mushroom Poisoning	Hallucinogenic Type
Species	Inocybe	Amanita phalloides	Amanita Muscaria
Toxin	Muscarine	Liver damage	Muscimol
Symptom	Dumbbells	Hepatotoxic	Hallucination/ Seizures
Antidote	Atropine	Hepatoprotective drugs • Thioctic acid • Silibinin	Atropine is contraindicated.

BIG QUESTION 4: Describe indirectly acting cholinergic drugs.

Broad Answer: Indirectly acting cholinergic drugs inhibit the enzyme **acetylcholinesterase**, which breaks down acetylcholine, thereby increasing its concentration at synapses. This enhances cholinergic transmission at both muscarinic and nicotinic receptors. Examples include **neostigmine**, **physostigmine**, and **donepezil**, used in conditions like **myasthenia gravis**, **Alzheimer's disease**, and **postoperative ileus.**

DETAILED QUESTIONS

Q4.1: What is the mechanism of action of indirectly acting cholinergic drugs?

Answer:

- Inhibits ACHE < PACHE
- Inhibits degradation of Ach: Increases endogenous Ach

Q4.2: Name the classes of indirectly acting cholinergic drugs.

Answer:

- 2 types:
  - Carbamates
  - Organophosphates

Q4.3: Elaborate on the differences between Tertiary amines and Quaternary amines

Answer:

Carbamates:

Tertiary amines: Nh_3	Quaternary amines: NH_4
• Lipid soluble • Cross BBB • Physostigmine: o DOC: Atropine Poisoning • Drugs for Alzheimer's Disease	• Water soluble • Don't cross BBB • Neostigmine o Directly stimulates Muscarinic receptors o Causes bradycardia o Excess secretions o Atropine is given to block muscaranic symtoms • Edrophonium: Shortest acting • Pyridostigmine: Longest acting o Blocks Nm receptor: Muscle paralysis • Uses o Cobra bite poisoning, Curare reversal, Myasthenia Gravis

Q4.4: What are the drugs used in the treatment of Alzheimer's disease?

Answer:

- Anti-cholineesterases
- Memantine
- Monoclonal antibodies

Q4.5: Which anticholinesterase drugs are used in Alzheimer's disease, and what are their key features and routes of administration?

Answer:

- Anticholinesterases increase Ach. Drugs include:
  - Tacrine: Banned due to hepatotoxicity
  - Donepezil: Longest acting / most effective / DOC
  - Galantamine
  - Rivastigmine: Used as transdermal patches

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Q4.6: What is the mechanism of action of Memantine, and its role in the management of Alzheimer's disease?

Answer:

- Memantine is an NMDA antagonist
- It improves memory in the treatment of Alzheimer's disease

Q4.7: Which monoclonal antibodies are used in Alzheimer's disease, and what is their target?

Answer:

- Monoclonal Antibodies used in the treatment of Alzheimer's disease:
  - Aducanumab
  - Lecanemab
- They act by blocking Beta (β) 1 amyloid protein

Q4.8: What are the drugs used in Myasthenia Gravis?

Answer:

Blocks Nm receptors

Indication	
Symptomatic Treatment Muscle weakness	DOC: Neostigmine/ Pyridostigmine • Combine with Atropine
Definitive Treatment	• Prednisolone (induction) • Azathioprine (maintenance)
Myasthenic Crisis	• Plasmapheresis • IV-Ig
Diagnosis	Edrophonium

Q4.9: Describe the Edrophonium Challenge test.

Answer:

- A 10 mg injection of Edrophonium shows improvement (eyes open)
  - Also known as the Tensilon test
- Diagnosis of Myasthenia Gravis

Q4.10: Name the drugs avoided in Myasthenia Gravis.

Answer:

- Antibiotics
  - Aminoglycosides
  - Fluoroquinolones
  - Macrolides
  - Colestine
- Beta (b) blockers: Propranolol
- Curare: Tubocurare

→ Blocks Nm:
Aggravates muscle paralysis

Q4.11: Write a short note on the drugs used in snake bite.

Answer:

- Cobra

- Krait
  - Venom: Neurotoxic
  - Blocks Nm receptor
  - Leads to Muscle paralysis
- DOC: **Polyvalent Antivenom**
- In Muscle paralysis: Neostigmine + Atropine is given

Q4.12: What are the drugs classified under irreversible anti-cholinesterase?

Answer:

- **Carbamates:**
  - Carbaryl
  - Aldicarb
  - Propoxur
- **Organophosphates:**
  - Malathion, Parathion
  - TIK-20
  - Chlorpyrifos
  - Nerve gases
    - → Tabun
    - → Sarin
    - → Soman: Used in wars
- Chlorpyrifos + Propoxur is known as Baygon

Q4.13: What is the mechanism, clinical presentation, and diagnostic method for carbamate and organophosphate (OP) poisoning?

Answer:

- Mechanism causing clinical features:
  - Inhibits ACHE, PACHE
  - Increased Ach levels
- **Clinical presentation:** Produces the symptoms of DUMBBELLS
- **Diagnosis:** Reduces the activity of PACHE and RBC esterase enzyme

Q4.14: What is the treatment difference between organophosphate and carbamate poisoning?

Answer:

Treatment	
Organophosphate Poisoning	Carbamate Poisoning
• IV Atropine (DOC) • Cholinesterase reactivation o Oximes → Pralidoxime (PAM) → Di acyl monoxime (DAM)	• IV Atropine (DOC) • Oximes are contraindicated

BIG QUESTION 5: Describe briefly about Anticholinergic Drugs.

Broad Answer: Anticholinergic drugs block the action of acetylcholine at muscarinic receptors, thereby inhibiting

parasympathetic nerve impulses. They are used to treat conditions like **asthma (e.g., ipratropium)**, **motion sickness (e.g., scopolamine)**, and **Parkinson's disease (e.g., benztropine)**. Common side effects include dry mouth, blurred vision, urinary retention, and constipation

DETAILED QUESTIONS

Q5.1: What are Anticholinergic drugs also known as?

Answer:

- Antimuscarinic drugs

Q5.2: Name the natural Anticholinergic drugs.

Answer:

- Only 2 drugs are natural; the rest are all synthetic
  - Atropine: Belladonna, Datura
  - Hyoscine: Scopolamine

Q5.3: Name the other classes of drugs that have anticholinergic action.

Answer:

1. TCAs
2. Antihistamine
3. Quinine
4. Amantadine

Q5.4: What are the clinical features of Atropine Poisoning?

Answer:

• Hot as hare	• Hyperthermia • MC: Children
• Red as Beat	• Flushing
• Dry as bone	• Dry eyes/dry mouth • MC: Adults
• Blind as Bat	• Mydriasis and Cycloplegia
• Mad as hatter	• Delirium and seizures • Constipation, Urinary retention, tachycardia

Q5.5: What is the antidote for atropine poisoning?

Answer:

- Antidote: **Physostigmine** (can cross BBB)
  - Not Neostigmine because it does not cross the BBB

Q5.6: What is the role of hyoscine (scopolamine) in the cortex, and what is it used for?

Answer:

- Hyoscine (Scopolamine) decreases cognition and produces sedation
- It is also known as truth serum and used in Narcoanalysis

Q5.7: What is the DOC in Narcoanalysis?

Answer: Thiopentone

Q5.8: What is the effect of anticholinergic drugs in the Basal ganglia, and what is their clinical significance?

Answer:

- Anticholinergic drugs increase dopamine levels by acting in the basal ganglia of the brain.
- It is used to treat drug-induced Parkinson's disease
  - DOC: Benzhexol
  - Muscle dystonia
  - Benztropine
  - Biperiden

Q5.9: Which drugs have both antihistaminic and anticholinergic properties, and where do they act in the brain?

Answer:

- Promethazine & Diphenhydramine have both antihistaminic and anticholinergic properties
- They act in the basal ganglia of the brain

Q5.10: Which antimuscarinic drugs act on the vestibule, and what is their clinical use?

Answer:

- **Indication:** Motion sickness
- **Drugs used:** Antimuscarinic drugs
  - Hyoscine - Transdermal patch (placed in post-auricular area)
  - Oral drugs:
  - Diphenhydramine
  - Promethazine
  - Cyclizine
  - Meclizine
  - Cinnarizine
- **Purpose:** Only for the prevention of nausea and vomiting
- **Timing:** Should be given at least 30 minutes before the journey
- **Side effect:** Sedation

Q5.11: What is the effect of Atropine on the heart, and where is it used?

Answer:

- Atropine blocks M2 receptors in the SA/ AV node
- It used to treat Bradycardia & AV node block

Q5.12: Which anticholinergic drugs are used in the respiratory tract, and what are their clinical applications?

Answer:

- Glycopyrrolate
  - Causes bronchodilation
  - Produces dryness of respiratory secretions
  - Used during surgery
- Inhalational anticholinergics (used in asthma and COPD):
  - Ipratropium

- Tiotropium
- Umeclidinium
- Aclidinium

Q5.13: What is the effect of Cycloplegic drugs on the eyes, and what are they used for?

Answer:

- Cycloplegic drugs cause paralysis of the ciliary muscles
- Used to treat Anterior Uveitis and used in the Refractive Error Test

Q5.14: What is the effect of Mydriatic drugs on the eyes, and what uses and contraindications of these drugs?

Answer:

- Mydriatic drugs cause paralysis of the sphincter pupillary muscle
  - DOC in fundoscopy in children: Atropine, used as 1% ointment
  - Treatment of Anterior Uveitis and Refractive Error Testing:
  - Cyclopentolate
  - Tropicamide
  - Homatropine
- Mydriatic drugs are contraindicated in Glaucoma

Q5.15: What is the effect of anticholinergic drugs on the bladder, its clinical significance?

Answer:

- Target:
  - Blocks M3 receptors in the detrusor muscle
  - Prevents contraction ▫ Reduces urination
- Indication:
  - Overactive bladder / Detrusor hyperactivity

Q5.16: Name the anticholinergic drugs acting on the bladder.

Answer:

- Mnemonic: OFF To School Days
  - Oxybutynin *(least vasicoselective)*
  - Flavoxate
  - Fesoterodine
  - Trospium
  - Does not cross the BBB
  - Preferred in Alzheimer's disease
  - Solifenacin
  - Darifenacin

Q5.17: Which anticholinergic drugs are used in the treatment of peptic ulcer, and what receptors do they target?

Answer:

- Pirenzepine & Telenzepine
  - Block M1 receptors
  - Used in peptic ulcer treatment to reduce gastric acid secretion

Q5.18: Which anticholinergic drugs are used as antispasmodic agents for their effect on the intestines, and which drug is contraindicated in colicky pain?

Answer:

- M3 receptor effects:
  - Causes diarrhoea and spasm of sphincters ▫ colicky pain
- Antispasmodic drugs:
  - Dicyclomine
  - Glycopyrrolate
  - Hyoscine
  - Solifenacin
  - Darifenacin
  - Drotaverine (a PDE4 inhibitor)
- Contraindicated drug in colicky pain: Opioids like Morphine

Q5.19: Name the conditions where anticholinergic drugs (atropine) are contraindicated.

Answer:

- Atropine: Anticholinergics are contraindicated in:
  - Benign prostate hypertrophy
  - Alzheimer's
  - Glaucoma

BIG QUESTION 6: Write briefly about Adrenergic Drugs.

Broad Answer: Adrenergic drugs stimulate the **sympathetic nervous system** by activating **alpha and beta adrenergic receptors**, mimicking the effects of adrenaline and noradrenaline. They can be **direct-acting** (e.g., epinephrine, salbutamol) or **indirect-acting** (e.g., amphetamines), and are used in conditions like **asthma, hypotension, and anaphylaxis**. These drugs increase heart rate, blood pressure, and bronchodilation, among other effects.

DETAILED QUESTIONS

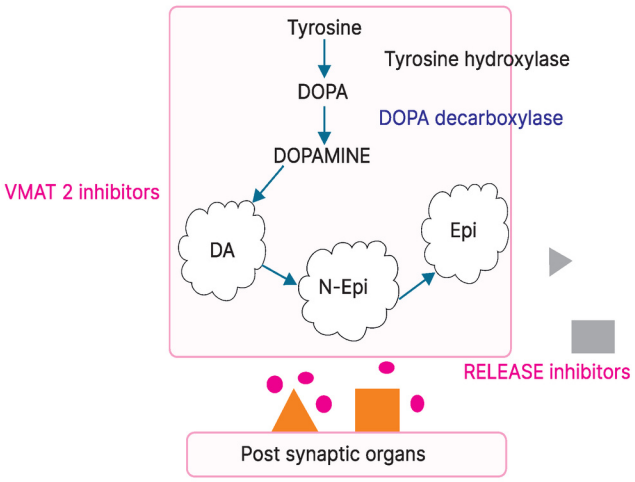
Q6.1: What are the endogenous catecholamines, their receptor selectivity, and clinical uses?

Answer:

- Endogenous Catecholamines (Mnemonic: DNA)
  - Dopamine does not act on ß-2 receptors.
  - Noradrenaline/ Norepinephrine: Doesn't act on Beta (b) 2 receptors
  - Adrenaline/ Epinephrine
    → Acts on all receptors
    → Used in anaphylactic shock

Q6.2: What are the key steps in catecholamine synthesis and release, and which drugs inhibit each step?

Answer:



Q6.3: Which enzymes involved in catecholamine synthesis are targeted by drugs, and what are the inhibitors and their clinical uses?

Answer:

- **Tyrosine hydroxylase** (rate-limiting step)
  - **Inhibited by:** Metyrosine
  - **DOC for:** Pheochromocytoma
- **DOPA decarboxylase**
  - Inhibited by: Carbidopa

Q6.4: Which dopamine-depleting drugs inhibit vesicle entry and what are their clinical indications?

Answer:

- **Dopamine depleters (inhibit vesicle entry):**
  - Tetrabenazine
  - Valbenazine
  - Deu-Tetrabenazine
- **Used in:**
  - Huntington's chorea
  - Tardive dyskinesia

Q6.5: What is the mechanism of action of guanethidine, its clinical use, and major side effects?

Answer:

- **Mechanism:** Inhibits the release of catecholamines, especially norepinephrine
- **Clinical use:** Treatment of hypertension (HTN)
- **Side effect:** Hypotension

Q6.6: What are the effects of cocaine on the sympathetic nervous system, and what is its clinical application?

Answer:

- **Mechanism:** Increases sympathomimetic activity
- **Effects:** Causes vasoconstriction
- **Clinical use:** Acts as a local anesthetic

Q6.7: Tabulate the different types of adrenergic agonist, antagonists and their receptors.

Answer:

Agonist	Receptors	Antagonist
Phenylephrine	Alpha (α) 1	Prazosin
Clonidine	Alpha (α) 2	Yohimbine
Dobutamine	Beta (β) 1	Atenolol/ Metoprolol
Salbutamol	Beta (β) 2	Butaxamine
Merabegron	Beta (β) 3	

Q6.8: What are the directly acting Adrenergic drugs? Elaborate on the receptors they act on and their clinical effect?

Answer:

- Stimulates alpha (α) and beta (ß) receptors
  - Dopamine
  - Noradrenaline

- Adrenaline
- Norepinephrine acts on beta (β) 1 receptor and increases HR
- Norepinephrine acts on the alpha (α) 1 receptor and increases BP
- Dobutamine only acts on beta (β) 1 receptor
- Dopamine acts on beta (β) 1 and D1 receptors - increases GFR

Q6.9: What are the drugs of choice for different types of shock, along with the preferred route and dose of adrenaline in emergencies?

Answer:

- Given in Shock
- Through IV: Not orally (Degraded by MAO enzymes in the GIT)

Shock	Drug of Choice
Anaphylactic shock	Epinephrine: 0.5 ml of 1:1000 IM
Cardiac arrest	Epinephrine: 1 ml of 1:10,000 IV, I/osseous(tibia)
Septic Shock	Norepinephrine
Neurogenic shock	Norepinephrine
Cardiogenic shock with Hypotension	Norepinephrine
Cardiogenic shock without Hypotension	Dobutamine
Cardiogenic shock with oliguria	Dopamine
Resistant shock	Vasopressin

Q6.10: Write a short note on Stress ECHO and the adrenergic drug used in it.

Answer:

- Stimulates heart
- Beta (β) 1 Agonist is given: Dobutamine

Q6.11: Name some vasopressors and their clinical use.

Answer:

- Hypotension in Pregnancy: Ephedrine
- Hypotension in spinal anaesthesia: Phenylephrine
- Postural hypotension: Midodrine

Q6.12: Which drugs are used as mydriatics for fundoscopy in adults and children, and how do their mechanisms and effects differ?

Answer:

- Acts on the (α) 1 receptors of Radial muscles of the iris: Mydriasis (active)
  - Phenylephrine: Eye drops
    - → Fundoscopy in Adults
    - → No cycloplegic effect
- Anticholinergics produce passive mydriasis: Paralysis of the sphincter pupils

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- Atropine
  - → Fundoscopy in children
  - → 1% ointment
  - → Cycloplegic
- Cyclopentolate
- Tropicamide
- Homatropine

Q6.13: Elaborate on routes of administration of nasal decongestants, and complications that arise from their prolonged or sudden discontinuation.

Answer:

- Vasoconstriction in the nose
- Used in Rhinorrhea

Nasal drops	Both tablet and drops	Oral tablet
• Oxymetazoline • Xylometazoline	• Phenylephrine	• Ephedrine • Pseudoephedrine

Chronic use of nasal decongestants
↓
Prolonged vasoconstriction
↓
Ischemia
↓
Atrophic Rhinitis

- Sudden discontinuation
  - Rebound Rhinorrhea (**Rhinitis medicamentosa**)

Q6.14: Which drugs are used as tocolytics, and what are their mechanisms and specific advantages?

Answer:

- Relax uterus: Given in premature deliveries
- Atosiban
  - Oxytocin receptor antagonist
  - Safe in heart disease
- Beta (β) 2 Agonist
  - Ritodrine
  - Isoxsuprine
- CCB: Nifedipine

Q6.15: Which β3 agonists are used to treat overactive bladder, what is their mechanism of action, and in which condition are they contraindicated?

Answer:

- Detrusor relaxation
- Mirabegron

- Vebegron
  - Treats overactive bladder
  - **Detrusor hyperactivity**
- Contraindicated in BPH
  - Urinary retention will aggravate

Q6.16: Tabulate the different indirectly and mixed acting adrenergic drugs.

Answer:

Indirectly Acting	Mixed Acting
• Increases the release of Norepinephrine	• Increases the release of Norepinephrine and stimulates alpha (α) beta (β) receptors
• Modafinil o Decreased sleep o Used to treat narcolepsy • Amphetamine o Used in ADHD o Increased attention span • Tyramine: present in cheese/ meat o Combined with MAO inhibitor o Hypertensive crisis: Cheese reaction o Treated by Phentolamine	• Mephentermine o Approved anti-obesity drug • Ephedrine
S/E: Rapid loss effect (Tachyphylaxis)	

Q6.17: What is the treatment approach for ADHD with tics, and how does the choice of medication impact symptoms like attention span and hyperkinesia?

Answer:

CBT
↓
If fails
↓
Methylphenidate (DOC)
↓
Increased attention spasm
↓
Increased Hyperkinesia (TICS)

- ADHD + TICS:
  - Atomoxetine
  - Clonidine/ Guanfacine

Q6.18: Tabulate the drugs used in Anti Obesity Drugs.

Answer:

Mephentermine + Topiramate (AED)	Weight loss
Bupropion + Zonisamide	Weight loss

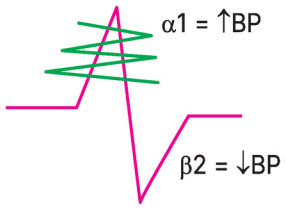
Bupropion + Naltrexonde	Weight loss
Liraglutide Semaglutide	GLP -1 peptide analogue (used in Type 2 DM) Injection
Tirzepatide	GLP -1 peptide analogue + GIP analogue (used in Type 2 DM) Injection
Orlistat , Cetilistat	Lipase inhibitors reduce fat absorption.

Q6.19: What are the effects of Epinephrine and Norepinephrine on BP and HR?

Answer:

Drug	BP	Direct Heart Rate	Indirect Heart Rate	Net Heart Rate
Norepinephrine	Increased BP	Increased HR	Decreased HR	• Bradycardia • Tachycardia in transplanted heart
Epinephrine	Biphasic change	Increased HR	No effect	Tachycardia

- Epinephrine + alpha (α) blocker
  - Unopposed fall in BP
  - Act only on beta (β) 2 receptors
  - **Vasomotor reversal of Dale**



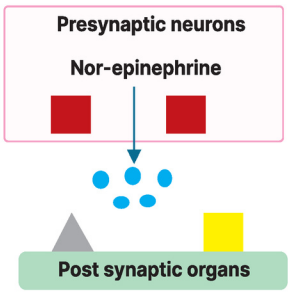
BIG QUESTION 7: Describe briefly about anti-adrenergic drugs.

Broad Answer: Anti-adrenergic drugs block the action of norepinephrine and epinephrine at adrenergic receptors, thereby inhibiting sympathetic nervous system effects. They include **alpha-blockers** (e.g., Prazosin) used for hypertension and **beta-blockers** (e.g., Atenolol, Propranolol) used for conditions like angina, arrhythmias, and anxiety. These drugs reduce heart rate, lower blood pressure, and may cause side effects like dizziness and fatigue

DETAILED QUESTIONS

Q7.1: Name the 3 classes of anti-adrenergic drugs.

Answer:



- Alpha (α) blocker
- Beta (β) blocker
- Alpha (α) 2a agonist: Reduce norepinephrine release

Q7.2: What are the clinical uses and side effects of α-2a agonists like clonidine?

Answer:

- Clonidine is a central sympatholytic that acts by stimulating ▫-2 adrenergic receptors
- Uses:
  - Post-menopausal hot flushes

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- Hypertensive crisis
- Diabetic diarrhoea

- S/E:
  - Hypotension
  - Apnea in <2 yr
  - Dry eyes/ mouth
  - Sedation
  - Erectile dysfunction

Q7.3: What is Dexmedetomidine used for, and how is it administered in clinical settings?

Answer:

- Dexmedetomidine is a central sympatholytic that acts by stimulating ¤-2 adrenergic receptors
- It is used as an IV sedative in a preoperative setting

Q7.4: Which α2a agonist is a centrally acting muscle relaxant?

Answer: Tizanidine

Q7.5: What is the mechanism of action of α-methyldopa, its use in pregnancy, and its notable side effects?

Answer:

- **Drug:** α-Methyldopa
- **Mechanism:** Acts as an α2 agonist ¤ central sympatholytic action
- **Clinical use:**
  - Chronic hypertension in pregnancy (safe and preferred)
- **Side effects:**
  - Drug-induced lupus erythematosus (DLE)
  - Hemolytic anemia due to warm antibody formation
  - Coombs test positive
  - RBC damage

Q7.6: Which centrally acting α2 agonist has the longest duration of action?

Answer: Guanfacine

Q7.7: Why shouldn't we abruptly stop clonidine in a patient with hypertension?

Answer:

- Clonidine blocks alpha (α) 2 receptors and inhibits the release of norepinephrine
- If stopped suddenly, super-sensitive alpha (α) 2B postsynaptic receptor produces
  - Vasoconstriction
  - Hypertensive crisis
  - Treated with Phentolamine

Q7.8: What are the clinical uses and mechanisms of action of non-selective alpha (α) blockers, and can you provide examples of these drugs?

Answer:

- Hypertension in pheochromocytoma: Phenoxybenzamine
  - (noncompetitive + irreversible blocker of the alpha (α) receptor)

YOURWISH

- Clonidine rebound hypertension: Phentolamine
- Cheese reaction Hypertension: Phentolamine
- Vasodilator during Angiographies: **Tolazoline**

} competitive + reversible blocker of alpha (α) receptor

Q7.9: Elaborate on the MOA, uses, and side effects of selective α-1 blockers.

Answer:

Prazosin, Terazosin, Doxazosin, Alfuzosin	Tamsulosin, Silodosin
• DOC: BPH + HTN • Blocks alpha (α) 1A (open internal ureteric sphincter) and alpha (α) 1B (vasodilation) • S/E: Postural Hypotension o First dose effect	• Alpha (α) 1 A blocker • DOC: BPH • Postural Hypotension is not seen

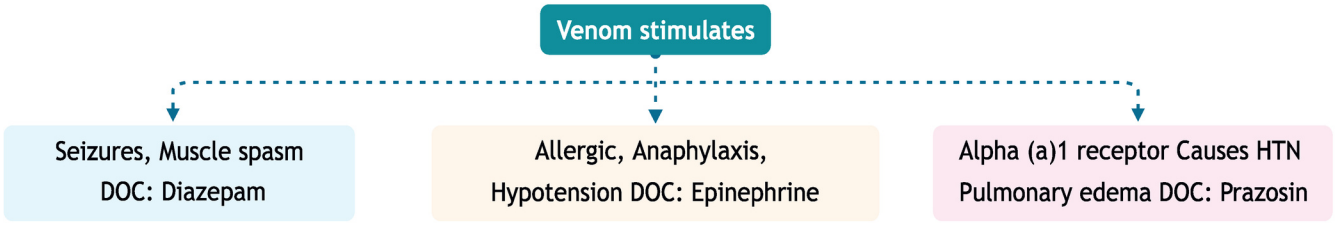
Q7.10: What are the drugs used in the treatment of Benign Prostatic Hypertrophy?

Answer:

- Open IUS to relieve urinary obstruction
  - o Tamsulosin
  - o Silodosin
- Reduce prostate size (5 alpha (α) reductase Inhibitor)
  - o Finasteride
  - o Dutasteride
- 5 alpha (α) - reductase
  - o Converts testosterone to Dihydrotestosterone
    - → Increases prostate size
    - → Alopecia
- 5 alpha (α) reductase inhibitors are also used to treat alopecia with Minoxidil

Q7.11: Write briefly about the clinical features and drugs used in scorpion sting.

Answer:



BIG QUESTION 8: Write a short note on beta blockers.

Broad Answer: Beta blockers are drugs that inhibit **beta-adrenergic receptors**, thereby reducing the effects of adrenaline and noradrenaline on the heart and blood vessels. They are commonly used to treat **hypertension, angina, arrhythmias**, and **heart failure**. Examples include **propranolol** (non-selective) and **atenolol or metoprolol** (cardio-selective for beta-1 receptors)

DETAILED QUESTIONS

Q8.1: Classify beta blockers.

Answer:

1st Generation	2nd Generation	3rd Generation
• Non Selective • Beta (β) 1 = Beta (β) 2 = Beta (β) 3	• Cardio Selective • Beta (β) 1 >>> Beta (β) 2/3	• Vasodilators
Mnemonic: **Pyari So TN** • **P**ropranolol • **P**indolol • **S**otalol • **T**imolol • **N**adolol	Mnemonic: **BEAMA** • **B**isoprolol • **E**smolol • **A**cebutolol • **M**etoprolol • **A**tenolol	

Q8.2: Which is the longest-acting beta blocker?

Answer: Nadolol

Q8.3: Which is the shortest-acting beta blocker?

Answer: Esmolol (Plasma esterase metabolism)

Q8.4: Name the beta blockers avoided in renal failure?

Answer:

- Atenolol
- Nadolol
- Sotalol

Q8.5: Name the most cardio-selective beta blocker.

Answer: Nebivolol (Additional property of increased Nitric oxide Production)

Q8.6: Name the beta blockers that affect the potassium channels.

Answer:

- Open potassium channel: Tilisolol
- Close potassium channel: Sotalol (Increase QT interval on ECG)

Q8.7: Which beta blocker also has anti-oxidant properties?

Answer: Carvedilol

Q8.8: Which beta blocker increases the HDL levels?

Answer: Bevantolol

Q8.9: Describe the Vasodilatory Action of 3rd Generation Beta (β) Blockers.

Answer:

- Produce nitric oxide

  - Nebivolol
  - Nipradilol
- Beta (β) 2 Agonist: Celiprolol
- Calcium channel blockers: Betaxolol
- Alpha (α) blocker: Labetalol
- Potassium channel opener: Tilisolol
- Combined alpha (α) + beta (β) blocker: Carvedilol and Labetalol

Q8.10: What are the other special actions of Beta (β) Blockers?

Answer:

- Partial agonist
  - Pindolol (bopindolol)
  - Acebutolol
- No bradycardia
- Local anaesthetic effect
  - Block Sodium channel
  - Maximum action: Propranolol
  - C/I: Topical eye drops in Glaucoma
    → Corneal anaesthesia

Q8.11: What are the uses of propranolol?

Answer:

- HOCM
- Thyroid storm (Inhibits conversion of T4 to T3)
- Essential tremors
- Performance anxiety
- Migraine prophylaxis

Q8.12: Which drug is a nonselective beta-blocker, and what receptors does it block?

Answer:

- **Nonselective beta-blocker:** Propranolol
- **Mechanism:** Blocks both β1 and β2 receptors equally

Q8.13: What are cardioselective beta-blockers, which receptors do they target, and in which conditions are they preferred or contraindicated?

Answer:

- **Cardioselective beta-blockers:** Preferentially block β1 > β2 receptors
- **Contraindicated in:** Bradycardia
- **Can be given in:**
  - Asthma
  - Diabetes Mellitus (DM)
  - Raynaud's disease

Q8.14: Which calcium channel blockers should never be combined with beta-blockers, and why?

Answer:

- **Drugs to avoid combining with beta-blockers:**
  - Verapamil
  - Diltiazem
- **Reason:**
  - Both cause additive bradycardia

Q8.15: What is the antidote for beta-blocker toxicity, and how does it work?

Answer:

- **Antidote: Glucagon**
- **Mechanism:**
  - Directly stimulates the SA node
  - Increases heart rate (HR)

Q8.16: What are the effects of beta-blockers in diabetic patients, and what is hypoglycemic unawareness?

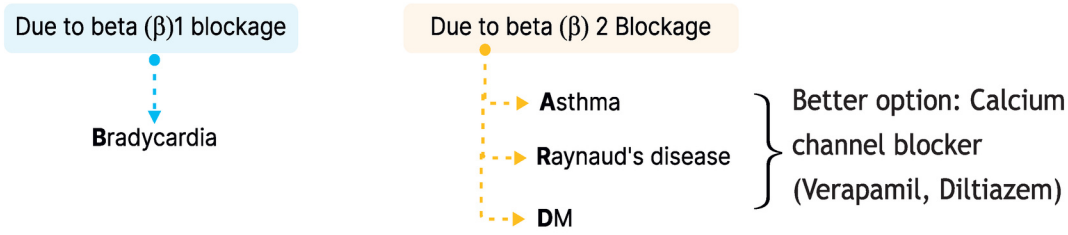
Answer:

- In starvation, it may cause hypoglycemia
- In the fed state, it may cause hyperglycemia
- Beta-blockers mask symptoms of hypoglycemia, leading to hypoglycemic unawareness.

Q8.17: What are the adverse effects of beta blockers?

Answer:

- Mnemonic: **BARD**



Q8.18: Write a note on the classes of drugs used in glaucoma.

Answer:

PGF2 agonist - DOC	• Latanoprost • Bimatoprost } Increase Uveoscleral outlow
Alpha (α) 2 Receptors	• Apraclonidine • Brimonidine
Pilocarpine	• Miotics - Open iridio corneal angle
Alpha (α) 1 + Alpha (α) 2 Agonist	• Dipivefrine(prodrug) • Epinephrine (alpha (α) 1&2 agonist)
Beta (β) blocker	• Timolol • Carteolol • Betaxolol - cardioselective
Carbonic Anhydrase Inhibitor	• Acetazolamide Brinzolamide

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Q8.19: Name the drug of choice in open-angle and closed-angle glaucoma. Name the add-on drugs used here as well.

Answer:

- The DOC for open-angle and closed-angle glaucoma are PGF2 agonists like Latanoprost and Bimatoprost.
- Add-on Drugs are:
  1. Alpha Agonist
  2. Beta Blocker
  3. Carbonic Anhydrase Inhibitors

Q8.20: Name the DOC and the definitive treatment in acute congestive glaucoma.

Answer:

- DOC for acute congestive glaucoma
  - IV Acetazolamide + IV Mannitol
  - Start the same treatment with eye drops
- Definitive Rx: Iridotomy (Surgery/Laser)

Q8.21: What are the side effects of prostaglandin analogs used in Glaucoma?

Answer:

- Heterochromia Iridis
- Cystoid Macular Edema: C/I in Diabetics
- Hypertrichosis

Q8.22: Which anti-glaucoma drug is most associated with allergic reactions?

Answer: Apraclonidine causes more allergic reactions than Timolol

Q8.23: Which class of drugs can cause bronchospasm?

Answer: Beta-blockers

Q8.24: Which drugs are associated with 2° angle-closure glaucoma, and what are their therapeutic classes?

Answer:

- **Drugs that can cause 2° angle-closure glaucoma:**
  - Carbonic anhydrase inhibitors
  - Antiepileptics
  - Zonisamide
  - Topiramate

Q8.25: Which drug used in the treatment of Glaucoma can cause a dark or black eye?

Answer: Dipivefrine

Q8.26: Which eye drop is known to cause pain upon instillation?

Answer: Pilocarpine

Q8.27: Which anti-glaucoma drug is avoided in children but considered safe in pregnancy, and why?

Answer:

- **Drug:** Brimonidine > Apraclonidine
- **Reason:** Can cause apnea in children
- **Clinical note:** Avoid in children, but safe in pregnancy

3. CENTRAL NERVOUS SYSTEM

BIG QUESTION 1: What are sedatives and Hypnotics?

Broad Answer:

- Sedatives: Induce calmness, remove anxiety
- Hypnotics: Induce sleep
- Sedatives in higher doses: Hypnotic effect

DETAILED QUESTIONS

Q1.1: Name the drugs that are categorized as sedatives and hypnotics.

Answer:

- Benzodiazepines: Sedatives
- Barbiturates: Hypnotics
- Atypical benzodiazepines (Z drugs)
- Melatonin
- Alcohols

Q1.2: What are the dose-dependent effects of sedatives and hypnotics, and what can occur with progressively higher doses?

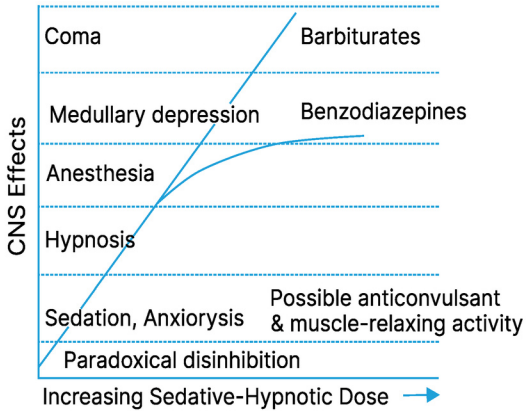
Answer:

Sedatives
↓
Higher dose
↓
Hypnotics
↓
Further increase in dose
↓
Muscle relaxation
↓
Higher dose
↓
Unconsciousness and loss of sensation (Anesthesia)
↓
Respiratory depression/Coma (Higher dose)
↓
Death due to overdose of sedatives and hypnotics

Q1.3: Illustrate the Dose-response curve for sedatives and hypnotics

Answer:

- Benzodiazepines (sedatives): Flat DRC
- Barbiturates (hypnotics): Steep dose response



Q1.4: What is the mechanism of action of Benzodiazepines & Barbiturates, and which is the safer drug among the two?

Answer:

- Benzodiazepines are safer drugs than Barbiturates

Barbiturates and benzodiazepine
↓
Acts on GABA A chloride channels
↓
Opening of the chloride pore
↓
Chloride moves inside the neuron
↓
Hyperpolarization of the neurons
↓
Neurons are suppressed

BIG QUESTION 2: What type of neurotransmitter is GABA, and what is the subunit composition of the GABA receptor?

PYQ: FMGE 2023

Broad Answer:

- GABA receptor is an inhibitory neurotransmitter
- It has five subunits:
  - 2 alpha (α)
  - 2 beta (β)
  - 1 gamma (γ)

DETAILED QUESTIONS

Q2.1: On which subunits of GABA do Benzodiazepines act, and what effect do they have on GABA binding?

Answer:

- Benzodiazepines: Acts on alpha (α) - gamma (γ) subunit
- Benzodiazepines are GABA facilitatory drugs: Increases the binding of endogenous GABA

Q2.2: On which subunits of GABA do Barbiturates act, and what effect do they have on GABA binding?

Answer:

- Barbiturates have no specific binding site.
- At low doses: GABA facilitatory action
- At high doses: GABA mimetic action
  - Leads to respiratory depression

Q2.3: What drugs or substances act at the alpha-beta junction of the GABA receptor?

Answer:

- Agonist
  - GABA (Endogenous)
  - Muscimol (Exogenous)
- Competitive antagonist: Bicucilline
- Direct chloride pore blocker: Picrotoxin

Q2.4: What drugs or substances act at the alpha-gamma junction of the GABA receptor?

Answer:

- Agonists: Benzodiazepines
- Competitive antagonist: Flumazenil
- Inverse agonist: Beta carboline (Side effects: Seizures)

Q2.5: What is the antidote for benzodiazepine poisoning?

Answer:

- The antidote for benzodiazepine poisoning is Flumazenil

BIG QUESTION 3: What are the different types of Barbiturates?

Broad Answer:

- Different types of Barbiturates include:
  - Ultrashort-acting barbiturates
  - Short-acting barbiturates
  - Long-acting barbiturates

DETAILED QUESTIONS

Q3.1: What are Ultrashort-acting barbiturates and drugs under them?

Answer:

- Ultrashort-acting barbiturates are highly lipid-soluble drugs (Redistributed into fats)
- Drugs include
  - Thiopentone
  - Methohexitone

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Q3.2: What are the effects of Thiopentone, and in which condition is it considered the DOC?

Answer:

- Thiopentone induces general anaesthesia
- Has cardioprotective, neuroprotective effects
  - Decreases the O_2 demand of the heart and neurons
- DOC: Narcoanalysis
  - Other Name: Truth-Serum: Hyoscine

Q3.3: What are the effects of Methohexitone, and what is it used for?

Answer:

- Methohexitone reduces seizure threshold: Easily provokes seizures
- DOC: Electroconvulsive therapy

Q3.4: What is the other drug used in the ECT?

Answer:

- Ketamine is used in ECT to treat Depression

Q3.5: Name the drugs classified as Short-acting barbiturates and their route of administration.

Answer:

- Drugs includes
  - Butabarbitone
  - Amobarbitone
  - Pentobarbitone
  - Secobarbitone
- ROA: IV in ICU patients pre-operatively

Q3.6: Name the drugs classified as Long-acting barbiturates.

Answer:

- Drugs include
  - Phenobarbitone
  - Primidone

Q3.7: What are the features and uses of primidone?

Answer:

- Primidone: Active form is phenobarbitone
- It is a first-line drug for Essential tremors
  - Propranolol is also used for Essential tremors

Q3.8: In what conditions is Phenobarbitone used as a DOC?

Answer:

- Phenobarbitone is DOC in:
  - Neonatal seizures
  - Neonatal jaundice: Deficiency of the **UDPGT enzyme**
  - Crigler-Najjar syndrome type 2
  - Gilbert syndrome: Deficiency of the UDPGT enzyme
- Phenobarbitone is an enzyme inducer

Q3.9: Explain why Phenobarbitone is used in conditions deficient in the UDPGT enzyme.

Answer:

Phenobarbitone
↓
Increases the activity of UDPGT enzyme
↓
Glucuronide will be attached to bilirubin
↓
Bilirubin will become water soluble
↓
Excretion of bilirubin through water

Q3.10: What are the side effects caused by Phenobarbitone?

Answer:

- Paradoxical excitation (inhibits inhibitory neurons, causing excitation): Seen in children
- Hyperkinesia
- Induce seizures
- Excessive sensation
- Excessive pain perception

Q3.11: Why are Barbiturates contraindicated in Acute Intermittent Porphyria?

Answer:

Barbiturates are CYP enzyme inducers
↓
CYP enzyme contains heme
↓
Increases the heme demand of the body
↓
Accumulation of abnormal porphyrin
↓
Barbiturates are contraindicated in Acute Intermittent Porphyria
↓
Benzodiazepines: Safe in porphyria

Q3.12: What are the features and management of barbiturate poisoning?

Answer:

- Barbiturate poisoning: Occurs due to respiratory depression
  - Respiratory stimulants are recommended --> Directly stimulate the respiratory centres in the brain.
- Other Name of respiratory stimulants: Analeptic drug - Doxapram
- Has no specific antidote
- Treatment: Forced alkaline diuresis with Sodium bicarbonate
  - Severe poisoning: Haemodialysis

BIG QUESTION 4: How are benzodiazepines classified, and what are their pharmacological uses?

Broad Answer: Based on their uses, benzodiazepines are classified into:

- Antiseizure drugs
- Drugs for insomnia
- Anti-anxiety drugs
- Pre-anesthetic drugs
- Muscle relaxants

DETAILED QUESTIONS

Q4.1: Write briefly about the drug used as an antidote in Benzodiazepine poisoning.

Answer:

- Antidote: Flumazenil
  - Also, an antidote for Atypical benzodiazepine poisoning
  - Half-life: 30-60 mins
  - Dose: 5mg
  - ROA: Repetitive IV injections
- Acts on the alpha-gamma subunit of GABA A chloride channels: GABA A facilitatory

Q4.2: Which benzodiazepines are used as anti-seizure drugs?

Answer:

- Diazepam: Febrile seizures
- Lorazepam: Status epilepticus
- Clonazepam
- Clonazepam
- Midazolam

Q4.3: Which benzodiazepines are used to treat insomnia?

Answer:

- Flurazepam: Longest acting benzodiazepine
- Temazepam
- Estazolam
- Quazepam
- Triazolam

Q4.4: Which benzodiazepines are used for the management of anxiety?

Answer:

- **Benzodiazepines are** recommended for the Acute attack of anxiety
  - Diazepam
  - Clonazepam
  - Oxazepam
  - Lorazepam
  - Alprazolam
- **Note:** SSRIs are used in the maintenance therapy of anxiety

Q4.5: What is the role of benzodiazepines as pre-anesthetic medication, and what are their adverse effects?

Answer:

- Benzodiazepines have anxiolytic effects
- Drugs include:
  - Diazepam
  - Lorazepam
  - Midazolam
  - Remimazolam: Shortest acting benzodiazepine
- Adverse effects:
  - Produce anterograde amnesia: Leads to loss of memory

Q4.6: How do benzodiazepines produce muscle relaxation?

Answer:

- Diazepam: Stimulate GABA A receptor
  - Addictive
  - Produces sedation
- Baclofen: Acts on GABA B receptor
  - Non benzodiazepines
  - Non-addictive and non-sedative

Q4.7: What is automatism?

Answer:

- Repetitive self-medication leads to overdose or poisoning
- Automatism: Seen with alcohol and opioids also
- Alcohol, opioids: Increase sedative effect of benzodiazepine, barbiturates

Q4.8: How is diazepam metabolied?

Answer:

Diazepam
↓
Goes to the liver
↓
CYP3A4 enzyme in liver
↓
Diazepam is converted to Oxazepam
↓
Excreted out in urine

Q4.9: Which Benzodiazepines are safe in liver disease, and why?

Answer:

- All BZD are metabolized by the CYP3A4 enzyme in the liver to another active form.
- Benzodiazepines with no CYP metabolism in liver are safe in patients with liver disease
- Drugs include:
  - Triazolam

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- Oxazepam
- Temazepam
- Estazolam
- Lorazepam

Q4.10: Which drugs are misused as date-rape drug?

Answer:

- Benzodiazepines cause Sedation and Amnesia and are misused as Date Rape drug
- Other drugs include:
  - Alcohol: Most commonly used
  - Ketamine
  - Barbiturates
  - Benzodiazepines:
  - Gamma hydroxybutyric acid
  - Flunitrazepam: Rohypnol-Banned drug as it is Tasteless and colourless

BIG QUESTION 5: What are Atypical Benzodiazepines?

Broad Answer:

- Atypical benzodiazepines are drugs that act on benzodiazepine receptors (BZ1/BZ2 on GABA-A) but are structurally different from classical benzodiazepines.
- AKA Z drugs

DETAILED QUESTIONS

Q5.1: What is the difference between normal and atypical Benzodiazepines?

Answer:

Normal Benzodiazepines	Atypical benzodiazepine
• Act on alpha and gamma subunits of GABA A receptors • Alpha (α) 1: Produce sedation, used to treat insomnia • Alpha (α) 2: Muscle relaxant, used to treat seizures	• Act on alpha (α) 1 gamma (γ) subunit • Produce sedation-Treat insomnia • Lack of muscle relaxant effect and anti-seizure activity

Q5.2: What are the drugs included under atypical Benzodiazepines?

Answer:

- Zopiclone: Longest acting
- Zolpidem
- Zaleplon: Shortest acting
  - Less sleep cycle distortion

Q5.3: What is the main use of atypical benzodiazepines?

Answer:

- Atypical Benzodiazepines are DOC in the treatment of Insomnia
  - Chronic insomnia
  - Transient insomnia
  - Sleep onset insomnia

Q5.4: What is the DOC in treating Jet lag?

Answer: Ramelton is DOC in treating Jet lag, but atypical Benzodiazepines are also used (off label use)

Q5.5: What are the side effects of atypical Benzodiazepines and what is the antidote used in its poisoning?

Answer:

- Side effect: Highly addictive
- Poisoning: Flumazenil (Antidote)
  - Blocks alpha-gamma junction

Q5.6: What are the advere effects of Barbiturates?

Answer:

- Barbiturates distort the sleep cycle (Not used in insomnia)
- Nightmare/night tremors
- Hangover

BIG QUESTION 6: What are the pharmacological options for treating insomnia apart from benzodiazepines?

Broad Answer:

- Melatonin
- Ramelteon
- Agomelatine
- Tasimelteon
- Miscellneous drugs like Suvorexant, Mirtazapine, antidepressants, antihistamines

DETAILED QUESTIONS

Q6.1: How does melatonin help in treating insomnia?

Answer: Melatonin maintains sleep-wake cycles (circardian rhythms), hence recommended for treatment of Insomnia

Q6.2: What are the features and indications of ramelteon?

Answer:

- Ramelteon is an MT1 and MT2 receptor agonist
- It used to treat insomnia in:
  - Shift or night workers
  - Elderly
  - Jet lag

Q6.3: What is the MOA and uses of Agomelatine?

Answer:

- Agomelatine is a MT1 and MT2 receptor agonist + **5HT2C antagonist**
- It is used to treat insomnia with depression

Q6.4: What is the MOA and uses of Tasimelton?

Answer:

- It is a MT1 and MT2 receptor agonist
- It is used to treat Insomnia by maintaining circadian rhythm in blind people

Q6.5: What the are the newer drugs used in the treatment of Insomnia?

Answer:

- New drugs used in the treating Insomnia are: Suvorexant, Lemborexant
- They are Orexin antagonists

Q6.6: Are antihistamines used in the treatment of Insomina?

Answer:

- 1st generation antihistamines are used to treat Insomina due to their sedative action
- Drug: Promethazine

Q6.5: What are the antidepressants used to treat insomnia and how do they act?

Answer:

- Antidepressant used to treat Insomina: Mirtazapine, Mianserin
- MOA: Blocks alpha-2 receptors in the brain and produce sedation
- Used for depression + insomnia

BIG QUESTION 7: What are the pharmacological properties of alcohol, and how is its poisoning, withdrawal and relapse managed?

Broad Answer:

- Alcohols, when ingested, are primarily processed in the liver by dehydrogenase enzymes. While some alcohols are relatively benign in small amounts, certain types, such as methanol and ethylene glycol, are highly toxic

DETAILED QUESTIONS

Q7.1: How is alcohols metabolized in the human body?

Answer: Alcohols are metabolised by Non-specific dehydrogenase enzyme in liver

Q7.2: What are the dangerous alcohols, their metabolic end products and adverse effects?

Answer:

- Dangerous alcohols: Methanol and ethylene glycol
- Formic acid: Neurotoxic and blindness
- Glycolic + Oxalic acid: Neurotoxic, blindness

Methanol	Ethylene glycol
↓	↓
Formaldehyde	**Glycolaldehyde**
↓	↓
Formic acid	Glycolic + oxalic acid

Q7.3: What is the sign of Ethylene glycol poisoning?

Answer: Formation of oxalate crystals in urine is a sign of Ethylene glycol poisoning

Q7.4: What is the MOA of Fomepizole and Disulfiram?

Answer:

- Fomepizole: Inhibits alcohol dehydrogenase
- Disulfiram: Inhibits aldehyde dehydrogenase

Q7.5: Write briefly about the treatment of alcohol poisoning.

Answer:

- Treatment of alcohol poisoning: Mnemonic: **SHAFE**
  - o **S**odium bicarbonate (High anion gap)

- Haemodialysis (Best)
- Antidote: Fomepizole (Orphan drug)
- Folinic acid
- Ethanol (To saturate enzymes)

Q7.6: How is alcohol withdrawal managed and prevented?

Answer:

- Acute withdrawal: Emergency
  - Delirium tremens: Diazepam (IV)
  - If liver failure: Lorazepam, Oxazepam
  - Korsakoff psychosis: Haloperidol + Thiamine
- Maintenance (Detoxification phase): To prevent withdrawal
  - Oral Chlordiazepoxide (Taper slowly)
  - If liver failure: Lorazepam, Oxazepam
- Prevent relapse (Abstinence/aversion therapy)
  - Anti-craving: Naltrexone (opioid antagonist), Acamprosate (NMDA glutamate receptor antagonist)
  - Deterrent (creates fear): Disulfiram (Antabuse)
  - Off-label (not approved) anti-craving drugs: Topiramate, Gabapentin (has anti-craving effect against ethanol)
  - Off-label deterrent drug: Metronidazole

Q7.7: How does Disulfiram act, and what are its adverse effects?

Answer:

- Disulfiram inhibits aldehyde dehydrogenase
- Accumulation of acetaldehyde causes symptoms like:
  - Vomiting
  - Headache
  - Flushing
  - Chest pain
  - Hypotension (Death)
- Hence, Disulfiram is contraindicated in active drinkers

Q7.8: What drugs have Disulfiram like reaction?

Answer:

- Drugs with disulfiram-like reaction: Should be avoided in active drinkers
  - Chlorpropamide, Cephalosporins: Due to the presence of methyl-thio tetrazole ring (MTT)
    - → Cefoperazone
    - → Cefamandole
    - → Cefotetan
    - → Moxalactam
  - Griseofulvin
  - Metronidazole
  - Procarbazine

BIG QUESTION 8: What are opioids, and what are their sources, receptors, pharmacological actions, uses, and the features and management of opioid addiction?

Broad Answer:

- Opioids are alkaloids obtained from opium, Papaver somniferum
- Other name: Poppy plant
- They are stupefying drugs.

DETAILED QUESTIONS

Q8.1: What are the natural opioids?

Answer:

- Natural opioids are called Opiates. They include:
  - Morphine
  - Codeine

Q8.2: What are the uses of opioids?

Answer:

- Opioids are used for their analgesic effect
- They are the most effective painkillers
- DOC: Severe pain (step ladder 3 pain by WHO classification)

Q8.3: Through which receptors do endogenous opioids produce their effect

Answer:

- Endogenous opioids produce their effect through opioid receptors
  - Mu: Endorphins (Morphine acts via this receptor)
  - Kappa (κ): Dynorphins
  - Delta: Enkephalins

Q8.4: What are the effects caused by stimulation of Mu receptors?

Answer:

- Sedation
- Analgesia (Spinal, Supraspinal)
- Constipation, Cough suppression
- Respiratory depression
- Euphoria
- Miosis: Pinpoint pupil (Stimulation of EDW nucleus)
- Nausea/Vomiting (+ CTZ)
- Gallstones
- Abdominal colic (Spasm of sphincters)
- Prolactin release

Q8.5: In what conditions are opioids contraindicated?

Answer:

- Opioids are not given for colicky pain
- Not given in head injury
  - Accumulation of CO_2
  - Increase in ICP

Q8.6: What are the effects caused by stimulation of kappa receptors?

Answer:

- All the effects caused by Mu receptors and
  - Dysphoria- Psychomimetic
  - Diuresis- Inhibits the ADH hormone

Q8.7: What are the effects caused by stimulation of Delta receptors?

Answer:

- Supraspinal/effective analgesia
- Convulsions

Q8.8: What are the effects and uses of Morphine?

Answer:

- Heart: Reduces heart rate and preload, oxygen demand
  - Treatment:MI and acute left ventricular failure
- Oral morphine: Produces miosis (morphine eyedrops do not)
- Morphine: Causes asthma and pruritus
  - Histamine release from mast cells

Q8.9: What are the drugs contraindicated in MI and why?

Answer: Pethidine, Pentazocine are contraindicated in MI as they increase heart rate and oxygen demand

Q8.10: Name the opioids contraindicated in renal failure.

Answer:

- Pethidine
- Codeine
- Morphine

Q8.11: What is the mechanism by which codeine suppresses cough?

Answer: Codeine is converted to Morphine in the body by the enzyme CYP2D6 and is given as an anti-tussive drug to suppress cough.

Q8.12: Name the opioid drugs that are used as anti-tussives, and what are their side effects?

Answer: PYQ: INICET 2021

Anti-tussive (cough syrups)	
Codeine	Morphine
Hydrocodone	Hydromorphone
Oxycodone	Oxymorphone
Pholcodeine	Levorphanol
S/E: Addiction, Sedation	

Q8.13: Name non-addictive cough syrups.

Answer:

- Non addictive cough syrups

- Dextromethorphan
- Noscapine

Q8.14: What are the shortest and longest-acting opioids?

Answer:

- Shortest acting opioid: Remifentanil
- Longest acting opioid: Methadone

Q8.15: What are the least and most potent opioids?

Answer:

- Least potent: Codeine
- Most potent: Sufentanil, most protein-bound also

Q8.16: What are the MOAs of Methadone, Tramadol, and Pethidine?

Answer:

- Mu agonist + NMDA antagonist: Methadone
  - Causes QT prolongation
- Mu agonist + SNRI (↑ serotonin norepinephrine receptor reuptake inhibitor): Tramadol
- Mu agonist + anticholinergic: Pethidine

Q8.17: What are the pharmacological properties of pethidine?

Answer:

- Safest opioid in pregnancy
- DOC
  - Pregnancy
  - Post anaesthetic shivering
- Pro-drug
  - Meperidine: Opioid like activity (MAO enzyme)
  - Nor-pethidine: Causes seizures

Q8.18: Why is Pethidine not combined with MAO inhibitors?

Answer: MAO inhibitors with Pethidine can be converted to nor-pethidine and cause seizures

Q8.19: What are the features, ROA, uses and side effects of fentanyl?

Answer:

- NOT given as Oral route: High first-pass metabolism
- Transdermal: Chronic cancer pain
- Epidural: Analgesics
- Sublingual and IV: Acute pain
- Side effects: Rigidity of chest muscles, which is known as Wooden chest syndrome

Q8.20: What are mixed acting opioids?

Answer:

Partial k agonist + μ antagonist	• **Mnemonic: PNB** o **P**entazocine o **N**albuphine o **B**utorphanol: Intranasal o Treatment: Migraine headache • Side effects: Dysphoria/psychosis • C/I: **Opioid addiction**
Pure k agonist	• Nalfurafine • Eluxadoline • Asimadoline
Partial μ agonist + k antagonist	• Buprenorphine PYQ: INICET 2023 o Treatment: **Opioid addiction** • Dezocine • Advantage: Less risk of respiratory depression
Pure Antagonist	• Naloxone: IV drug o DOC: Opioid poisoning **(Antidote)** • Nalmefene • Naltrexone o Oral drugs o Prevent relapse in opioid addiction • Other drugs: Naloxol, Naloxegol, Naldemedine

Q8.21: Which effects of opioids do not develop tolerance even with prolonged use?

Answer:

- Constricted pupil
- Constipation
- Convulsion

Q8.22: What are the treatment strategies and preventive measures for opioid addiction?

Answer:

- Acute overdose/poisoning: IV Naloxone repetitive injection (antidote)
- Maintenance (detoxification phase: To prevent withdrawal)
  - Opioids: Oral (Mnemonic: **BMT)**
    - → **B**uprenorphine
    - → **M**ethadone
    - → **T**ramadol (taper slowly)
  - Non-opioids which prevent withdrawal: Clonidine, Lofexidine
- Prevent relapse (Abstinence): Oral Naltrexone

Q8.23: What opioids are used in the treatment of diarrhea?

Answer:

- Loperamide: Non addictive opioid
  - Doesn't enter BBB
  - DOC: Diarrhoea

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→ IBS (irritable bowel syndrome)
→ Drug-induced diarrhoea by Irinotecan and Imatinib

- Diphenoxylate: Addictive
  - Atropine is added to it to reduce addiction
- Racecadotril: Enkephalinase inhibitor
  - Safest drug in children

Q8.24: What are the drugs used in the treatment of opioid induced constipation?

Answer:

- Drugs
  - Alvimopan: μ opioid receptor antagonist
  - Naloxone
  - Naldemedine
  - Methylnaltrexone
- ROA: Oral

BIG QUESTION 9: What are the properties, mechanisms, uses and adverse effects of anti-epileptic drugs?

Broad Answer: Anti-epileptic drugs (AEDs) are a diverse group of drugs used to **prevent or control seizures** in patients with **epilepsy** or other seizure-related conditions. They act by inhibiting deploarization of neurons.

DETAILED QUESTIONS

Q9.1: What are the first-line drugs used in the treatment of various types of epilepsy?

Answer:

Type	First Line Drugs
• GTCS (Grand mal epilepsy)	Valproate, Lamotrigine
• Absence (Petit mal epilepsy) • EEG: 3Hz wave spike pattern	Valproate, Lamotrigine, Ethosuximide
• Atypical absence • Myoclonic • Atonic • Tonic seizures	Valproate, Lamotrigine, Topiramate
• Focal seizures	Lamotrigine, Oxcarbazepine/Eslicarbazepine, Carbamazepine, Phenytoin, Levetiracetam

Q9.2: Write briefly about Juvenile myoclic epilepsy

Answer:

- Other Name: Janz Syndrome
- First-line drugs
  - Valproate(Most teratogenic)
  - Lamotrigine
  - Topiramate
- Safe drug in pregnancy: Levetiracetam
- Drugs contraindicated: Phenytoin, Carbamazepine

Q9.3: How is epilepsy managed in pregnancy?

Answer:

- If a female is taking epileptic drugs, then continue the old epileptic drug (do not stop AED) + high dose of folic acid (4 mg) + Vitamin K should be added
- Safe drug in pregnancy - Levetiracetam

Q9.4: List the anti-epileptic drugs used in the treatment of various epileptic disorders.

Answer:

Epileptic disorder	Anti-epileptic drugs
Febrile seizure in children (due to high-grade fever)	DOC- Rectal diazepam > Intranasal midazolam
Infantile spasm (West syndrome) isolated	ACTH
Infantile spasm + Tuberous sclerosis	Vigabatrin
Lennox-Gastaut Syndrome	Valproate (DOC), Rufinamide, Felbamate
Dravet's Syndrome (Severe Myoclonic Epilepsy of Infancy)	Valproate (DOC), Stiripentol
Status epilepticus (Acute seizure > 5 min)	IV Lorazepam (DOC), BZD (e.g., IM Midazolam)

Q9.5: Classify anti-epileptic drugs based on their MOA

Answer:

Blocks the dependent sodium channels	• **Mnemonic: PCV TOLL** o **P**henytoin o **C**arbamazepine o **V**alproate o **T**opiramate o **L**amotrigine o **L**acosamide, Zonisamide, Rufinamide
Blocks T type of Calcium channels	• **Mnemonic: VEL** • Treatment: Absence seizures o First-line drugs → **V**alproate → **E**thosuximide → **L**amotrigine o 2nd line drugs → Zonisamide → Clonazepam • Phenytoin and Carbamazepine are not effective

Q9.6: What are the different types of GABA receptor agonists and their mechanisms?

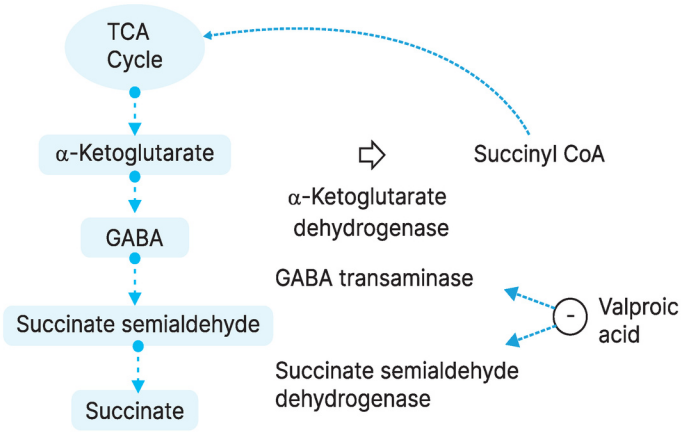
Answer:

- Inhibitory neurotransmitter
- Increases the level of GABA: Sedative drug

GABA receptor Agonist	Barbiturates, Benzodiazepines
GABA Transaminase Inhibitor	Vigabatrin, Valproate
GABA Transporter Inhibitor	Tiagabine
Gaba release increase (block P/Q type of Calcium)	Pregabalin, Gabapentin

Q9.7: Illustrate the mechanism of GABA receptor agonists?

Answer:



Q9.8: What are the uses of vigabatrin?

Answer:

- GABA transaminase inhibitor
- Side effect: Visual field contraction
- Use: Infantile spasm + Tuberous sclerosis

Q9.9: Which drugs target NMDA, AMPA receptors, potassium channels, cannabinoids, and neurosteroids in seizure management?

Answer:

NMDA Blocker	Felbamate
AMPA Blocker	Perampanel, Telampanel
Open K channel (KCN-Q)	Ezogabine (Retigabine)
Cannabinoids	Cannabidiol
Neurosteroids	Ganoxolone

Q9.10: What are the side effects of Felbamate and the open K^+ channel agents?

Answer:

- Side effects of Felbamate: Aplastic anaemia
- Side effects of open K^+ channel: Visual disturbance, Blue skin colour

Q9.11: Cannabidiol, Ganaxolone are approved for the treatment of which conditions?

Answer:

- Dravet syndrome
- Infantile spasm
- Lennox gestraud syndrome

Q9.12: Write briefly about the pharmacokinetics of Phenytoin

Answer:

- Also known as Hydantoin
- ROA: Oral
- Fos-phenytoin: Water soluble

- ROA: Faster IV injection
- Metabolism: CYP2C9
- Kinetics: Zero/pseudo-zero order kinetics

Q9.13: What are the side effects of Phenytoin?

Answer:

Side effects in high doses	Side effects in normal dose

• Cerebellar neurotoxicity
  o Ataxia
  o Diplopia
  o Slurred speech
• Cardiac arrhythmias
	• Gum hyperplasia- Seen with Phenytoin, Amlodipine, and Cyclosporine
	  o Treatment - Maintaining good oral hygiene & Azithromycin
	• Hirsutism
	• Hyperglycemia: PCOD
	• Heavyweight: PCOD
	• Hamper vitamin K and D absorption:Osteomalacia
	• Hamper folic acid absorption: Megaloblastic anaemia
	• Hypersensitivity

Q9.14: Which AED is the only CYP enzyme inhibitor?

Answer:

- Valproate is a CYP enzyme inhibitor whereas all the other AEDs are CYP inducers

Q9.15: What is the MOA and the side effects of Carbamazepine?

Answer:

- MOA
  - Carbamazepine is a CYP enzyme inducer and auto-inducer preferred in old age groups
- Side effects- Mnemonic: **SHADES**
  - **S**teven-Johnson syndrome: HLA-B*1502
  - **H**epatotoxic
  - **A**plastic anemia
  - **D**iplopia, ataxia: Cerebellar neurotoxicity
  - **E**osinophilia
  - **S**IADH: Syndrome of inappropriate ADH secretion causes Hyponatremia in old age

Q9.16: What are the features of Oxcarbazepine & Eslicarbazepine?

Answer:

- Oxcarbazepine
  - More risk of causing SIADH
  - Less risk of Stevens-Johnson syndrome
  - Preferred in children
- Eslicarbazepine: Longer acting

Q9.17: What are the drugs causing Stevens-Johnson syndrome in children?

Answer:

- Carbamazepine
- Lamotrigine

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Q9.18: What are the therapeutic range values of anti-epileptic drugs?

Answer:

Therapeutic range values	
Phenytoin	10-20 mg/dl
Valproate	50-100 mg/dl
Phenobarbitone	15-40 mg/dl
Carbamazepine	4-12 mg/dl

Q9.19: Which AEDs are recommended for the management of neuropathic pain?

Answer:

Trigeminal Neuralgia	DOC →	Carbamazepine
Post-Herpetic Neuralgia	DOC →	Pregabalin = Gabapentin
Diabetic Neuropathy	DOC →	Pregabalin > Gabapentin

Q9.20: In what conditions is Valproate recommended?

Answer:

- Recommended for all types of epilepsy
- Mood stabilizers in bipolar disorder
- Prevention of migraine

Q9.21: What are the side effects of valproate?

Answer:

- Nausea/Vomiting: Most common
  - o Divalproex: Less risk of nausea/vomiting
- Alopecia
- Liver toxicity in children: <2 years of age
- Rashes
- Obesity
- Pancreatitis, PCOS: Gender-specific side effects
- Tremors
- Enzyme inhibitors
- Ammonia increase: Encephalopathy (Treatment: L-Carnitine)

Q9.22: Which AED causes maximum teratogenicity?

Answer:

1. Most teratogenic: Valproate
2. Causes neural tube defects such as spina bifida

Q9.23: What are the uses, MOA, and side effects of Topiramate?

Answer:

- Use- Weight loss: anti obesity drug
- MOA- Has Carbonic anhydrase inhibiting properties like Acetazolamide
- Side effects

- Secondary angle closure glaucoma (frequent eye check-up needed)
- Nephrolithiasis: Calcium stones in the kidney

- Similar drug- Zonisamide

Q9.24: Write briefly about Levetiracetam and Brivaracetam.

Answer:

- MOA: SV2A inhibitor- Inhibits glutamate release
- Uses:
  - Increases memory: Nootropic
  - Antioxidant: Neuroprotective
- Piracetam: Used in Alzheimer's dementia

Q9.25: How do commonly used AEDs differ in terms of pregnancy and lactation?

Answer:

	Pregnancy	Lactation
Valproate	Most teratogenic	Least in milk
Levetiracetam	Safest drug	Maximum in milk

BIG QUESTION 10: What are the drugs used in the management of Parkinson's disease?

PYQ: NEET PG 2021
PYQ: FMGE 2022

Broad Answer:

- Parkinson's disease (PD) is a progressive neurodegenerative disorder primarily affecting motor function caused by degeneration of the dopaminergic neurons in substantia nigra.
- Toxin involved is MPTP toxin

DETAILED QUESTIONS

Q10.1: What is the drug of choice in the treatment of Parkinson's disease?

Answer:

- DOC in treating Parkinson's disease: Levodopa
- Other Name: L-DOPA
- Crosses the BBB

Q10.2: What are the MOA, drug interactions, contraindication, and prodrug of Levodopa?

Answer:

- Prodrug: Converted to dopamine by dopa decarboxylase
- Inhibits peripheral dopa decarboxylase: Carbidopa, benserazide
  - Combined with levodopa
  - Shows synergism
- Never combine Levodopa with vitamin B6 as it increases the peripheral conversion of levodopa into dopamine
- Contraindication: Angle closure glaucoma and Melanoma
  - It causes mydriasis

Q10.3: What are the peripheral and CNS adverse effects of Levodopa?

PYQ: INICET 2022

Answer:

Peripheral	• Reduced by Carbidopa • It includes o Nausea/vomiting: Most common → Treatment: Domperidone (blocks D2 receptor in CTZ area) o Postural hypertension o Mydriasis o Arrhythmia
CNS	• It includes o Dyskinesia → Treatment: Levetiracetam, Amantadine o Psychosis → Treatment: Clozapine, quetiapine, pimavanserin

Q10.4: What is On-Off phenomenon?

Answer:

- Prolong On: Inhibit the degradation of dopamine
  - o Administer MAO-B and COMT inhibitors
  - o New drug to prolong on phase: Istradefylline (Adenosine A2 blocker)
- Rescue from Off: Injection of apomorphine

Q10.5: What are the different classes of drugs used in Parkinson's disease and their examples?

Answer:

Mao-B Inhibitors (Irreversible)	Seligiline, Rasagiline (Neuroprotective)
Mao-B Inhibitors (Reversible)	Safinamide
COMT Inhibitors	Entacapone, Opicapone (Do Not Cross BBB), Tolcapone (Cross BBB): Hepatotoxic (Drug of Last Resort)
NMDA Antagonist > D2 Agonist > Anticholinergic	Amantadine
Dopamine Agonist	• Ropinrol, Pramipexole (Oral) • Rotigotine (Transdermal/Cranial Patch) • Apomorphine (Injection)

Q10.6: What is the preferred order of using COMT inhibitors in Parkinson's disease and why?

Answer:

- Started first - Entacapone, Opicapone
- Tolcapone: Started last (Hepatotoxic)

Q10.7: What are the side effects and additional properties of Amantadine?

Answer:

- Amantadine is an antiviral drug that causes vasodilation of veins
- Side effects of Amantadine: Livedo reticularis

YOURWISH

Q10.8: What are the drugs of choice for treating restless leg syndrome in general and in CKD patients?

Answer:

- DOC for restless leg syndrome: Pregabalin, gabapentin
- Restless leg syndrome due to CKD: Clonidine
  - Earlier: Ropinirole

Q10.9: What are the drugs used to manage chorea in Huntington's disease?

Answer:

- DOC for Huntington's disease (excessive chorea): Dopamine depleters
  - Tetrabenazine
  - Deutetrabenazine
  - Valbenazine
- In resistant cases: Antipsychotic drugs

Q10.10: What are the drugs used to manage chorea in Tourette syndrome?

Answer:

- DOC for tourette syndrome: Alpha (α) 2 agonist
  - Guanfacine/Clonidine
- In resistant cases: Antipsychotic drugs

Q10.11: What are the drugs used to manage chorea in Rheumatic chorea?

Answer:

- DOC for Rheumatic Chorea: Valproate or Carbamazepine
  - Other Name: Sydenham's chorea
- In resistant cases: Antipsychotic drug like Haloperidol

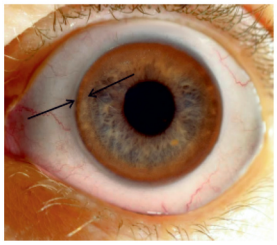
PYQ: NEET PG 2020

PYQ: FMGE 2021

Q10.12: How does Wilson disease occur and how is it treated?

Answer:

- Deposition of copper in the various body parts
- DOC: Zinc
  - Organ damage (CNS): Tetrathiomolybdate
  - Liver: Penicillamine, trientine



KF ring

Q10.13: What is the DOC for managing Amyotrophic lateral sclerosis?

Answer:

- DOC for Amyotrophic lateral sclerosis, AKA Lou Gehrig's disease is:
  - Riluzole
  - Edaravone
  - Tofersen

Q10.14: What are DOC in Retts syndrome, Progeria, and Friedreich ataxia?

Answer:

Retts syndrome		• **DOC for Retts syndrome: Trofenatide**
Progeria		• **DOC for progeria: Lonafarnib**
Friedreich ataxia		• **DOC for Friedreich ataxia: Omaveloxolone**

BIG QUESTION 11: What is Multiple sclerosis and what are the disease modifying drugs used in its treatment?

Broad Answer:

- **Multiple sclerosis (MS)** is a chronic autoimmune demyelinating disease of the CNS.
- Disease-modifying therapies (DMTs) **do not cure** MS but **reduce relapse rates, delay progression**, and **slow accumulation of disability.**

DETAILED QUESTIONS

Q11.1: What are the Disease modifying drugs for multiple sclerosis?

Answer:

Relapsing-remitting multiple sclerosis	DOC: Interferon Beta + glatiramer
Secondary progressive multiple sclerosis	DOC: Mitoxantrone or natalizumab or high dose of interferon beta
Primary progressive multiple sclerosis	DOC: Ocrelizumab

Q11.2: Which drug shows the maximum improvement in EDSS scale?

Answer:

- Maximum improvement is seen via the Expanded disability status scale: Mitoxantrone > Natalizumab

Q11.3: What is the adverse effect of Natalizumab?

Answer:

- Natalizumab: Causes JC polyomavirus infection in the brain causing Progressive multi focal leukoencephalopathy (PMLE)

Q11.4: Which drugs shows symptomatic improvement in multiple sclerosis?

Answer:

- Symptomatic improvement like weakness, gait is seen in:
  - Modafinil
  - Dalfampridine (Aminopyridine)

BIG QUESTION 12: What are the drugs used in psychiatric diseases, and what are the mechanisms of action, uses and side effects of anti-psychotics?

Broad Answer:

- Drugs in psychiatric disease are divided in to:
  - Drugs to treat Psychosis- Insight absent
  - Drugs to treat Neurosis- Insight present

DETAILED QUESTIONS

Q12.1: Explain psychosis and neurosis and disorders classified under them.

Answer:

Psychosis	Neurosis
Insight absence of disease They are further divided into • Schizophrenia: DOC: antipsychotics • Mood disorders o Mania: Mood stabilisers o Depression: Antidepressants (SSRI) o Bipolar disorder: Mood stabilisers	Insight presence of disease • Generalised anxiety disorder • OCD • PTSD • Anorexia • PMTS DOC-SSRI

Q12.2: What is the MOA of anti-psychotic drugs and what are their uses?

Answer:

- MOA: Block dopamine D2 and 5HT2 in brain
- Uses: Mnemonic: **ANTIPSYCHOTIC**
  - **Anti**emetic drugs: Blocks CTZ
  - **Psy**chosis: Blocks mesolimbic and mesocortical
  - **Cho**rea: Blocks basal ganglia
  - **TIC** disorder: Blocks basal ganglia

Q12.3: What are the differences between typical and atypical antipsychotics drugs?

Answer:

Typical Antipsychotics 1st Generation	Atypical Antisychotics 2nd Generation
Block Dopamine (D2) More	Block 5HT-2 (Serotonin) More and Other Actions
Control Positive Symptoms (Aggression, Hallucination)	Control Positive + Negative Symptoms (Also Depression, Apathy, Amnesia, Anhedonia)

- 2nd generation antipsychotics are more effective than 1st generation

Q12.4: Classify the drugs under typical antipsychotics.

Answer:

Phenothiazine	-AZINE	• Chlorpromazine • Thioridazine • Fluphenazine • Perphenazine	Least Dopamine Blockage ↓
Thioxanthenes	-THIX-	• Thiothixene • Flupenthixol • Zuclopenthixol	↓
Butyrophenone	-RIDOL	• Haloperidol • Droperidol • Benperidol • Penfluridol	↓ Maximum Dopamine Blockage

Q12.5: What are the risks and uses of typical antipsychotics?

Answer:

- Other Name: Neuroleptics
- Maximum risk of Parkinson's disease
- Maximum risk of increase in prolactin levels
- Uses
  - o DOC for intractable hiccups: Chlorpromazine
  - o Droperidol + Fentanyl: Neurolept analgesia
  - o Droperidol + Fentanyl + N2O: Neurolept analgesia

Q12.6: Classify atypical antipsychotics based on their MOA

Answer:

Receptors	How to identify	Drugs	
5-HT2A Antagonist > D2 Antagonist	- PINE - DONE	• Clozapine. • Olanzapine. • Zotepine. • Asenapine. • Quetiapine.	• Ziprasidone • Risperidone • Iloperidone • Sertindole • Paliperidone • Lurasidone
D1/2 Partial Agonist + 5 HT2A Antagonist	- PIPRAZOLE	• Aripiprazole • Brexipiprazole	
D2 + D3 Antagonist	- SULPIRIDE	• Sulpiride • Levosulpiride • Amisulpiride	
5-HT2A Inverse Agonist	- SERIN	Pimavanserin	

Q12.7: Which atypical antipsychotics has the maximum and least risk of causing Parkinson's disease and increasing prolactin levels?

Answer:

- Risperidone: Maximum risk for causing parkinson's disease, prolactin increase
- Least risk: Clozapine

Q12.8: What is Levosulpiride used for?

Answer:

- Levosupiride is an antiemetic drug
- As a prokinetic drug it is used to treat GERD

Q12.9: What are the effects and uses of Pimavanserin?

Answer:

- No risk of parkinson's disease, prolactin increase
- No dopamine action
- DOC: Psychosis in parkinson's disease

Q12.10: What is the route of route of administration of anti-psychotic drugs?

Answer:

- All anti-psychotic drugs are given via oral
- Poor oral compliance: Intramuscular depot injections

Q12.11: Which anti-psychotic drugs are given as Intramuscular depot injections?

Answer:

High	Haloperidol
Five	Fluphenazine
P	Paliperdone
A	Aripiprazole
R	Risperidone
O	Olanzapine

Q12.12: Which are the anti-psychotic drugs given via intranasal and sublingual route?

Answer:

- Intranasal: Loxapine
- Sublingual: Asenapine
  - Recommended in acute attack of psychosis

Q12.13: What are the adverse effects of D2 receptor blockage and which drugs have the maximum and least risk of casuing them?

Answer:

- Prolactin increase
  - Blocks D2 in hypothalamic-pituitary axis
  - Galactorrhea, amenorrhea, infertility
- Extrapyramidal symptoms
  - Blocks D2 in basal ganglia

YOURWISH

- Maximum risk of causing prolactin increase: Haloperidol
- Maximum among atypical: Risperidone
- Least risk of causing extrapyramidal symptoms
  - Pimavanserin > Clozapine > Aripiprazole

Q12.14: What are the different types of extrapyramidal symptoms, and how are they managed pharmacologically?

Answer:

- Mnemonic- Never APART

PYQ: FMGE 2022 PYQ: NEET PG 2020

Extrapyramidal symptoms (EPS)	Pharmacotherapy
• Neuroleptic malignant syndrome • (Emergency)	• Extreme rigidity o Hyperthermia o Rhabdomyolysis → Myoglobinuria, kidney damage and cola coloured urine. • DOC: Dantrolene o Muscle relaxant o Also Bromocriptine can be given: D2 agonist
• Acute muscle dystonia • 1st EPS	• Spasms of head and neck • Torticollis, Oculogyric crisis • DOC: Anticholinergic drugs o Benzhexol o Promethazine
• Parkinsonism	• Resting tremors, bradykinesia • DOC: Anticholinergic drugs
• Akathisia • Most common EPS	• Anxiety like restlessness • DOC: Propranolol
• Rabbit syndrome	• Perioral tremors • Treatment: Anticholinergic drugs o Benzhexol o Promethazine
• Tardive dyskinesia • Last EPS • Permanent EPS	• Chorea • DOC: Dopamine depleters o Tetrabenazine o Valbenazine

Q12.15: Elaborate on the MOA, effects and uses of Dantrolene.

Answer:

- Dantrolene is a muscle relaxant
- MOA: Inhibits the release of calcium from smooth endoplasmic reticulum
- SERCA-2 Blocker
  - Other Name: Ryanodine antagonist
- DOC: Malignant hyperthermia

Q12.16: Name the drugs causing malignant hyperthermia.

Answer:

Mnemonic: **SHAL**

- Succinylcholine

- Halothane
- Atropine
- Lignocaine

Q12.17: What are the uses of clozapine?

Answer:

- Most effective anti-psychotic drug
- Chemically: Di-benzodiazepine
- Uses
  - o DOC: Resistant cases of psychosis
  - o Used as a Anti-suicidal drug (Lithium is the other drug)

Q12.18: What are the side effects of Clozapine?

PYQ: NEET PG 2020
PYQ: FMGE 2020
PYQ: INICET 2023

Answer:

Non-serious side effects	• **Mnemonic: MOTHS** o Metabolic syndrome o Obesity o Type 2 DM o Hypersalivation: Wet pillow syndrome o Sedation
Serious side effects	• **Mnemonic: SAM** o Seizures o Myocarditis o Agranulocytosis: Occurs at any dose → Dose independent side effect - Other Name: Idiosyncratic reaction → Monitor - WBC - Absolute neutrophil count • C/I: Absolute neutrophil count <2000/mm3

Q12.19: Which anti-psychotic drugs causes cataract?

Answer:

- Clozapine > Quetiapine

Q12.20: Which anti-psychotic drugs causes QT prolongation?

Answer:

- Quetiapine, Ziprasidone, Sertindole

Q12.21: Which anti-psychotic drugs can cause maximum and least weight gain?

Answer:

- Obesity (weight gain): Olanzapine > Clozapine
- Least weight gain: Aripiprazole, Ziprasidone

Q12.22: Which anti-psychotic is used off label for treating OCD?

Answer:

- Risperidone

Q12.23: Which anti-psychotic is approved for treating unipolar depression?

Answer:

- Quetiapine

BIG QUESTION 13: What are mood stabilizers, and what are the features, uses and adverse effects of lithium?

Broad Answer:

- Mood stabilizers are drugs used in treating Bipolar disorders
- Drugs include: Mnemonic: Low VOLTAGe
  - Lithium
  - Valproate
  - Oxcarbazepine, Carbamazepine
  - Lamotrigine
  - Topiramate
  - Antipsychotics
  - Gabapentin

DETAILED QUESTIONS

Q13.1: Which drugs are used off label for treating Bipolar disorder?

Answer:

- Oxcarbazepine and Topiramate

Q13.2: Which drugs are used to treat acute Mania?

Answer:

- IV lithium
- Antipsychotics
- Valproate

Q13.3: Which drug is used in maintainance therapy of Bipolar disorder?

Answer:

- Oral lithium

Q13.4: Define rapid cycling Bipolar disoder and what is the drug used to treat it?

Answer:

- Rapid cycling bipolar disorder: > 4 attacks of BPD per year
- Valproate is used to treat Rapid cycling bipolar disorder

Q13.5: Which drug is used in treating resistant Mania?

Answer:

- Clozapine

Q13.6: What is the DOC in Bipolar diasease in pregnanacy?

Answer:

- Antipsychotic (DOC)

Q13.7: Which is the most teratogenic anti-psychotic drug?

Answer:

- Valproate
- Causes neural tube defects

Q13.8: What are the uses and contraindications of lamotrigine in mood disorders?

Answer:

- Recommended in depression and BPD
- Contraindicated in Mania

Q13.9: Which anti-depressants precipitate the attack of mania in Bipolar disorder?

Answer:

- SSRIs
- TCA

Q13.10: What are the uses of lithium?

PYQ: FMGE 2023
PYQ: NEET PG 2021
PYQ: INICET 2023
PYQ: FMGE 2020

Answer:

- Mnemonic: **BHAR**
  - **B**ipolar disorder
  - **H**ypnic headache
  - **A**nti-suicidal drug
  - **R**esistant depression

Q13.11: Elaborate the pharmacokinetics of Lithium.

Answer:

- Salts of Lithium: Lithium citrate and Lithium carbonate
- ROA: Oral, IV
- Half-life: 24 hrs
- Therapeutic drug monitoring (TDM): Blood sample taken
  - 12 hrs after the last dose
- Metabolism: No
- Excretion: Urine > Sweat, saliva, milk
- Contraindication: During breastfeeding
- Lithium is stopped: 24 hrs before surgery

Q13.12: What are the various ranges of serum lithium levels, and their clinical implications?

Answer:

0.6-1.0 meq/L	Maintenance of bipolar disorder
1.0 - 1.5 meq/L	Acute mania

YOURWISH

> 1.5 meq/L	Toxicity
> 4 meq/L	Hemodialysis

Q13.13: How is Lithium toxicity managed?

Answer:

- Hydration with NaCl
- Mannitol diuresis
- Amiloride

Q13.14: What are the adverse effects of Lithium?

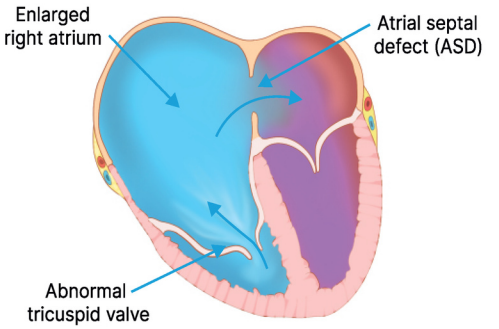
Answer:

- Mnemonic: LITHIUMS
- Leukocytosis: Increase WBC
  - Leukocytosis can be used therapeutically to increase neutrophil counts in Felty syndrome.
- Increase weight
- Tremors
  - Normal dose: Fine tremors
  - Toxic dose: Coarse tremors
- Hypothyroid goiter
  - Inhibition of T3/T4 synthesis
  - Increase in TSH
- Increased nausea, vomiting, diarrhoea
- Urination: Nephrogenic diabetes insipidus
- Mental changes: Ataxia, tinnitus, seizures
- Skin: Acneiform eruption

Q13.15: What is the tetratogenic condition caused by Lithium?

Answer:

- Ebstein's anomaly- Type of cardiac malformation
  - Abnormal tricuspid valve
  - Box-shaped heart



Ebstein anomaly due to lithium used in bipolar disorder

BIG QUESTION 14: What are anti-depressant drugs and what are their MOA, uses, adverse effects?

Broad Answer:

- Drugs used to treat **depressive disorders**, anxiety, OCD, PTSD, and other mood-related conditions by modulating neurotransmitters
- MOA: Increases the levels of serotonin and norepinephrine in brain

DETAILED QUESTIONS

Q14.1: What is the MOA of SSRIs and name the drugs classiifed under them?

Answer:

- MOA of Selective serotonin reuptake inhibitors: Inhibits serotonin transporter
- Drugs include

- Fluoxetine
- Fluvoxamine
- Paroxetine
- Dapoxetine
- Escitalopram
- Citalopram
- Sertraline

Q14.2: Which is the longest and shortest acting SSRI?

Answer:

- Longest acting: Fluoxetine
  - Converted to another active form: Nor-fluoxetine
  - Duration: 250 hrs
- Shortest: Paroxetine > Fluvoxamine

Q14.3: Which enzyme metabolizes SSRIs?

Answer:

- Metabolised by: CYP2D6
- Except: Escitalopram (safest SSRI in Heart disease)

Q14.4: What are the indications of SSRIs?

Answer:

- DOC for depression- Only for maintenance: Action >4 weeks
- Anxiety disorders
  - Generalised anxiety disorder
  - Obsessive-compulsive disorder
  - Premenstrual tension syndrome

Q14.5: What class of drugs are used in treating acute anxiety attack?

Answer:

- Benzodiazepines

Q14.6: What are the side effects of SSRIs?

Answer:

- Nausea/vomiting/Diarrhoea: Most common
- Decreased secretions
  - Dry eyes
  - Dry mouth
  - SSRIs: Has mild anticholinergic action
- Increased risk for seizures
- Increase the risk of suicides
- Severe anxiety in initial 4 weeks
  - For initial 4 weeks: SSRIs + Benzodiazepines
  - Benzodiazepines: Addictive drugs

→ Not recommended for long-term use

- Sexual dysfunction
  - Characteristic side effect
  - Delayed ejaculation
    → DOC in Premature ejaculation are SSRI
  - Anorgasmia
- Loss of libido
- SIADH

Q14.7: What is the MOA of SNRIs and what are the drugs classiifed under them?

Answer:

- MOA of Selective norepinephrine reputable Inhibitors (SNRI): Inhibit both serotonin and norepinephrine transporters
- Drugs include: Mnemonic: **Very Difficult MD**
  - **V**enlafaxine
  - **D**esvenlafaxine
  - **M**ilnacipran: Approved fo fibromyalgia pain
  - **D**uloxetine (Longest ating): Approved for diabetic neuropathy and DOC: Stress urinary incontinence
- Given in Resistance cases of SSRIs

Q14.8: What are the side effects of SNRIs?

Answer:

- Same as SSRIs
- Others include: Hypertension due to increase in norepinephrine levels

Q14.9: What class of drug does atomoxetine belong to, and what is its mechanism of action and clinical use?

Answer:

- **Atomoxetine is a Norepinephrine reuptake inhibitor**
- MOA: Inhibition of norepinephrine transporters
- Use:
  - Attention deficit hyperactivity disorder
  - Tourette syndrome

Q14.10: What drugs are classified under Tricyclic antidepressants?

Answer:

- Imipramine: active form→ Desipramine
- Clomipramine
- Trimipramine
- Amitriptyline: Active form→ Nortriptyline

Q14.11: What are the side effects of TCAs?

Answer:

Histamine blockage	Sedation, Anti-pruritus effect
Alpha blockage	Hypotension
Muscarinic blockage (atropine like effects)	Hyperthermia, tachycardia, Urinary retention Dry eyes/mouth Mydriasis (c/l angle closure glaucoma)
Potassium blockage	QT prolongation: Torsade's de pointes (quinidine like arrhythmia)

Q14.12: Which drug is approved for nocturnal enuresis?

Answer:

- Imipramine

Q14.13: Why does TCAs need therapeutic drug monitoring?

Answer:

- TCA has a narrow therapeutic index
- SSRIs are safe drugs requirng no TDM

Q14.14: How is TCA poisoning managed?

Answer:

- Antidote: Sodium bicarbonate (DOC)
  - Protects from arrhythmias
- Atropine-like symptoms: Physostigmine
- Resistant arrhythmia: Lignocaine

Q14.15: Elaborate on uses, MOA, side effects of other atypical antidepressants.

Answer:

Bupropion	• Norepinephrine, dopamine reuptake inhibitor
	• Use
	  o Anti-smoking drug
	  o Anti-obesity drug
	• Side effects: Seizures (Maximum)

Trazodone	• **Other Name:** Serotonin antagonist and reuptake inhibitor
	  o Has serotonin-blocking property
	  o 5HT2, 5HT3 antagonist
	  o Has SSRI activity
	• Advantage: No risk of impotence
	• Side effect: Priapism
	  o Prolonged painful penile erection PYQ: NEET PG 2020

Mirtazapine and Mianserin PYQ: NEET PG 2022	• Noradrenaline and selective serotonin antagonist
	  o Blocks alpha 2 A receptor of noradrenaline
	  o Blocks 5HT 3 receptors
	• Produces sedation and has antiemetic effect
	• DOC: Depression + Insomnia

YOURWISH

Buspirone and Gepirone	• 5HT1A agonist • Treat anxiety disorder o Generalised anxiety disorder
Vortioxetine PYQ: INICET 2021	• Serotonin stimulator and modulator • Just like SSRI
Vilazodone	

Q14.16: What are the two types of MAO enzymes?

Answer:

- MAO-A
- MAO-B

Q14.17: Write briefly about Irreversible MAO inhibitors.

Answer:

- Other Name: Hit and Run drug or Suicide inhibitor
- Drugs includes
  - o Tranylcypromine
  - o Phenelzine
- Causes dangerous drug interactions
  - o Cheese reaction: Tyramine-containing food
  - o Seizures when used with Pethidine
  - o Serotonin syndrome: SSRIs/SNRIs

Q14.18: What are reversible MAO-A inhibitors?

Answer:

- Inhibits MAO-A enzyme
- Safest drugs
- Drugs include: Mnemonic: CM
  - o Clorygiline
  - o Moclobemide

Q14.19: What are MAO-B inhibitors?

Answer:

- Inhibits MAO-B enzyme
- Drugs include: Mnemonic:SR
  - o Selegiline: Available as transdermal patches
  - o Rasagiline
- Treat depression, Parkinson's disease

Q14.20: What are the newer MOA inhibitors?

Answer:

- Esketamine: nasal spray
- Used in treating depression

Q14.21: What are the Congeners of progesterone hormone and their uses?

Answer:

- Drugs includes
  - Brexanolone: IV
  - Zuranolone: Oral
- Treatment: Postpartum depression
- DOC for depression: SSRIs

Q14.22: What is the complication of using SSRIs and SNRIs during pregnancy?

Answer: Pulmonary artery hypertension in the fetus

Q14.23: What is drug discontinuation syndrome?

Answer:

- Drug discontinuation syndrome: sudden stoppage of anti-depressants
  - Maximum seen with: Venlafaxine and paroxetine (Shortest)
  - Least seen with: Fluoxetine (Longest)

4. AUTACOIDS

BIG QUESTION 1: What are the roles, preparations, and clinical uses of prostaglandins?

Broad Answer: Autocoids are local hormones that produce local effects and include prostaglandins, leukotrienes, and other locally acting agents. Prostaglandins are a major class of autacoids that mediate inflammation, smooth muscle tone, and reproductive functions. Their synthetic analogs are clinically used in abortions, ductus arteriosus management, glaucoma, peptic ulcers, and pulmonary hypertension. The section also covers uterine stimulants and relaxants (tocolytics), along with prostaglandin synthesis pathways and medical abortion protocols. Understanding their mechanisms and applications is essential for therapeutic decision-making

DETAILED QUESTIONS

Q1.1: What are autocoids, and what kind of effects do they produce?

Answer: Autocoids are local hormones that produce local effects

Q1.2: What are the synthetic preparations of prostaglandins and their clinical uses?

PYQ: NEET PG 2021, 2023

PYQ: FMGE 2023

Answer

Prostaglandins	Synthetic Preparation
PGE1	Misoprostol • DOC for MTP/Abortions in 1st trimester (63 days) • NSAIDs-induced peptic ulcer (DOC: PPIs) • S/E of Misoprostol: Diarrhoea (Chloride Secretion) • Teratogenic: Moebius syndrome (6th Cranial nerve damage)
	Alprostadil • DOC in open Ductus arteriosus
	Lubiprostone (chloride secretors have a laxative property) • Treats constipation in inflammatory bowel syndrome
PGE2	Dinoprostone • DOC for cervical ripening, MTP in the 2nd trimester
PGF2 Alpha	Dinoprost • DOC for MTP in the 2nd trimester

YOURWISH

	Carboprost • Control PPH resistant to oxytocin • MTP in 2nd trimester • Contraindicated in Asthma • Dose: 250 mcg injection • Maximum dose: 2000 mg or 8 injections/day
	DOC for glaucoma (POAG, ACG) • Latanoprost • Bimatoprost • Travoprost • Tafluprost
PGI2 (Prostacyclin) • **Vasodilation** • **Antiplatelet effect**	DOC for PAH • Treprostinil • Iloprost • Epoprostenol

Q1.3: What are the contrasting effects of TXA_2 and PGI_2 on vasculature and platelets?

Answer

TXA_2 and PGI_2 are known as physiological antagonists

- TXA_2 (Thromboxane A_2):
  - Vasoconstriction
  - ↑ Platelet aggregation
- PGI_2 (Prostacyclin):
  - Vasodilation
  - ↓ Platelet aggregation

Q1.4: What is the mechanism and protocol of medical abortion using prostaglandins?

Answer

Medical Abortion

- Day 1: Mifepristone (RU-486) 200 mg
  - Blocks progesterone receptors, causing the death of the fetus
- Day 3: Misoprostol - Expels the baby
  - Upto 49-day pregnancy: 400 micrograms oral or S/L
  - Upto 63 days: 800 micrograms vaginally or S/L

Q1.5: How are prostaglandins used in managing the ductus arteriosus?

Answer

- Maintain patency of the ductus arteriosus
  - PGE1: Alprostadil
- Close patency of the ductus arteriosus: decrease PG by NSAIDS
  - DOC: Ibuprofen
  - MC Used: Indomethacin

YOURWISH

YOURWISH

Q1.6: What are the effects of prostaglandins on the uterus?

Answer

Uterine Stimulant	Uterine Relaxant (Tocolytics)
• Oxytocin o DOC: Induction and augment labour o DOC: controls PPH • Carbetocin: Longer-acting alternative of oxytocin. • Carboprost (PGF-2 alpha drugs) • Ergometrine • Methyl ergometrine } To control PPH in oxytocin resistance cases Contraindicated the induction of the labour as it can lead to fetal hypoxia	• Used in premature labour • Atosiban: Blocks oxytocin receptor o Safe for heart disease patients. • Beta (β)-2 agonists: Ritodrine, isoxsuprine • CCB: Nifedipine • GA with maximum tocolytic effect: Halothane • Avoid NSAIDS during labour pain: Due to tocolytic effects as it days child delivery

BIG QUESTION 2: What is the mechanism of action, classification, clinical applications, and toxicity profiles of NSAIDs?

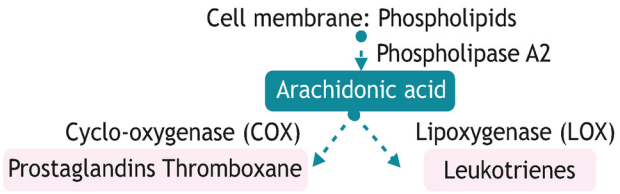
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Broad Answer: NSAIDs act by inhibiting cyclooxygenase (COX) enzymes, thereby blocking prostaglandin synthesis from arachidonic acid. Their anti-inflammatory, analgesic, and antipyretic properties are utilized in various conditions, including pain, fever, inflammation, and specific syndromes such as Reye's syndrome. NSAIDs are classified into non-selective and selective COX inhibitors, each with distinct side effects and indications. Understanding their biochemical origin, mechanism, and toxicity helps guide their safe use

DETAILED QUESTIONS

Q2.1: How are prostaglandins synthesized from cell membrane phospholipids?

Answer



Q2.2: What are the various anti-inflammatory drugs, and what is their mechanism of action?

Answer

Anti-inflammatory drugs blocking:

- Phospholipase A2 enzyme: Corticosteroids
- COX: NSAIDS
- LOX: Zileuton
- Dual COX + LOX: Lecofelone (used in osteoarthritis).

Q2.3: What is the mechanism of action of Aspirin?

Answer

Only irreversible COX inhibitor (suicide inhibitor)

Q2.4: What are the dose-dependent actions of aspirin?

Answer

- Low dose (40-325 mg): Antiplatelet → MI or stroke.
- Medium dose (<2 grams): Analgesic and Antipyretic
- High dose (2-5 grams): Anti-inflammatory
- > 5g/d: Increased urate excretion (uricosuric) - Good for gout

Q2.5: What are the side effects of aspirin?

Answer

- All NSAIDs: Rashes, SJS, and allergic reactions
- Peptic ulcer (Iron trapping in the stomach): PPI > Misoprostol
- < 2g/d: Increase uric acid in the blood - Bad for Gout
- 2-5 g/d: Variable effects

Q2.6: How is aspirin poisoning managed?

Answer

- Aspirin poisoning antidote: Sodium bicarbonate (Forced alkaline diuresis)
- Severe poisoning: hemodialysis is done

Q2.7: What are the contraindications of aspirin intake?

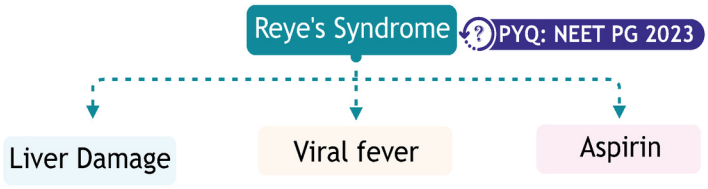
Answer

Contraindicated as an antipyretic and in children, and Reye's syndrome except in Kawasaki disease

Q2.8: What is Reye's syndrome?

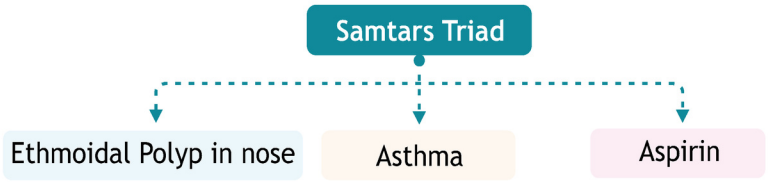
Answer

Occur in children with viral infections treated with aspirin



Q2.9: What is Samter's triad?

Answer



Q2.10: What is the mechanism of COX-1 and COX-2, and how do NSAIDs affect them?

Answer

- COX-1 - S/E: Peptic ulcer
- COX-2: Inflammation
- Non-selective COX inhibitor: For COX-1 and COX-2
- Preferential COX-2 inhibitors: COX-2 >> COX-1
  - Least risk of peptic ulcer

Q2.11: What are the various non-selective COX inhibitors?

Answer

Non-Selective Cox Inhibitors	
Piroxicam > tenoxicam	Longest, undergo enterohepatic circulation
Ketorolac	Intravenous NSAID
Ibuprofen > Indomethacin	Closure of PDA
Mefenamic acid	Dysmenorrhea
Banned Nsaids	
Phenylbutazone	Banned : Agranulocytosis
Phenacitin	Banned: Analgesic Nephropathy

Q2.12: What are the side effects of non-selective COX inhibitors?

Answer

- A specific side effects of Ibuprofen is aseptic meningitis
- Specific side effects of Indomethacin are pancreatitis and epilepsy
- Side effect of mefenamic acid: Autoimmune hemolytic anemia

Q2.13: What are the preferential COX-2 inhibitors?

Answer

- Nimesulide (S/E: Stevens-Johnson syndrome)
- Meloxicam · Diclofenac (best topical)
- Aceclofenac
- Etodolac

Q2.14: What are the selective COX-2 inhibitors?

Answer

- Celecoxib
- Etoricoxib
- Parecoxib
- Rofecoxib, Valdecoxib: MI, stroke (thromboembolism) (banned)
- Advantages: Less risk of peptic ulcer

Q2.15: What is the mechanism of action of Paracetamol?

Answer

- Paracetamol (Acetaminophen) is analgesic + antipyretic with a poor anti-inflammatory action
- Acts on the COX-3 and TRPV1 receptor

Q2.16: What is the safety profile of Paracetamol?

Answer

- Safest NSAID in children - No risk of Reye's syndrome
- Safest NSAID in Renal disease
- Safest in Peptic ulcers

Q2.17: How is PCM metabolised?

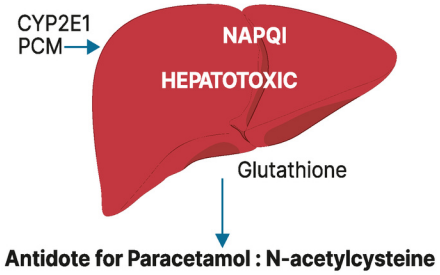
Answer

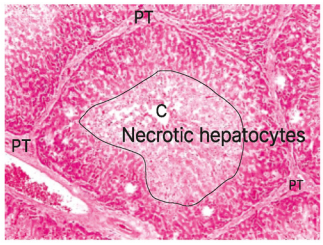
PCM is converted to NAPQI in the presence of CYP2E1 and is removed by glutathione

Q2.18: What is the toxic form of paracetamol, and what are the pathological findings?

Answer

- Toxic form of paracetamol: NAPQI
  - Causes zonal necrosis: Centrilobular necrosis with periportal sparing





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Q2.19: What is the antidote for paracetamol?

Answer

Antidote for paracetamol: N-Acetylcysteine

Q2.20: What is a Nomogram? What are the Nomograms used for different drugs?

Answer

- A technique to monitor plasma levels of the drug in case of toxicity
  - Paracetamol - Rumack Matthew Normogram
  - Vancomycin- Kuller's Normogram

BIG QUESTION 3: What are the types, mechanisms, and clinical uses of antihistamines?

Broad Answer: Antihistamines, primarily H1 antagonists, act on histamine receptors distributed in the CNS and periphery. They are used to manage allergic conditions, motion sickness, and other histamine-mediated responses. Based on their sedative effects and receptor selectivity, they are categorized into first- and second-generation drugs, each with specific clinical applications and side effect profiles

DETAILED QUESTIONS

Q3.1: How is histamine synthesised?

Answer

- Synthesis: Histidine → Histamine (via Histidine Decarboxylase)
- Receptors: H1, H2, H3, H4 (all are GPCRs)

Q3.2: What are the effects of H1 receptors based on location?

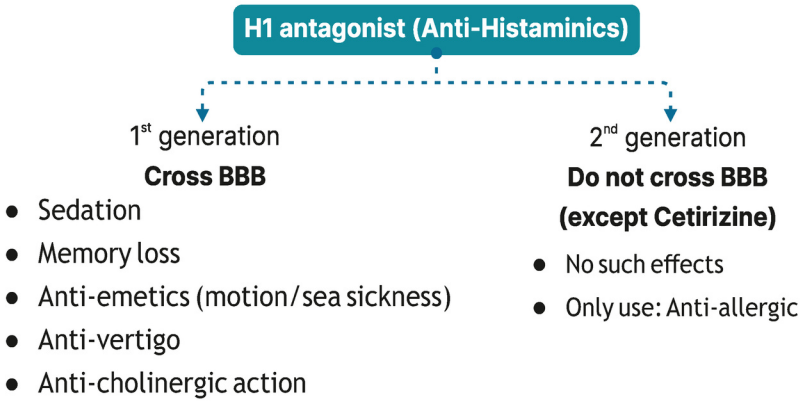
Answer

Effects by location:

- **CNS:**
  - Wakefulness
  - Memory increase
  - Vomiting (motion/sea/morning sickness)
  - Vertigo
- **Periphery (Mast Cells):**
  - Allergy (Type I Hypersensitivity)
  - Triple response: Red, wheal, flare

Q3.3: How are H1 antagonists classified, and what are their features?

Answer



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Q3.4: What are the contraindications for antihistamines (H1 antagonists)?

Answer:

Contraindications:

- Pilots, divers, and machinery workers
- During daytime (except Chlorpheniramine: Least sedative 1st Gen)

Q3.5: Which drugs belong to the first-generation antihistamines, and what are their uses?

Answer:

1st generation
Highly Sedative 1. **Promethazine:** Max. sedation, anticholinergic (use: Parkinson's) 2. **Diphenhydramine:** Post auricular patch for motion sickness 3. **Hydroxyzine:** Longest, active form is Cetirizine 4. **Doxepin:** Is a TCA also 5. **Doxylamine (along with Vitamin B6):** Morning sickness (DOC)
Moderate Sedative 1. **Cyclizine, meclizine:** Max antiemetic effect (in motion and sea sickness) 2. **Cinnarizine:** Also block Calcium on vestibular nerves 3. **Cyproheptadine:** Additional Anti-serotonin (use: Migraine) 4. **Pheniramine**
• **Least sedative: Chlorpheniramines** (given During day time)

Q3.6: What are the uses of second-generation antihistamines?

Answer

- Used in mild allergy (rashes, dry cough, urticaria)
- Severe Anaphylaxis: Adrenaline (0.5 ml of 1:1000 intramuscular)
- Loratidine: Most potent
- Rupatadine: Inhibits PAF (Antiplatelet)
- New drug that inhibits PAF are
  - Apafant
  - Modipafant

Q3.7: What are the 2nd Gen antihistamines causing QT prolongation?

Answer

- Terfenadine, Astemizole:
  - CYP3A4 substrate - Banned as it causes QT prolongation (Torsades de pointes)
- Fexofenadine: Active form of terfenadine
  - No risk of QT prolongation

Q3.8: What is the 2nd Gen antihistamine that crosses the BBB?

Answer

- Cetirizine is the only drug in 2nd generation antihistamines that crosses the BBB
- Causes sedation (Levo-cetirizine: Requires half dose: less sedation)

Q3.9: What is the most potent 2nd Generation antihistamine drug?

Answer

Loratidine

Q3.10: What are the drugs that inhibit PAF?

Answer

Inhibit PAF (Antiplatelet)

- Rupatadine: Inhibits PAF
- New drug that inhibits PAF are
  - Apafant
  - Modipafant

Q3.11: What is Betahistine?

Answer

- Betahistine: H1 Partial Agonist
- Use: Anti-vertigo
- Brand name: Vertin

Q3.12: How is motion sickness and sea sickness treated?

Answer

Motion sickness and Sea sickness can be treated via

- Hyoscine
- All 1st generation Antihistaminic
  - Diphenhydramine
  - Promethazine
  - Cyclizine
  - Meclizine
  - Cinnarazine

Q3.13: How is morning sickness treated?

Answer

Doxylamine + Vitamin B6

Q3.14: What is the treatment of mountain sickness?

Answer

Acetazolamide

Q3.15: What are the topical antihistamines, and their uses?

Answer

- Eye or nasal drops
- Treatment: Allergic conjunctivitis or rhinitis
- Azelastine - Maximum topical activity
- Levocarbastine
- Additional mast cell stabilizers
  - Olopatidine
  - Ketotifen

Q3.16: What is H3 inverse agonist, and its uses?

Answer:

- Tiprolisant (Pitolisant) - Increases wakefulness, treats Narcolepsy
- Modafinil : DOC- Narcolepsy

BIG QUESTION 4: What are the pharmacological features and clinical uses of drugs acting on serotonin (5-HT) receptors?

Broad Answer: Serotonin receptors (5-HT1 to 5-HT7) are primarily GPCRs, with 5-HT3 being the only ionotropic receptor. Various agonists and antagonists act on these receptors and are used in conditions like migraine, anxiety, nausea, vomiting, and GI motility disorders

DETAILED QUESTIONS

Q4.1: What is serotonin, and what are its receptors?

Answer:

- Serotonin = 5-hydroxytryptamine (5-HT)
- Synthesised from tryptophan
- Receptors: 5-HT1 to 5-HT7
  - All are GPCRs, except 5-HT3 (ionotropic)

Q4.2: What drug acts as a 5-HT1A partial agonist, and what is its clinical use?

Answer:

- Buspirone
- Clinical use: Anti-anxiety (GAD)

Q4.3: Which drugs act as 5-HT1B/1D agonists?

Answer:

- Triptans (e.g., sumatriptan)
- Ergotamine
- Use: Acute migraine

Q4.4: What is Lasmiditan, and what is it used for?

Answer:

- Lasmiditan is a 5-HT1F agonist
- Used in acute migraine (new drug)

Q4.5: What are triptans?

Answer:

Triptans are specific 5-HT1B/1D agonists

Q4.6: What is the drug of choice (DOC) for acute migraine?

Answer:

- Sumatriptan (Overall DOC)
- Routes: Oral, SL, Nasal spray

Q4.7: What are the notable properties of other triptans?

Answer:

- Zolmitriptan: Given as a nasal spray (esp. if vomiting)
- Eletriptan: Most effective
- Rizatriptan: Fastest acting
- Frovatriptan: Longest acting

Q4.8: What are Ergotamines?

Answer:

- Ergotamines are non-specific drugs
- When 5-HT1B/1D agonists are combined with alpha blockers, the hydrogenated form (e.g., dihydroergotamine) increases the alpha-blocking effect

Q4.9: What are the adverse effects of ergotamine?

Answer

- Causes vasoconstriction
- In the end arteries of the fingers, vasoconstriction caused by ergotamine can lead to ischemic necrosis or ergotism, also known as dry gangrene
- Treatment: Nitroprusside, vasodilator



Ergotism

Q4.10: What are the drugs used for the prophylaxis of chronic migraine?

Answer

- Beta blockers: Propranolol (overall DOC)
  - Contraindicated (C/I) in asthma; in such cases, antiepileptics and calcium channel blockers (CCBs) are used
- Antiepileptics: Valproate, Topiramate, Gabapentin
- CCBs: Flunarizine, Verapamil
- TCAs: Amitriptyline, Nortriptyline
- Anti-serotonin: Cyproheptadine, Methysergide
- MAO inhibitors: Phenelzine

Q4.11: What are some additional treatments used for migraine prophylaxis?

Answer

- Botulinum toxin
- Clonidine and Captopril

Q4.12: What is the role of CGRP in migraine, and how is it targeted?

Answer

- CGRP-2 in neurons causes migraines
- CGRP-2 inhibitor drugs end with - **Gepant**
  - Calcitonin gene-related peptide-2 inhibitor
  - Mainly given in acute migraine
  - Ubrogepant, Rimegepant, Zavagepant
- Recently, Erenumab, a monoclonal antibody, blocks CGRP-2: Prophylaxis of Migraine

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Q4.13: What are the drugs acting on 5HT-2 receptors, and their uses?

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Answer

5HT-2C agonist	5HT-2 A/B/C antagonist	5HT-2 to 5HT 4 antagonist
• Lorcaserin • Suppress appetite • Anti-obesity drug, but banned due to the increased risk of colorectal cancer.	• Antipsychotics o Olanzapine (Causes maximum obesity) o Clozapine • Increases appetite • S/E: Obesity	• Anti-serotonin o Ketanserin, o Ritanserin o Cyproheptadine • DOC: Serotonin syndrome, and also used in migraine prophylaxis

Q4.14: What are 5-HT3 antagonists (setrons) and their mechanism?

Answer

Setrons block 5-HT3 in the GIT and CTZ

Q4.15: What are the effects of setrons (5HT-3 antagonists) on GIT?

Answer

- In GIT, serotonin increases motility, setrons blocks 5HT-3 receptors and produces an anti-motility effect
- Alosetron: Given for diarrhea in IBS, only given to females
  - o C/I in males as it causes ischemic colitis

Q4.16: What are the setrons acting on CTZ?

Answer

- Setrons acting on the CTZ area of the brain have antiemetic action
- Drugs:
  - o Ondansetron
  - o Granisetron
  - o Tropisetron
  - o Ramosetron
  - o Palonosetron

Q4.17: What are the uses and side effects of 5HT-3 antagonists acting on the CTZ?

Answer

Uses

- Chemotherapy-induced nausea and vomiting (CINV)
- Radiotherapy-induced nausea and vomiting
- GIT infections causing vomiting
- Not effective in motion sickness- Antihistaminics are used

Side effects

- Constipation
- QT prolongation

Q4.18: What is the treatment protocol for Chemotherapy-induced nausea and vomiting (CINV)?

Answer

1. Setron (5-HT3 Antagonist): Ondansetron, Granisetron, Palonosetron
↓
2. Pitant (NK-1 Antagonist): Aprepitant, Fosaprepitant, Rolapitant, Netupitant
↓
3. Dexamethasone
↓
4. CB1 (cannabinoid) agonist: Dronabinol, Nabilone

Important Information

- Maximum vomiting is caused by cisplatin, an anticancer drug
- Setrons are only effective up to 24 hours - Early phase of CINV except Palonosetron
- If vomiting persists beyond 24 hours, pitant are used - Delayed phase of CINV
- Dexamethasone and CB1 agonists (Drugs identified by -nabi-) are added in the delayed phase of CINV
- CB1 agonists can increase or stimulate appetite, as the cancer patient has severe weight loss or ataxia

Q4.19: What are 5-HT4 agonists and their clinical use?

Answer

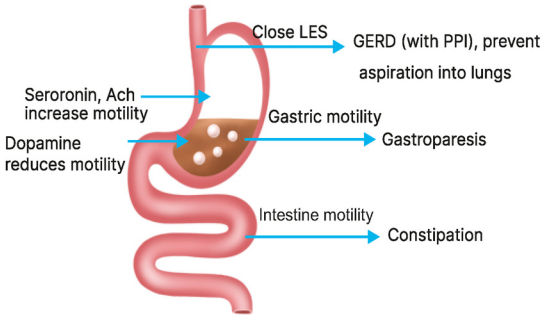
Prokinetics - Increase GIT motility

Q4.20: What are the various prokinetic drugs and their uses?

PYQ: NEET PG 2021

Answer

- **5HT-4 Agonist** (End with -Pride)
  - Cisapride, Mosapride, Renzapride, Itopride, Prucalopride, and Tegaserod
  - Cisapride and Tegaserod are banned as they cause QT prolongation (Torsades de pointes)
- **D2 (Dopamine) antagonist:** Domperidone also has antiemetic action, as dopamine receptors are also present in the CTZ area
  - Cannot cross the BBB
- **Anticholinesterase** (Increase Ach): Neostigmine
  - Use: Postoperative paralytic ileus
- **Motilin receptors** on the stomach: Erythromycin (Use: Gastroparesis)
- **Metoclopramide**



Q4.21: What is the MOA, side effects of metoclopramide?



Answer

- Prokinetic and antiemetic
- **Action**
  - 5-HT 4 receptor agonist
  - D2 antagonists
  - ↑↑ Ach
- **Side effects:**
  - It can cross the blood-brain barrier causing drug-induced Parkinson's disease (DIPD) or muscle dystonia
  - Abnormal posture is observed
  - Treatment: Benzhexol

Q4.22: What is the relationship between Metoclopramide and Domperidone?

Answer

- Metoclopramide can cross the BBB, while domperidone cannot
- Both drugs block D2 receptors

BIG QUESTION 5: What are the drugs used in the treatment and prophylaxis of gout, and how do they act?

Broad Answer: Gout is treated using NSAIDs, colchicine, corticosteroids for acute attacks, and uric acid-lowering agents for chronic management. These drugs either reduce inflammation or decrease uric acid levels through xanthine oxidase inhibition, uricosuric action, or enzymatic breakdown of uric acid.

DETAILED QUESTIONS

Q5.1: What are the effects of gout?

Answer

- Increases blood uric acid levels
- Causes deposition in joints → Arthritis

Q5.2: What are the treatment options for acute gout?

Answer

NSAIDS (all except Aspirin and PCM) → Colchicine → Corticosteroids

Q5.3: What is the mechanism of action, effect, and side effects of colchicine?

Answer

- Microtubule inhibitor → Inhibits the migration of WBC
- Also inhibits the movement of spindle fibers, which suppresses the growth of rapidly dividing cells
- Side effects: BM suppression, GIT ulcers

Q5.4: What is the feature of NSAIDs in gout?

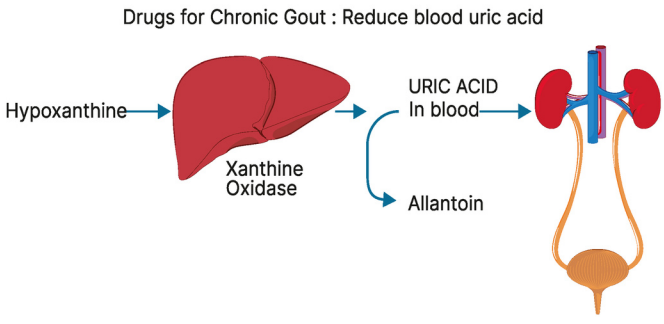
Answer

- Aspirin leads to increased blood uric acid concentration
  - Aspirin, low dose: < 2g/day causes gout
  - Aspirin high dose: > 5g/day is beneficial in gout
- Paracetamol has no anti-inflammatory effect

Q5.5: How are drugs for chronic gout categorized?

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Answer



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Xanthine oxidase inhibitors	Uric Acid Oxidase Enzyme	URICOSURIC AGENTS (inhibit OATR/URAT)
1. Allopurinol 2. Oxypurinol 3. Febuxostat	1. PEGLOTICASE (Mammal) 2. RASBURICASE (Birds)	1. Probenecid 2. Sulfinpyrazone: (NSAID like action). So used in Acute and chronic gout 3. Benzbromarone(safe in renal disease) 4. Lesinurad

Q5.6: What are the features of Allopurinol?

Answer

- Allopurinol and oxypurinol are fake purines and act as competitive inhibitors
- Allopurinol, associated with hypersensitivity
  - In such cases, febuxostat is given

Q5.7: What is the difference between Allopurinol and Febuxostat?

Answer

Febuxostat is a non-competitive inhibitor

Q5.8: What are the features of uric acid oxidase enzymes?

Answer

- Uric acid oxidase enzymes are proteins, thus given only via injections
- Used in allopurinol-resistant gout. E.g. Tumour lysis syndrome

Q5.9: What is the action of uricosuric agents?

Answer

Promote the excretion of uric acid in urine

Q5.10: What are the key drug interactions involving xanthine oxidase inhibitors?

Answer

- 6-Mercaptopurine and Azathioprine are also fake purines that are degraded by Xanthine Oxidase enzymes
- If we combine these 2 drugs with Allopurinol, Allopurinol will inhibit Xanthine Oxidase and increase the toxicity of Azathioprine and 6-Mercaptopurine, causing Bone Marrow Toxicity
- So, reduce the dose of 6MP/AZP if combined with allopurinol by 75%, to reduce the toxicity

Q5.11: What drugs can cause gout?

Answer

- Pyrazinamide
- Aspirin (low dose)
- Immunosuppressant (cyclosporine, tacrolimus)
- Niacin
- Ethambutol
- Diuretics: Thiazide/loop

Q5.12: What drugs are beneficial in gout?

Answer

- Fenofibrate

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- Aspirin (high dose)
- Losartan
- Statins

BIG QUESTION 6: What are the drugs used in the management of rheumatoid arthritis, and how are they categorized?

Broad Answer: Rheumatoid arthritis is treated with anti-inflammatory agents like NSAIDs and corticosteroids for symptom relief, and DMARDs (Disease-Modifying Anti-Rheumatic Drugs) for disease control. DMARDs are categorized into conventional and newer agents with specific mechanisms and uses

DETAILED QUESTIONS

Q6.1: What is Rheumatoid arthritis, and what are the most common joints involved?

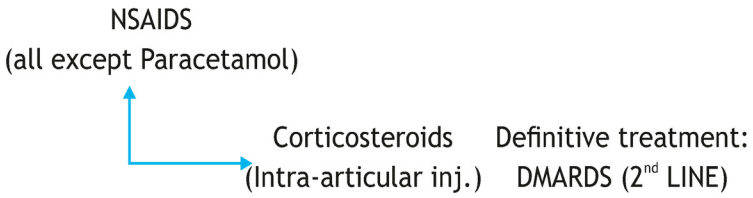
Answer

- Type 3/4 HS, inflammation in the body, causing arthritis
- MC involved joints: MCP, ICP

Q6.2: How is acute RA managed?

Answer

- Acute RA: Arthritis (Anti-inflammatory): 1st line drugs (NSAIDs + Corticosteroids)
- Paracetamol has poor anti-inflammatory action
- Immunosuppressants, DMARDs, are used for definitive treatment
  - o Conventional
  - o Newer



Q6.3: What are the features of conventional DMARDs?

Answer

Methotrexate	• Inhibit DHFR • Adenosine efflux • Most effective for RA, considered as DOA for RA • C/I: Pregnancy
Sulfasalazine	• Prodrug. Active forms are: • Sulfapyridine → RA • 5-ASA → UC (Drugs identified by -sala-) • Other drugs for UC: o Mesalazine o Olsalazine
Penicillamine: Gold	• Penicillamine: Copper chelator • Gold compounds and Leflunomide (100 mg) • S/E:Nephrotoxic

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Leflunomide (100 mg)	• Inhibit pyrimidine synthesis via inhibiting DHOD (Dihydro orotate dehydrogenase)
Chloroquine or Hydroxy CQ	• Immunosuppression → ↓ IL-6, ↓ IL-1, ↓ TNF-alpha • Safest in pregnancy

Q6.4: What are the features of newer DMARDs used for RA?

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Answer

Target	New DMARDS for RA
Anti-TNF-alpha	• Infliximab • Certolizumab • Adalimumab • Golimumab • Etanercept
Anti-IL-6	• Tocilizumab • Sarilumab
Anti-CD-20	• Rituximab
Anti-IL-1	• Anakinra
Recombinant CTLA4	• Abatacept
JAK1, 3 inhibitor JAK1, 2 inhibitor JAK 1 inhibitor	• Tofacitinib • Baricitinib • Upadacitinib

Q6.5: What are the routes of administration and key precautions to be taken for selected biological DMARDs

Answer

I/V: Infliximab	S/C
• Use: RUPA (RA, UC/CD, Psoriatic arthritis, ankylosing spondylitis) • Used in methotrexate-resistant cases • S/E: Reactivation of latent TB, so the Mantoux test is done before administration	• Certolizumab • Adalimumab • Golimumab • Etanercept

Q6.6: What are the uses of Tofacitinib?

Answer

Recently, Tofacitinib was approved for

- RA
- UC/CD

5. CARDIOVASCULAR SYSTEM

BIG QUESTION 1: What is the classification , mechanism of action, uses and adverse effects of diuretics?

Broad Answer: Diuretics are drugs that promote sodium and water excretion by acting at different sites of the nephron. They are classified as:

- Carbonic Anhydrase Inhibitors (e.g., Acetazolamide) → act at PCT, cause HCO_3^- loss.
- Osmotic Diuretics (e.g., Mannitol) → increase plasma osmolarity, reduce ICP/IOP.
- Loop Diuretics (e.g., Furosemide) → act on the thick ascending limb, inhibit $Na^+K^+2Cl^-$, cause loss of all ions.
- Thiazides (e.g., HCTZ) → act on DCT, inhibit Na^+Cl^- symporter, retain calcium, used in HTN and nephrolithiasis.
- Potassium-Sparing Diuretics (e.g., Spironolactone, Amiloride) → act on the collecting duct, retain K^+, used in hyperaldosteronism and heart failure. Choice of diuretic depends on clinical condition: Loop in oedema, Thiazide in mild HTN, Spironolactone in liver failure, Mannitol in cerebral oedema.

DETAILED QUESTIONS

Q1.1 Describe Carbonic anhydrase inhibitors

Answer:

- **MOA**
  - Act at PCT of nephron
  - Inhibits carbonic anhydrase enzyme
  - Loss of sodium and bicarbonate in urine

PYQ: FMGE 2020

- Drugs are derivatives of sulphonamide
- Drugs are noncompetitive and reversible inhibitors of carbonic anhydrase enzyme
  - Acetazolamide
  - Methazolamide
  - Dichlorphenamide

Q1.2 What are the clinical uses and side effects of acetazolamide?

PYQ: FMGE 2019

Answer:

Uses (Mnemonic: GAME Plan)	Side effects of acetazolamide like drugs (Mnemonic: BASE)

• Glaucoma
• Alkalinization of urine
  o As they cause bicarbonate loss in urine
• Metabolic acidosis
  o Increased H^+ ions in blood
  o Stimulates respiratory centre
  o **DOC** for mountain sickness (Acetazolamide)
• Epilepsy treatment
• Plan: Familial periodic muscle paralysis
  o Occur due to electrolyte imbalance (potassium)
	• Bone marrow suppression (sulfa allergy)
	• Ammonia level in blood is increased
	  o Contraindicated: Liver diseases
	• Stones in the kidney: Calcium phosphate stone
	• Electrolyte imbalance
	  o Hyperchloremic + hypokalemic + metabolic acidosis

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Q1.3 What are the pharmacological properties of osmotic diuretics?

Answer:

- Act at the descending limb, loop, and the thick ascending limb of Henle
- Drugs
  - Mannitol I/V as 20% osmolar solution
  - Isosorbide
  - Glycerol
  - Urea

Q1.4: What are the pharmacological properties of mannitol?

Answer:

Increases plasma osmolarity (plasma volume expands)	• Decreases CSF production o Decreases intracranial pressure o Hence, mannitol is used in the treatment of cerebral edema • Decreases aqueous production o Decreases intraocular pressure o Used in acute glaucoma • Given during dialysis o To maintain plasma osmolarity o Called Dialysis Disequilibrium
Mannitol excrete metals in urine	• Hence used in the treatment of o Lithium toxicity o Cisplatin toxicity (anti-cancer drug)
Mannitol is contraindicated in	• Heart failure • Renal failure

Q1.5 What are loop diuretics and their mechanism of action?

Answer:

- Acts on the thick ascending limb of Henle in the medullary portion of nephron
- Inhibits Na+K+2Cl- transporter in medullary portion of the thick ascending limb
- Drugs are

PYQ: INICET 2019

Mercury containing

Mersaryl
Highly ototoxic
Lead to permanent deafness

Phenoxy-acetic acid

Ethacrynic acid

Sulfa containing

Furosemide

Torsemide
- Longest acting drug
- More potent than furosemide

Bumetanide
- Most potent drug
- Least dose enough

- Known as High-ceiling diuretics
  - DOC for edema

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Q1.6 What are the mechanisms of action and uses of Thiazide diuretics?

PYQ: NEET PG 2020
PYQ: INICET 2021
PYQ: FMGE 2023

Answer:

- Act at the cortical portion of the thick ascending limb and inhibit Na+Cl- symporter
- Drugs are

Thiazides	• Chlorothiazide • Hydro-chlorothiazide
Thiazide like	• Chlorthalidone - Longest acting drug • Metolazone - Safe in renal failure (GFR: 15-30 ml/min) • Indapamide - Most potent drug

- DOC: hypertension
  - Not effective in severe hypertension (BP > 160/100)
  - Then loop diuretics are given
- Used in the treatment of hypercalciuria
  - Calcium renal stones
- Used to treat diabetes insipidus
  - Due to the antidiuretic effect

Q1.7 Compare the adverse effects of Loop vs Thiazide diuretics

Answer:

- Have the same side effects except calcium
  - Loop loses all ions in urine, causing
    - → Hyponatremia
    - → Hypokalemia
    - → Hypomagnesemia
    - → Hypocalcemia
- Thiazide also loses all ions except calcium
  - Preserve calcium in the blood
- Cause hyperglycemia
  - Hence, loop and thiazide diuretics are bad for diabetes mellitus
- Increases blood lipid level
  - Hence bad for hyperlipidemia patients
- Increases uric acid level
  - Contraindicated in gout

Diuretics	Blood Calcium	Uses
Loop diuretics	Hypocalcemia	Treatment of Hypercalcemia in blood
Thiazide diuretics	Hypercalcemia	Treatment of hypercalciuria (Calcium-containing renal stones)

Q1.8 How are potassium-sparing diuretics classified?

Answer:

Classification: Potassium-sparing diuretics are divided into two classes based on their mechanism of action:

- **Aldosterone receptor antagonists:**
  - Spironolactone
  - Eplerenone

- **Epithelial sodium channel (ENaC) inhibitors:**
  - Amiloride
  - Triamterene

Q1.9: What is the site and mechanism of action of potassium sparing diuretics

Answer:

- These drugs act on the collecting duct of the nephron.
- They block sodium reabsorption and potassium excretion by:
  - Spironolactone and Eplerenone → Inhibit aldosterone receptors from the basolateral side.
  - Amiloride and Triamterene → Block ENaC channels from the luminal side.
    → Active form of spironolactone - Canrenone
- All diuretics act from the luminal side of the nephron
- Only Spironolactone and Eplerenone act from the basolateral side of the nephron

Q1.10: What are the clinical uses and side effects of potassium sparing diuretics?

Answer:

Clinical Uses:

- Spironolactone is the drug of choice (DOC) for:
  - Primary hyperaldosteronism (Conn's syndrome).
  - Secondary hyperaldosteronism in liver cirrhosis (CLD) and congestive heart failure (CHF).
- Amiloride is used in:
  - Liddle syndrome (ENaC channel defect).
  - Lithium-induced nephrogenic diabetes insipidus.
- Finerenone, a newer drug, is approved for diabetic nephropathy.
- Spironolactone also blocks androgen (testosterone) receptors:
  - Can cause gynecomastia in males.
  - Used to treat hirsutism and PCOS in females.
- Triamterene may cause folic acid deficiency and renal stones.
- These diuretics spare potassium, making them useful in patients prone to hypokalemia.

Q1.11 What are the diuretics of choice in edema?

Answer:

Heart failure	• Pulmonary edema • Pedal edema • DOC: loop diuretic • Mannitol is contraindicated
Renal failure	• Periorbital edema (due to a decrease in albumin level) • **DOC:** loop diuretic • Mannitol is contraindicated
Liver failure	• Ascites • DOC: Spironolactone • Acetazolamide is contraindicated o As it increases ammonia levels

Cerebral edema	• Cerebral edema
	  o Due to increased intracerebral pressure
	  o DOC: Mannitol

Q1.12 How do different diuretics affect serum, Na+, K+, H+ levels, and what acid-base imbalance do they cause?

Answer:

Diuretic	Blood Na^+	K^+	H^+
Carbonic anhydrase inhibitors (Low ceiling diuretics)	Decreases	Decreases (hypokalemia)	Increases (Metabolic acidosis)
Loop diuretics (High ceiling diuretics)	Decreases (maximum)	Decreases (hypokalemia)	Decreases (Metabolic alkalosis)
Thiazides diuretics (Medium ceiling diuretics)	Decreases	Decreases (hypokalemia)	Decreases (Metabolic alkalosis)
K+ sparing diuretics (Low ceiling diuretics)	Decreases	Increases (Hyperkalemia)	Increases (Metabolic acidosis)

Q1.13 How is nocturnal enuresis managed?

Answer:

- Child requires treatment if age > 6 years
- 1st treatment: train the child
  - o Alarm method
    - → When the child is about to pass urine, the alarm rings
    - → That wakes up the child
- 2nd treatment: drugs
  - o Desmopressin
    - → Decreases urine volume
    - → Nasal spray or oral drug
    - → Drug of choice
  - o Oxybutynin
    - → Anticholinergics drug
    - → Relaxes bladder
  - o Imipramine
    - → Tricyclics antidepressants
    - → Have an anticholinergic effect

Q1.14 Differentiate Nephrogenic and Neurogenic Diabetes Insipidus

Answer:

Neurogenic Diabetes Insipidus	Nephrogenic Diabetes Insipidus
• Brain does not produce ADH • ADH deficiency occur • DOC: Desmopressin o Carbamazepine - antiepileptic drug o Chlorpropamide - diabetic mellitus drugs o These drugs increase ADH production	• ADH is present, but kidney receptors are not responding • Receptors are resistant to ADH hormone • DOC: Thiazide diuretics + NSAIDS (indomethacin) o Contraindicated in lithium-induced nephrogenic DI : Amiloride (DOC)

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Q1.15: What are the drugs responsible for development of SIADH and diabetes insipidus?

Drugs Causing SIADH (Mnemonic: CVS)	Drugs Causing Diabetes Insipidus (Mnemonic: LAP Dog)
Carbamazepine Chlorpropamide Vincristine SSRI (fluoxetine)	Lithium Alcohol - decreases the secretion of ADH from the brain Phenytoin Demeclocycline

Q1.16: What is vasopressin?

Answer:

- AKAADH (antidiuretic hormone)
- Vasopressin agonist

Natural	Synthetic Hormone
• Arginine vasopressin o Human form • Lysine vasopressin o Swine form o Longer acting • Given as i/v • Increase BP • T/t: resistant shock to epinephrine and norepinephrine	• Terlipressin o V-1 agonist (vasoconstriction) o DOC: bleeding esophageal varices o DOC: Hepatorenal syndrome • To increase blood supply to the kidney • Desmopressin o V-2 agonist o Increases synthesis of clotting factor A o T/t: Haemophilia (A) o DOC: neurogenic diabetes insipidus o DOC: nocturnal enuresis o Can be given orally and as a nasal spray

Q1.17: What are vasopressin antagonists?

Answer:

- These drugs are given for
  - o T/t: chronic SIADH
    - → To treat hyponatremia
    - → But in acute hyponatremia - Hypertonic saline is given
- Conivaptan
  - o Blocks both V1 and V2 receptors
- Tolvaptan - V2 blocker
- Lixivaptan - V2 blocker
- Mozavaptan - V2 blocker
- Demeclocycline - Antibiotic (V2 blocker)

BIG QUESTION 2: What are RAAS inhibitors? Describe their types, mechanism of action, therapeutic uses, and adverse effects?

Broad Answer:

- RAAS inhibitors are drugs that block the Renin-Angiotensin-Aldosterone System, which plays a key role in

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regulating blood pressure and fluid balance. They include ACE inhibitors, ARBs, direct renin inhibitors, and aldosterone antagonists, and are commonly used in hypertension, heart failure, and chronic kidney disease. These agents help reduce vasoconstriction, sodium retention, and cardiac remodeling.

DETAILED QUESTIONS

Q2.1: What is aliskiren? Describe its mechanism of action.

Answer:

- Angiotensinogen converted to angiotensin I by renin
- Aliskiren inhibits renin in the blood

Q2.2: What are ACE inhibitors? Explain their mechanism of action, therapeutic uses, and common side effects.

Answer:

Angiotensin I converted to angiotensin II by ACE	• ACE inhibitors inhibit this step • Used in the treatment of hypertension • ACE-Inhibitors are Pro-drugs. Not prodrugs are o Captopril o Lisinopril • IV drug - enalapril o Used in the treatment of hypertensive emergency • Inhibiting ACE enzyme- increases the level of bradykinin cause allergic reactions • Like dry cough • Angioedema  Angioedema

Q2.3: What are ARBs? What are their mechanism of action, clinical applications, and major adverse effects?

Answer:

Angiotensin II increases blood pressure and hence acts on AT 1 receptor	• Angiotensin II increases blood pressure and hence acts on AT 1 receptor o That causes aldosterone secretion o ARBs block it o Used in the treatment of hypertension o Losartan → Have uricosuric effect → Used in gout treatment → Have anti-platelet effect (blocks thromboxane A2) o Telmisartan → PPAR Gamma agonist property → Only drug that is renal safe → Because it gets excreted in bile PYQ: NEET PG 2020 PYQ: NEET PG 2023 PYQ: AIIMS 2019

Q2.4: What are the adverse effects of ACE inhibitors and ARBs?

Answer:

Adverse Effects:

- **Hyperkalemia** → avoid with K^+-sparing diuretics:
  - o Spironolactone, Eplerenone, Amiloride, Triamterene
- Contraindicated in pregnancy: Category X → renal agenesis

- Avoid in bilateral renal artery stenosis (↑ risk of renal failure)

Q2.5: What investigations are done before starting ACEi and ARBs?

Answer:

- **Urine pregnancy** test
- Renal Doppler

Q2.6: What is a specific adverse effect of ARBs (Sartans)?

Answer: **SPRUE (diar**rhea) by blocking gut angiotensin receptors

BIG QUESTION 3: What are calcium channel blockers? Describe their classification, mechanism, uses, and side effects.

Broad Answer: Calcium Channel Blockers (CCBs) are drugs that inhibit L-type calcium channels, reducing calcium influx into cardiac and smooth muscle cells. They are mainly used to treat hypertension, angina, and certain arrhythmias by causing vasodilation and decreasing cardiac workload.

DETAILED QUESTIONS

Q3.1: What is the mechanism of action of CCBs?

Answer: Calcium Channel Blockers: Blocks L type of calcium channels on muscles

Q3.2: What are the types of CCBs, and what are their features?

PYQ: INICET 2020,2022

	Non -DHP type		DHP type
Drugs	Verapamil	Diltiazem	Amlodipine, Nifedipine, Nicardipine, Nimodipine, Clevidipine
Action	Heart >> blood vessels	Heart = blood vessels	Only blood vessels
	Inhibits SA node - bradycardia Inhibits AV node - AV node block	Inhibits SA node - bradycardia Inhibits AV node - AV node block	Artery dilator
Combined	Beta-blockers not combined	Beta-blockers not combined	It can be combined with beta-blockers

Q3.3 Why should verapamil not be given with beta-blockers?

Answer: Verapamil inhibits the SA and AV nodes, reducing heart rate and conduction. When combined with beta-blockers, which also depress cardiac function, there's a high risk of severe bradycardia and AV block. This combination is therefore contraindicated.

Q3.4: What are the indications of CCBs?

Answer:

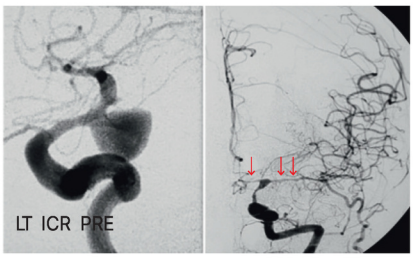
- **Verapamil:** Treatment of - supra ventricular tachyarrhythmias (arrhythmias) > angina SVT
- **Diltiazem:** Treatment: angina > SVT
- DHP type of calcium channel blockers: Treatment of angina
  - Contraindicated in SVT
  - S/E: Reflex tachycardia due to artery dilatation

Q3.5 Discuss the pharmacological features and clinical uses of commonly used DHP calcium channel blockers.

Answer:

Nifedipine	• Short-acting drug • Cause maximum reflex tachycardia • So combined with beta-blockers
Amlodipine	• Longest-acting oral drug • DOC: hypertension
Nimodipine	• Can cross BBB PYQ: FMGE 2020 • DOC: cerebral vasospasm after 3 days of SAH
Nitrendipine	• Increases nitric oxide synthesis
Nicardipine	• Longest-acting IV drug • DOC: hypertensive emergency
Clevidipine	• Shortest-acting IV drug • Because they are metabolized by esterase enzyme in plasma

Q3.6: What is the diagnosis, and Which CCB is used in its treatment?



Answer:

- The image shows Subarachnoid Hemorrhage having cerebral vasospasm
- Nimodipine is used.

Q3.7: What are the side effects of CCBs?

Answer:

- Headache (Most common)
- Urinary retention
- GERD
- Tocolytic effect
- Constipation
- Cause ankle edema due to vasodilation

Q3.8: How is CCB toxicity managed?

Answer: Calcium gluconate is the antidote

BIG QUESTION 4: What are arterial vasodilators? Briefly describe their types, mechanism of action, uses, and adverse effects

Broad Answer: Arterial dilators are drugs that reduce systemic vascular resistance by directly relaxing arterial smooth muscle, thereby lowering blood pressure. They include nitric oxide (NO) donors like hydralazine and sodium nitroprusside, and potassium channel openers like minoxidil and diazoxide, which cause hyperpolarization and vasodilation.

DETAILED QUESTIONS

Q4.1: What is the mechanism of action of nitric oxide donors?

Answer:

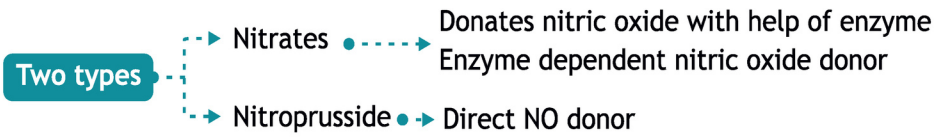
Nitric oxide goes inside smooth muscles

↓

Stimulates soluble guanylyl cyclase enzyme
↓
Increase cGMP
↓
Vasodilation

Q4.2: How are Nitric oxide donors grouped?

Answer:



Q4.3 What are the pharmacological properties and uses of nitrates?

Answer:

Nitrates

- Mechanism
  - Venodilator
  - MAD enzyme (mitochondrial aldehyde dehydrogenase)
- Tolerance
  - MAD enzyme stops working
  - Decrease in effect
  - Nitrate show tolerance
  - With time, the activity of enzymes reduces
  - Less amount of NO is produced
- Never combine with Phosphodiesterase 5 inhibitors
  - Sildenafil
  - Tadalafil
  - Due to massive increase in cGMP- hypotension and death

Q4.4: What are the features of nitroprusside?

Answer:

Nitroprusside

- Artery + vein dilator
- Donates NO without any enzyme
- No tolerance seen
- Stored in a black/amber-colored bottle
  - Because it gets degraded in the presence of light
- S/E: Cyanide poisoning

Q4.5 Write a short note on potassium channel openers

Answer:

- K+ efflux leads to hyperpolarization of muscle
  - Muscles become relaxed

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Minoxidil	• Used in males - alopecia PYQ: FMGE 2023 • Along with finasteride and dutasteride as a topical cream on the scalp • They are 5-alpha reductase inhibitors - inhibits the conversion of testosterone to dihydrotestosterone • Scalp cream: 2-5% concentrated
Diazoxide	• Opens potassium channel on beta cells of the pancreas • Leads to hyperpolarization of beta cells • Insulin is not secreted • So contraindicated in DM • Uses in the treatment of insulinoma
Hydralazine	• Potassium channel opener • Also, nitric oxide donor • Uses- treatment of o Hypertension o Heart failure • S/E - it's a SHIP drug (sulphonamide, hydralazine, isoniazid and propionamide) o These drugs undergo acetylation o Cause drug-induced lupus erythematosus (DLE)

BIG QUESTION 5: What are antihypertensive drugs? Classify them and what are their mechanisms, uses, and common side effects?

Broad Answer: Antihypertensives are drugs used to lower elevated blood pressure and reduce the risk of cardiovascular complications. They include various classes like diuretics, RAAS inhibitors (ACE inhibitors, ARBs, renin inhibitors), calcium channel blockers, beta-blockers, and vasodilators, each acting through different mechanisms

DETAILED QUESTIONS

Q5.1 What are the first-line drugs used in essential hypertension and their rationale?

Answer: Essential hypertension: No comorbidity except HTN

First-line drugs in essential HTN (BP >130/80 mmHg) include:

- CCBs (DHP types): effective vasodilators
- ACE inhibitors/ARBs: especially helpful in younger patients
- Thiazide diuretics: reduce sodium and volume load
- Mnemonic: CAT

Q5.2 What is resistant hypertension and how is it treated?

Answer: Resistant hypertension is when BP remains uncontrolled despite the use of 3 antihypertensives. The DOC in this case is an aldosterone antagonist like:

- Spironolactone
- Eplerenone

Q5.3 How does hypertension management vary in pregnancy?

Answer: Safe drugs for hypertension in pregnancy include:

- Labetalol - DOC

- Hydralazine
- Methyldopa - safest
- Nifedipine - for CCF
- ACE inhibitors/ARBs are contraindicated due to risk of renal agenesis in the fetus.

Q5.4 How do you manage a hypertensive crisis?

Answer:

In a hypertensive crisis (BP >180/120 mmHg):

- Urgency: No end-organ damage
- Emergency: End-organ damage present
- Drugs used (Mnemonic: Now Nobody CAN HELP):
- Nicardipine (DOC)
- Nitroprusside (IV)
- Clonidine (oral)
- Enalapril
- Nifedipine, Clevidipine
- Hydralazine, Esmolol, Labetalol, Loop diuretics, Phentolamine

Q5.5: Which drugs are not given in hypertensive crisis?

Answer: Thiazides diuretics

Q5.6: What are the uses of antihypertensive drugs in hypertension with comorbidities, and where are they contraindicated?

Answer:

ACE inhibitors/ARBs	• DOC for HTN with comorbidities like; o CKD, microalbuminuria, ESRD o Diabetes o Metabolic syndrome o Stroke o Retinopathy o Scleroderma • Avoided in; o Black ethnicity person o Pregnancy and bilateral afferent renal artery stenosis
CCB-DHP type	• DOC for HTN with comorbidities like; o Peripheral vascular disease o Renal artery stenosis o Atherosclerosis o Isolated systolic hypertension
Beta-blockers	• DOC for treatment of HTN with comorbidities like; o Stable angina o HOCM o Aortic dissection o Atrial fibrillation o Migraine o Hyperthyroidism • C/I - asthma o Verapamil and diltiazem are given instead of b blockers

Hypertension with Comorbidity	Drug of Choice
Benign prostate hypertrophy	Prazosin
Osteoporosis	Thiazides (increase bone mineral density)
Post-menstrual hot flushes	Clonidine
Hyperaldosteronism	Spironolactone
Pheochromocytoma	Phenoxybenzamine PYQ: FMGE 2023
Cheese reaction Clonidine sudden withdrawal	Phentolamine

Q5.7: Which antihypertensive drugs are contraindicated in certain comorbid conditions and why?

Answer:

Condition	Drugs Contraindicated
Gout	Thiazide/loop diuretic (losartan is used)
Hyperkalemia, Renal artery stenosis, Pregnancy, Angioneurotic edema	ACE inhibitors
Hyperkalemia Serum creatinine > 2.5 mg/dl	Spironolactone
Asthma/COPD	Beta-blockers
Bradycardia, AV node block	Beta blockers, verapamil and diltiazem

BIG QUESTION 6: Describe the pharmacological management of different types of angina and the rationale behind drug choices.

Broad Answer: Angina pectoris is chest pain caused by myocardial ischemia due to an imbalance between oxygen supply and demand. Anti-anginal drugs, such as nitrates, beta-blockers, calcium channel blockers, and newer agents like ranolazine, aim to restore this balance by reducing cardiac workload or improving oxygen delivery

DETAILED QUESTIONS

Q6.1 How are different types of angina managed?

Answer: Angina: Ischemic pain due to coronary artery blockage

Stable angina - classical angina/exertional angina	Unstable angina	Prinzmetal angina/vasospastic angina or variant angina
• Acute stable angina o S/L nitrates • Chronic stable angina o Beta-blockers • If angina is not controlled o Transdermal nitrates are used	• Part of acute coronary syndrome • Treated like MI	• Sudden spasm of coronary artery occurs • Acute angina o S/L nitrates → Glyceryl trinitrate (0.5 mg) → Isosorbide dinitrate (5 mg) • Chronic vasospastic angina o CCBs o Beta blockers are C/I → As they provoke vasospasm o If angina not controlled → Transdermal nitrates are used

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Q6.2 What are the first line drugs used in angina?

Answer:

First-line drugs:

- Nitrates: Venodilators → reduce preload
- Beta-blockers: ↓ HR and contractility
- CCBs: Vasodilators (DHP), ↓ HR (non-DHP)

Q6.3 What are the 2nd line drugs used in the management of angina?

Answer:

Second-line drugs:

- Nicorandil: K^+ channel opener
- Dipyridamole: Increase the amount of adenosine
- Ranolazine: Sodium channel blocker (↓ late Na^+ influx)
- Ivabradine: Blocks funny channels (↓ HR)
- Trimetazidine: pFOX inhibitor → shift metabolism to glucose
- Fasudil: Rho kinase inhibitor → coronary dilator

Q6.3: What are the drug interactions seen among 1st line anti-anginal drugs?

Answer:

- Beta-blockers with CCBs (Verapamil/Diltiazem)
  - Marked Bradycardia
  - Die suddenly
- Nitrates with PDE 3 inhibitors (Sildenafil, Tadalafil)
  - Marked hypotension, due to vasodilation
  - Die suddenly
  - Gap between Nitrates and Sildenafil is at least 24 hours
  - The gap between Nitrates and Tadalafil is at least 72 hours

Q6.4: What is the role of nitrates in the management of angina?

Answer:

- MOA: Venodilators
  - Reduce preload on heart
- Drugs
  - GTN (NTG) Glyceryl trinitrate
  - ISDN (Isosorbide dinitrate)
  - ISMN (Isosorbide mononitrate)
  - PETN
- All are organic drugs
- Highly lipid soluble
  - Non-ionic
- Given orally, undergoes first-pass metabolism in the liver
- To avoid this, NTG and ISDN are prepared. Sublingual
- ISMN is not degraded in the liver
  - 100% oral bioavailability
- Prodrug: ISDN

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  - Active: ISMN
- Shortest acting: GTN

Q6.6: What is the MOA and adverse effects of Dipyridamole?

Answer:

MOA:

- Coronary dilator
- Increase the amount of adenosine
- Efflux of adenosine cause coronary dilation in non-ischemic area

Adverse effects:

- Banned in Angina
- Cause coronary steal syndrome

Q6.7: What are the pharmacological properties of Ranolazine?

Answer:

- Sodium channel blocker
- Recently approved as the first-line drug for Chronic stable angina
- Side effects: QT prolongation (block potassium channel also)
- Has minor action of pFOX

Q6.8: What are the side effects of Ivabradine?

Answer: Bradycardia- Visual abnormality (Blocks funny channels on the retina)

Q6.9: What are the uses of Fasudil?

Answer:

- Rho kinase inhibitor
- Coronary dilator
- Treatment of Vasospastic angina

Q6.10: What are the pharmacological features of Trimetazidine?

Answer:

- pFOX (Partial Fatty acid oxidation) inhibitor
- Inhibit oxidation of fatty acid in the heart
- Heart shifts metabolism from fatty acid to carbohydrates
- Carbohydrates require less oxygen

Q6.11 What are the drugs causing coronary steal syndrome?

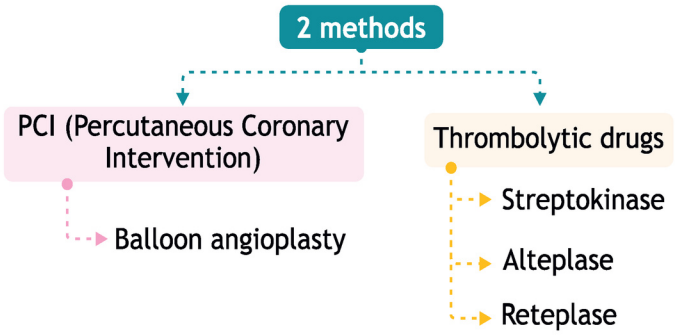
Answer:

- Never given in angina, (HIND Mnemonic):
  - Hydralazine
  - Isoflurane (General anaesthetic)
  - Nitroprusside
  - Dipyridamole

Q6.12 Write a short note on management of Acute coronary syndrome/MI.

Answer:

- Initial symptomatic treatment with (MONA Mnemonic:)
  - Morphine: chest pain relief
  - Oxygen
  - NTG, reduce preload
  - **DAPT** (Dual Antiplatelet Therapy) Aspirin (325 mg) + other antiplatelet
    - → Clopidogrel
    - → Ticagrelor
    - → Prasugrel
- Statins, anti-atherosclerotic action
  - Atorvastatin, 80mg
  - Rosuvastatin, 40 mg
- Definitive treatment, Reperfusion therapy
  - Opening of the coronary artery to maintain blood perfusion again
  - Within 12 hours
- In Unstable angina, NSTEMI streptokinase is contraindicated



Unstable angina	NSTEMI	STEMI
PCI	PCI	Thrombolytic drugs → PCI

BIG QUESTION 7: Discuss the complete pharmacological management of Chronic Heart Failure (CHF), period.

Broad Answer:

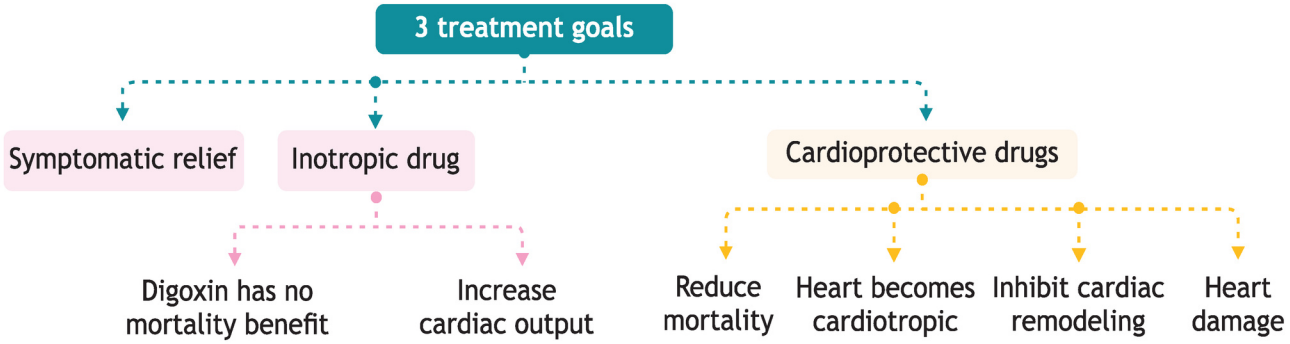
Management of CHF includes:

- Cardioprotective drugs (reduce mortality): ARNI (Sacubitril + Valsartan), ACE inhibitors, ARBs, aldosterone antagonists (spironolactone, eplerenone), ß-blockers (New BMC), SGLT-2 inhibitors (-flozins), hydralazine, and ivabradine.
- Symptomatic relief: Loop diuretics > thiazides (for pulmonary congestion), venodilators (nitrates), and combined vasodilators like nitroprusside, nesiritide.
- Inotropic support: Dobutamine, milrinone, levosimendan, digoxin, etc. used in decompensated heart failure. Verapamil and diltiazem are contraindicated as they increase mortality in CHF.

DETAILED QUESTIONS

Q7.1 What are the treatment goals in CHF?

Answer: CHF is characterized by heart damage and gradual decrease in cardiac output.



Q7.2 What are the cardioprotective drugs used in CHF and how do they reduce mortality?

Answer: Cardioprotective drugs improve survival by preventing remodeling and neurohormonal activation. These include:

- ARNI (Sacubitril + Valsartan): Sacubitril inhibits neprilysin → ↑ natriuretic peptides → vasodilation; Valsartan blocks AT1 receptors.
- ACE inhibitors / ARBs: Inhibit RAAS → ↓ preload, afterload & cardiac remodeling (1st drug of choice for CHF)
- Aldosterone blockers: Spironolactone, Eplerenone
- Beta-blockers (New BMC): Nebivolol, Bisoprolol, Metoprolol succinate, Carvedilol → ↓ sympathetic stimulation.
- SGLT-2 inhibitors (-flozins): Empagliflozin, Dapagliflozin, Canagliflozin → osmotic diuresis, ↓ hospitalization.
  - Treatment of Diabetes mellitus also
- Hydralazine
- Ivabradine: Slows heart rate by blocking SA node funny channels. PYQ: FMGE 2023
  - Used in angina
  - Cardioprotective effect
- Verapamil/ Diltiazem do not have cardioprotective effect and increase mortality - Contraindicated

Q7.3 What drugs produce symptomatic relief in patients with CHF?

Answer:

Symptom relieving drugs:

PYQ: INICET 2022

Artery dilator	• Increased afterload → Artery constriction → Hypertension • To treat: CCN-DHP (Calcium channel blocker DHP type) is given o Amlodipine
Veins dilator	• Venodilators reduce preload • Increase in preload in CHF causes pulmonary edema • Treatment: Loop > Thiazide diuretics, Nitrates • Contraindications: Mannitol o Increase preload, worsens edema

Combined dilators	• Treat both hypertension and edema
	• Drugs
	  o Nitroprusside
	  o Natriuretic peptides
	  → Vasodilatory actions
	  o Nesiritide: Recombinant form of brain Natriuretic peptides

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Q7.4: What are natriuretic peptides, and what is their role in CHF?

Answer:

Important Information

Natriuretic Peptides

- Nesiritide
  - o Injection
- Natriuretic peptides are good for CHF
- They are degraded by Neprilysin enzyme
  - o AKA: Neutral Endo Peptidase (NEP) enzyme
- Endogenous Natriuretic peptides are increased by inhibiting Neprilysin
  - o Neprilysin/NEP inhibitor
    - → Sacubitril
      - Approved drug
  - o Neprilysin inhibitor + ACE inhibitor
    - → Dual drug
    - → Omapatrilat
      - Under trial

Q7.5: What are inotropic drugs?

Answer:

Inotropic agents:

- Increase myocardial contractility, force of contractions and cardiac output
- Given treatment of decompensated heart failure
- Drugs
  - o Beta-1 agonist
  - o Intravenous injection

Stimulating Beta 1 stimulates cyclic AMP
↓
Opens calcium channel
↓
Calcium binds to troponin C
↓
Myosin activation
↓
Myosin binds to actin
↓
Increases the force of contraction

Examples

- Dobutamine (β1 agonist): DOC in ADHF.

Q7.6: What are the other inotropic drugs?

Answer:

- Norepinephrine: For ADHF + hypotension (acts on α and β).
  - o DOC: Cardiogenic shock

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- Increases blood pressure
- Milrinone, Inamrinone: PDE-3 inhibitors → ↑ cAMP.
- DOC: ADHF due to Beta blocker overdose
- Levosimendan: PDE-3 inhibitor + calcium sensitizer + K^+ channel opener.
  - Increases binding of calcium to troponin C
  - Intravenous injection
- Omecamtiv: Myosin activator (↑ contractility), intravenous injection
- Digoxin: Na^+/K^+ ATPase inhibitor; only oral inotrope, used in CHF

BIG QUESTION 8: Explain the pharmacological actions, clinical uses, and toxic effects of Digoxin.

Broad Answer: Digoxin is a positive inotropic drug that increases the force of cardiac contraction and improves cardiac output by inhibiting the Na^+/K^+-ATPase pump in myocardial cells. It also exhibits vagomimetic effects—negative chronotropic and dromotropic actions—by inhibiting the SA and AV nodes, making it useful in supraventricular tachyarrhythmias like atrial fibrillation and flutter. However, digoxin has a narrow therapeutic index and toxicity can cause arrhythmias, notably ventricular premature beats and potentially fatal ventricular fibrillation. Digoxin toxicity is managed with Digibind (Fab fragment antibodies). It's contraindicated in hypokalemia, hypomagnesemia, HOCM, and WPW syndrome.

DETAILED QUESTIONS

Q8.1 What is the mechanism of action of Digoxin?

Answer:

- Inhibits Na^+/K^+-ATPase → ↑ intracellular Na^+ → ↑ Ca^{2+} via Na^+/Ca^{2+} exchange → ↑ myocardial contractility (positive inotropy)
  - Increase cardiac output

Q8.2 What are the vagomimetic effects of Digoxin?

Answer:

- Negative chronotropy: ↓ SA node activity
- Negative dromotropy: ↓ AV node conduction
  - Used in atrial fibrillation/flutter.

Q8.3 What are the most common and most fatal arrhythmias seen with Digoxin toxicity?

Answer:

- Most common: Ventricular premature beats (bigeminy) - AKA ventricular extrasystole
- Most fatal: Ventricular fibrillation
  - Patient undergoes hypotension and sudden death
- Never causes: Atrial flutter → Digoxin converts Atrial flutter → Atrial fibrillation

Q8.4 What is the treatment for Digoxin-induced ventricular arrhythmia?

Answer: Lignocaine > Phenytoin (Class IB antiarrhythmics)

Q8.5 What is the therapeutic and toxic range of Digoxin?

Answer: Blood levels of digoxin should be monitored continuously

- Therapeutic range: 0.5-2.0 ng/mL; Toxicity: >2.0 ng/mL

- Antidote: Digibind aka Digifab (Antibody against digoxin- FAB fragment antibody against digoxin)
- No role of Hemodialysis

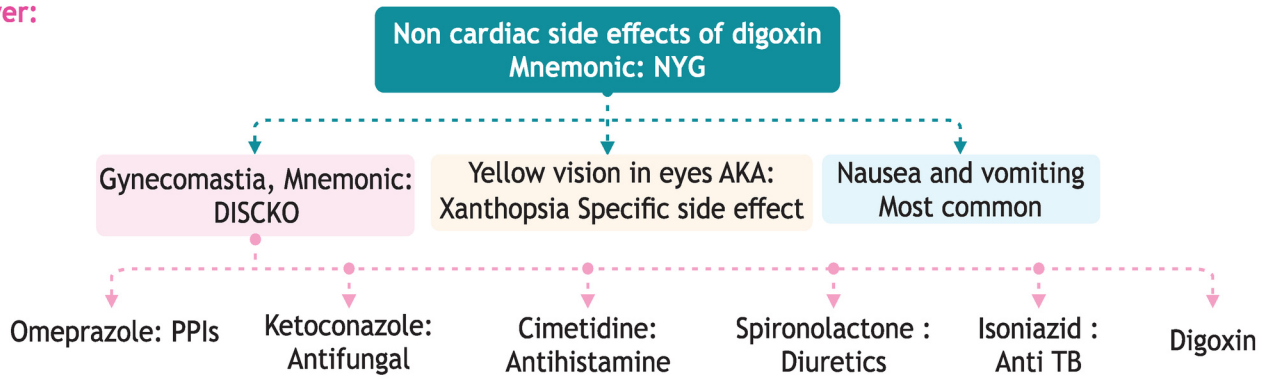
Q8.6 In which conditions is Digoxin contraindicated?

Answer:

- Electrolyte imbalance
  - o Hypokalemia, Hypomagnesemia
  - o Caused by loop/thiazides
    - → Increases digoxin toxicity
- WPW syndrome (↑ conduction via accessory pathway)
  - o Abnormal conductive pathway between atria and ventricle
    - → **Bundle of Kent**
  - o Digoxin blocks AV node
    - → Normal conduction pathway
    - → Conduction from abnormal pathway increases
  - o Treatment:
    - → Radiofrequency ablation of abnormal pathway
    - → Drugs indicated if
  - o Structural heart disease (MI)
    - → Procainamide
  - o No Structural heart diseases: Flecainide
- HOCM (↑ obstruction due to inotropy)
  - o Hypertrophy of the heart
    - → Inotropes increase obstruction
  - o Treatment: DOC: Beta-blocker
    - → Cardiac Suppressive drugs
- Negative inotropes
  - o In asthma patients: CCBs
    - → Verapamil/ Diltiazem
  - o New: Mavacamten
    - → Myosin inhibitor
    - → Inhibition of hypertrophy of the heart

Q8.7 What are non-cardiac side effects of digoxin?

Answer:



NOTE:

- Sildenafil causes blue-green color blindness
- Ethambutol (Anti TB) causes red-green color blindness

BIG QUESTION 9: What are the classes of antiarrhythmic drugs, and what are their mechanisms, uses, and adverse effects?

Broad Answer: Antiarrhythmic drugs are classified into five main classes based on the Vaughan-Williams classification. Class 1 drugs block sodium channels (further divided into 1a, 1b, 1c), Class 2 are beta-blockers, Class 3 block potassium channels, Class 4 block calcium channels, and Class 5 are miscellaneous. These drugs act on different phases of cardiac action potentials to correct arrhythmias. Common side effects include bradycardia, hypotension, QT prolongation, torsades de pointes, and specific toxicities (e.g., amiodarone ¤ pulmonary fibrosis, thyroid dysfunction).

DETAILED QUESTIONS

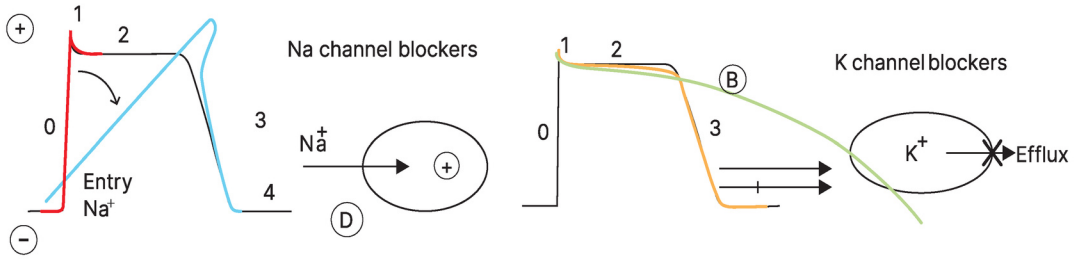
Q9.1 Classify anti-arrhythmic drugs

Answer:

- Classified by the William-Vaughan-Singh system into five classes:
  - Class I (Na^+ channel blockers): e.g., Quinidine, Lignocaine - act on depolarization
  - Class II (ß-blockers): e.g., Metoprolol - reduce SA/AV node activity
  - Class III (K^+ channel blockers): e.g., Amiodarone - prolong repolarization
  - Class IV (Ca^{2+} channel blockers): e.g., Verapamil - slow AV conduction
  - Class V (Misc): e.g., Adenosine, Digoxin - varied mechanisms

Q9.2 Explain the phases of the cardiac action potential and describe how Class I and Class III antiarrhythmic drugs affect the action potential?

Answer:



The cardiac action potential consists of five phases:

- Phase 0 (Depolarization): Rapid influx of Na^+ through voltage-gated Na^+ channels.
- Phase 1 (Initial repolarization): Slight efflux of K^+.
- Phase 2 (Plateau): Balance between Ca^{2+} influx and K^+ efflux.
- Phase 3 (Repolarization): Dominated by K^+ efflux restoring resting membrane potential.
- Phase 4 (Resting phase): Maintained by Na^+/K^+ ATPase.

Class I Antiarrhythmics (Na^+ Channel Blockers):

- Shown in the left diagram, these drugs block Phase 0, slowing the influx of sodium, and reduce the slope of depolarization.
- Class Ia drugs also block K^+ channels → prolong action potential duration.
- Class Ib drugs shorten action potential duration (Potassium channel opener)
- Class Ic drugs markedly slow Phase 0 without affecting repolarization (No effect on the potassium channel)

} Artery dilator

Class III Antiarrhythmics (K^+ Channel Blockers):

- Shown in the right diagram, these drugs block Phase 3 (K^+ efflux).
- This leads to prolongation of repolarization and action potential duration, which increases the effective refractory period.

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- Useful in preventing reentrant arrhythmias but may cause QT prolongation and torsades de pointes.

Clinical Implication:

- Class I drugs are used for ventricular or atrial tachyarrhythmias, depending on subclass.
- Class III drugs like Amiodarone and Sotalol are broad-spectrum antiarrhythmics.
  - o **NOTE:** All beta blockers are under class 2 except: Sotalol → Under class 3 (Additional potassium channel blocker property)

PYQ: NEET PG 2020,2023

Q9.3 Briefly describe Class 1 anti-arrhythmic agents

Answer:

	1a	1b	1c
Na channel	Block	Block	Block
Duration	Intermediate	Rapid	Slowest
K channel	Block	Open	No effect
Action potential Reduce phase 0 slope.	Increase APD (Action potential duration)	Reduce APD	No effect
Use	Atrial tachyarrhythmias • SVT • VT	Only VT	Atrial tachyarrhythmias • SVT • VT
Drugs	Mnemonic: QuPid • Quinidine • Procainamide • Disopyramide	Mnemonic: Leave-PMT • Lignocaine • Phenytoin • Mexiletine • Tocainide	Mnemonic: Famous Prime minister • Flecainide • Propafenone • Moricizine

Q9.4: What are the pharmacological properties, adverse effects of class I anti-arrhythmic agents?

Answer:

- Quinidine is metabolized by CYP2D6
  - o Causes hypoglycemia
  - o Given with 5% dextrose
- Procainamide
  - o Undergoes acetylation
  - o Side effects: DLE (Drug-induced SLE)
  - o Sulfa-containing drugs
    - → Cause Bone marrow suppression AKA: Agranulocytosis
- Disopyramide is an Atropine derivative
  - o Reduce all secretions in the body
    - → Dry eyes and mouth
- Lignocaine is an IV drug
  - o High first-pass metabolism in the liver
  - o Treatment: Ventricular tachycardia
  - o Side effects:

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→ Perioral numbness (Most common)
→ High dose: Seizure, Bradycardia

- Mexiletine is an oral prodrug of Lignocaine
  - Approved for treating diabetic neuropathy
- 1c agents are contraindicated in MI patients
  - Increase mortality

Q9.5 Name Class 2 drugs used as antiarrhythmics.

Answer: Propranolol, Metoprolol, Atenolol, Esmolol (All beta-blockers except Sotalol)

Q9.6 What is propranolol the DOC for?

Answer: Sympathetic tachycardia (hyperthyroidism, anxiety, fever)

Q9.7: What is the role of metoprolol and atenolol in the management of arrhythmias?

Answer:

- Metoprolol and atenolol block SA and AV node
  - To prevent VT

Q9.8 What is the DOC for intraoperative tachycardia?

Answer:

- Esmolol (shortest-acting β-blocker)

Q9.9 What is the antidote for beta-blocker-induced bradycardia?

Answer: Glucagon (Increases heart rate; causes tachycardia)

Q9.10 Which is the shortest-acting anti-arrhythmic drug?

Answer: Adenosine

Q9.11 Describe the pharmacology of Class III antiarrhythmic drugs.

Answer:

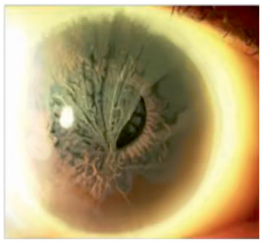
Drugs

- Pure potassium channel blockers
- Treatment of only SVT
  - Dofetilide
  - Ibutilide
- Multi-ion channel blocker
  - Block Na , Beta receptor, K , Ca2
  - Treatment of all types of Arrhythmias SVT/VT (Except in QT prolongation/Torsades de pointes)
    → Vernakalant
    → Amiodarone

PYQ: NEET PG 2020, 2023

1. Most effective anti-arrhythmic drug
2. Maximum reduction in mortality
3. DOC- VT after MI
4. Sotalol

Q9.12 What are the side effects of Amiodarone?





Purple Man Syndrome

- Amiodarone has 37% Iodine
  - Thyroid: Hypo > Hyperthyroidism
  - New: Dronedarone has no Iodine
- Cornea verticillate- AKA: Vortex keratopathy
- Liver cirrhosis
- Interstitial lung fibrosis
  - Hypoxia measured by (Diffusion Lung Capacity for Carbon monoxide) is reduced DLCO
- Purple man syndrome
  - Skin photosensitivity
  - AKA: Smurf syndrome

Q9.13 Differentiate between purple toe syndrome and purple glove syndrome

Answer:



Purple Toe



Purple Glove

- Purple toe syndrome is due to deposition of warfarin
  - Cholesterol embolisation
    - → Block blood vessels
- Purple glove syndrome is due to Phenytoin
  - Extravasate out of blood vessels

Q9.14 What are the features of class 4 anti-arrhythmic drugs?

Answer:

- Verapamil, Diltiazem given in SVT
- Contraindicated in VT
- Never combined with beta-blockers

Q9.15 What are the properties, MOA, and uses of class 5 drugs?

Answer:

Atropine	• DOC: Bradyarrhythmias
Digoxin: CHF with SVT	• Avoid beta blockers and CCBs in CHF
Adenosine	• DOC: Acute attack of PSVT (Paroxysmal Supra ventricular tachycardia) o Shortest-acting drug: 10 seconds PYQ: INICET 2021 o Given IV in the proximal vein (jugular vein) as fast bolus injection o Dose: 6-12-12 (30 mg max) o Side effects: Asthma
Magnesium sulphate	• DOC: Torsades de pointes • AKA: Long QT syndrome

Q9.16 Discuss the ECG of PSVT, VT, Torsades de Pointes

Answer:

PSVT



- If the arrhythmic patient is hemodynamically unstable, DC shock is given
- In PSVT, hemodynamically unstable treatment is
  - Vagal manoeuvres: Valsalva, Carotid massage, Eye massage
  - Block AV node
  - Drugs (Mnemonic: ABC)

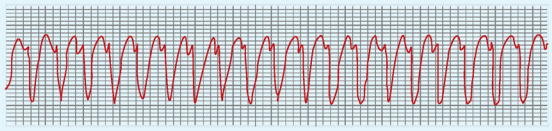
IV. Adenosine
- DOC for PSVT
- Contraindicated in asthma

Oral beta blockers
- Maintenance of PSVT/ any SVT
- Contraindicated in asthma

CCBs
- Verapamil/ Diltiazem
- Maintain PSVT in asthma

VT

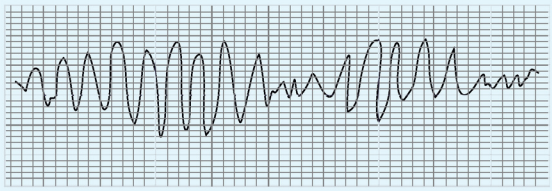
Monomorphic ventricular tachycardia



- Monomorphic ventricular tachycardia
- Hemodynamically unstable: DC shock
- DOC: Amiodarone
  - Sodium channel blocker
    - → Lignocaine
    - → Sotalol

PYQ: FMGE 2022

Torsades de pointes



- Polymorphic ventricular tachycardia
- Hemodynamically unstable: DC shock
- DOC: Magnesium sulphate

PYQ: FMGE 2021

PYQ: NEET PG 2022

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6. RESPIRATORY SYSTEM

BIG QUESTION 1: What is the pathophysiology and classification of asthma, and how is it managed in acute and chronic settings?

PYQ: FMGE 2021-22

Broad Answer: Asthma is a type 1 hypersensitivity reaction that leads to inflammation and bronchoconstriction of airways.

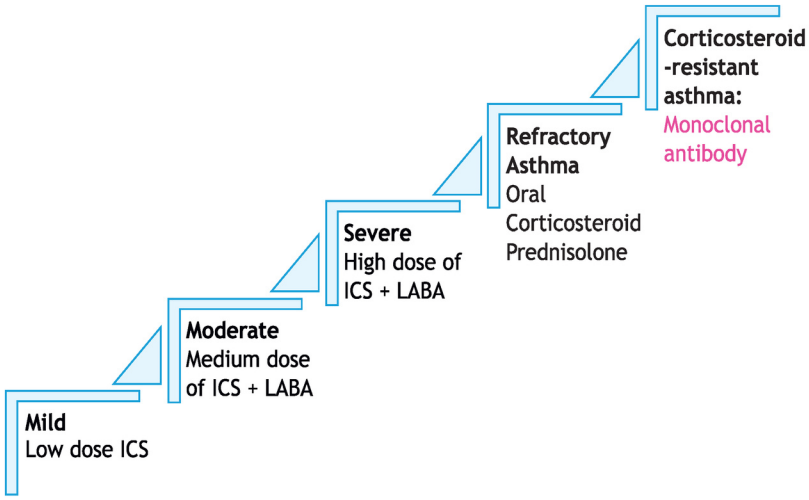
- In acute attacks, the first-line drug is formoterol, a β2 agonist, often combined with budesonide (an inhaled corticosteroid)
- For chronic asthma, the mainstay of treatment is inhaled corticosteroids (ICS), with step-up therapy depending on severity

PYQ: INICET 2020

DETAILED QUESTIONS

Q1.1: What is stepwise management strategy for asthma based on severity?

Answer:



Q1.2: What is the difference in drug types between acute and chronic asthma?

Answer:

Acute Asthma	Chronic or persistent Asthma
• Bronchodilators are given • Reliever therapy • Drugs o Beta (b) 2 agonists o Anticholinergics o Theophylline o Magnesium sulfate • Mnemonic: **BATMan**	• Anti Inflammatory drugs are given o Controller therapy o Drugs → Mast cell stabilizers → LOX inhibitors → Leukotriene receptor antagonist → Corticosteroids • Monoclonal Antibodies

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BIG QUESTION 2: What are the mechanisms of action and adverse effects of drugs used in asthma management?

Broad Answer: Asthma treatment includes bronchodilators, anti-inflammatory agents, and monoclonal antibodies targeting various receptors and pathways and hence, they may produce a variety of adverse effects

DETAILED QUESTIONS

Q2.1: What is the mechanism of action of ß2 agonists in the respiratory system, and how does phosphodiesterase-4 influence this pathway?

Answer:

- Mechanism of action of ß2 agonists:

Activates beta (β) 2 agonist on Bronchial muscles
↓
This is a Gs type G protein-coupled receptor.
↓
Activates **adenylyl cyclase**
↓
Increases **cAMP**
↓
Bronchodilation

- Phosphodiesterase 4 causes degradation of cAMP
- Phosphodiesterase 4 Inhibitor: Theophylline
- Additional action of Beta (β) 2 agonist: Increases mucus production

Q2.2: What are the classifications and examples of ß2 agonists?

Answer:

SABA	LABA	Ultra Laba
• Short-acting beta (b) 2 agonist • Given in acute Asthma • Drugs o Salbutamol (known as Albuterol) o Terbutaline (active form of Bambuterol)	• Long-acting beta (b) 2 agonist • Given in chronic Asthma • Works for 12 hrs • Drugs o Salmeterol o Bambuterol (prodrug)	• Given in chronic Asthma • Works for 24 hrs • Drugs o Indacaterol o Vilanterol o Clenbuterol → Got banned → Due to anabolic effect

Q2.3: Which drug can be used in both acute & chronic asthma?

Answer:

- Formoterol
  - o SABA + LABA action

Q2.4: What are the routes of administration for ß2 agonists, and which drugs are preferred for specific asthma conditions?

Answer:

- Inhalational

- Oral
- Subcutaneous (S/C): Terbutaline → DOC for brittle asthma type 1
- Intravenous (IV): Salmeterol

Q2.5: What are the side effects of β2 agonists?

Answer:

- Side Effects (Mnemonic: 3T 2H):
  - Tremors (most common)
  - Tachycardia
  - Tachyphylaxis
    - → Rapid loss of effect due to desensitization of β2 receptors
    - → To regain the activity, corticosteroids are added
  - Hypokalemia
  - Hyperglycemia

Q2.6: What are the MOA and route of administration of anti-cholinergic drugs for respiratory disorders?

Answer:

- MOA: Blocks M3 receptors of acetylcholine
- More effective in COPD > Asthma
- Route of administration: Inhalational

Q2.7: Which anticholinergic drugs are used in asthma and COPD, and how do their duration of action and specific uses differ?

Answer:

- **Ipratropium**
  - Shortest acting
  - Used in status asthmaticus
  - May cause paradoxical bronchoconstriction
- **Tiotropium**
  - Used in chronic COPD or asthma
- **Umeclidinium**
  - Used in chronic COPD or asthma
- **Aclidinium**
  - Longest acting
  - Used in chronic COPD or asthma

Q2.8: What are the common side effects of inhaled anticholinergic drugs used in respiratory conditions?

Answer:

- Dry eyes
- Dry mouth
- Decreased mucus production
- Constipation

Q2.9 : What are the natural sources of methylxanthines?

Answer:

- Natural methylxanthines are found in:
  - Tea
    - → Maximum Theophylline
    - → Bronchodilator in asthma and COPD
  - Coffee
    - → Maximum caffeine
    - → Treatment of migraine headache
  - Chocolate:
    - → Maximum theobromine
- Both tea and coffee can be given in apnea of newborn

Q2.10: What is the mechanism of action of Theophylline?

Answer:

- Mechanism:
  - PDE-4 inhibitor → ↑ cAMP → Bronchodilation
  - Adenosine receptor blocker

Q2.11: What are the key pharmacological properties of Theophylline?

Answer:

- Narrow therapeutic index drug
- Requires Therapeutic Drug Monitoring (TDM)
- **Therapeutic range:** 5 to 15 micrograms/mL
- **Toxicity:** Occurs at >15 micrograms/mL
- **Metabolized by:** CYP1A2 enzyme in the liver

Q2.12: What are the side effects of Theophylline?

Answer:

- Side Effects (Mnemonic: SUAGH):
  - Seizures (Adenosine A1 receptor blockade)
  - Urination (diuresis due to adenosine A1 receptor blockade)
  - Arrhythmia due to:
    - → Adenosine A1 receptor blockade
    - → PDE4 Inhibition
  - GIT upset (PDE4 Inhibition)
  - Headache (PDE4 Inhibition)

Q2.13: Name some specific PDE-4 inhibitors.

Answer:

- Roflumilast
- Cilomilast
- Ibudilast

Q2.14: What is the MOA and uses of Magnesium sulfate

Answer:

- Mechanism:
  - Blocks Ca^{2+} channels → Smooth muscle relaxation
- Uses (Mnemonic: TABLETS):
  - Torsades de pointes
  - Antacid (MgOH)
  - Barium and calcium poisoning
  - Laxative
  - Eclampsia
  - Tocolytic
  - Status asthmaticus

Q2.15: What is the earliest sign of $MgSO_4$ toxicity, and what is the antidote used?

Answer:

- The earliest sign of $MgSO_4$ toxicity
  - Loss of deep tendon reflexes, like the knee jerk
  - Also called the patellar effect
- Antidote: Calcium gluconate

Q 2.16: What is the earliest sign of magnesium toxicity and what is its antidote?

Answer:

- Loss of deep tendon reflexes (patellar effect)
- Antidote: Calcium gluconate

BIG QUESTION 3: What are the roles of anti-inflammatory and monoclonal antibody drugs in asthma?

Broad Answer: Anti-inflammatory and monoclonal therapies are essential for long-term control and refractory asthma

DETAILED QUESTIONS

Q3.1: Which drugs act as mast cell stabilizers, what are their routes of administration, and in which conditions are they used?

Answer:

- **Drugs:**
  - Nedocromil
  - Cromoglycate (Cromolyn)
- **Route:** Inhalational
- **Used in:**
  - Seasonal asthma
  - Exercise-induced asthma
  - **Note**: Inhaled corticosteroids (ICS) are the drug of choice (DOC)

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Q3.2: Which drug is a 5-lipoxygenase inhibitor, and what is its major side effect?

Answer:

- **Drug:** Zileuton
- **Major Side Effect:** High risk of hepatotoxicity

Q3.3: Which leukotriene receptor antagonists are used in asthma management, and what is a notable side effect?

Answer:

- **Drugs:** Montelukast, Zafirlukast, Pranlukast
- **Uses:**
  - Chronic asthma
  - Aspirin-induced asthma (AERD)
  - **Note:** Inhalational corticosteroids remain the DOC
- **Side Effect:** Churg-Strauss syndrome

Q3.4: What is the mechanism of action of corticosteroids and their route of administration?

Answer:

- Corticosteroids are broad spectrum anti-inflammatory drugs
- Mechanism of action: Inhibit phospholipase A2 enzyme
- Routes of administration:

PYQ: FMGE 2020

Inhalational route

- Beclomethasone
- Fluticasone
- Mometasone
- Triamcinolone
- Budesonide
- Ciclesonide

Oral route

- Prednisolone
- Used in refractory asthma

IV

- Hydrocortisone
- Used in Status asthmaticus
- 100 mg IV stat

Q3.5: What are the indications, advantages and side effects of inhalational corticosteroids (ICS)?

Answer:

- DOC for (Mnemonic: **CASE**):
  - Chronic asthma
  - Aspirin-induced asthma
  - Seasonal asthma
  - Exercise-induced asthma
- Advantages over oral steroids:
  - Safe in pregnancy
  - Less systemic side effects
  - Do not cause Cushing's syndrome or ACTH suppression
- Side Effects:
  - Oral candidiasis
    - → Prevention
      - Mouth gargle
      - Using plastic spacer

→ Localized candida: Nystatin paint
→ Widespread or esophageal candida: Oral fluconazole tablet

Q3.6: Which corticosteroid drug is least likely to cause oral thrush?

Answer: Ciclesonide (soft steroid)

Q3.7: What monoclonal antibodies are used in asthma and their targets?

Answer:

Drug	Target
Omalizumab	Blocks IgE on mast cells (S/C injection every 4 weeks)
Mepolizumab, Reslizumab	Block IL-5
Benralizumab	Blocks IL-5 receptor
Dupilumab	Blocks IL-4 receptor
Tezepelumab	Blocks TSLP (thymic stromal lymphopoietin)

BIG QUESTION 4: What are the pharmacological treatments for different types of cough, and how do their mechanisms and indications differ?

Broad Answer: Cough medications are classified into expectorants and antitussives, used based on whether the cough is productive (wet) or dry

- Expectorants are used to clear mucus in productive/infective cough
- Antitussives are used to suppress cough in dry cough but are contraindicated in productive cough

DETAILED QUESTIONS

Q4.1: What are expectorants, and how do they work?

Answer:

- Expectorants help in expelling mucus from the airways and are used in productive/infective cough
- Types:

Type	Mechanism	Drugs
Mucokinetics	↑ Ciliary movement to propel mucus	Guaifenesin
Mucolytics	Break disulfide bonds in mucus to liquefy it	Bromhexine, Ambroxol, N-acetylcysteine

Q4.2: What are antitussives and when should they be used or avoided?

Answer:

- Antitussives act by suppressing the cough centre in the CNS and are used in dry cough only
- They are avoided in infective or productive cough to prevent mucus retention

Q4.3: What are the types and examples of antitussive drugs?

Answer:

Drug Class	Examples	Mechanism	Addictive Potential
Non-opioid	Dextromethorphan	NMDA receptor blocker	Nonaddictive
Opioid	Morphine, Codeine	CNS suppression of cough reflex	Addictive
Others	Noscapine	Stimulates sigma receptors	Nonaddictive

BIG QUESTION 5: What are the pharmacological treatments for Cystic Fibrosis and Pulmonary Arterial Hypertension (PAH), and what are the mechanisms and key features of these drugs?

Broad Answer: Cystic Fibrosis (CF) and Pulmonary Arterial Hypertension (PAH) are treated using targeted therapies addressing their respective pathophysiological mechanisms

- Cystic Fibrosis is caused by a defect in the CFTR transporter, and is treated with CFTR potentiators like Ivacaftor, Lumacaftor, Tezacaftor, and Elexacaftor
- Pulmonary Arterial Hypertension (PAH) involves vasoconstriction of pulmonary arteries, leading to right heart failure. Treatment focuses on vasodilators such as PGI2 analogues, endothelin receptor antagonists, PDE-5 inhibitors, and other agents like Riociguat, Selexipag, and calcium channel blockers

DETAILED QUESTIONS

Q5.1: What is the underlying defect in Cystic Fibrosis, and how is it pharmacologically treated?

Answer:

- Defect: Mutation in CFTR (Cystic Fibrosis Transmembrane Conductance Regulator) transporter
- Treatment: Use of CFTR potentiators, which help restore or enhance CFTR function
  - Drugs include:
    - → Ivacaftor
    - → Lumacaftor
    - → Tezacaftor
    - → Elexacaftor

Q5.2: What is the pathophysiology of Pulmonary Arterial Hypertension (PAH), and how does it lead to right heart failure?

Answer:

- In PAH, there is vasoconstriction of the pulmonary arteries
- This increases pulmonary artery pressure, placing strain on the right side of the heart, eventually causing right heart failure

Q5.3: What are the drugs used in PAH?

Answer:

- Drugs (Mnemonic: **PEPSI COCA COLA**):
  - **P**GI analogues
  - **E**ndothelin receptor antagonists
  - **P**DE-5 inhibitors

- Soluble guanylyl cyclase activators
- Inhaled nitric oxide
- Calcium channel blockers
- Oral agents like Selexipag

Q5.4: What are the different classes of vasodilator drugs used in PAH?

Answer:

Drug Class	Examples	Route	Notes
PGI_2 analogues	Treprostinil Iloprost Epoprostenol	Not given orally	DOC for PAH
Endothelin receptor antagonists	Bosentan Macitentan Ambrisentan	Oral	Blocks endothelin receptor Contraindicated in pregnancy
PDE-5 inhibitors	Sildenafil Tadalafil	Oral	Sidenafil is also used in erectile dysfunction
Soluble guanylyl cyclase activators	Riociguat Vericiguat	Oral	Riociguat is used in PAH Vericiguat is used in CHF
PGI_2 receptor agonist	Selexipag	Oral	Mimics PGI2
Calcium channel blockers	Amlodipine Nifedipine	Oral	Used if PAH coexists with systemic HTN
Inhaled nitric oxide	–	Inhalational	Continuous inhalation therapy

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7. GIT

BIG QUESTION 1: What are the major drug classes and mechanisms for treating acid peptic diseases?

Broad Answer:

Drugs used in acid peptic disease either reduce acid secretion, neutralize existing acid, or protect the gastric mucosa. The main classes include acid suppressants (PPIs and H2 blockers), antacids, prostaglandin analogs, mucosal protective agents, and antibiotics against *H. pylori*.

DETAILED QUESTIONS

Q1.1: What are acid suppressants and how do they work?

Answer:

- Acid suppressants reduce HCl production from parietal cells and provide round-the-clock protection.

Q1.2: What are Proton Pump Inhibitors (PPIs) and key features?

Answer:

- Irreversible inhibitors of H^+/K^+ ATPase.
- End with -prazole.
- Drugs: Dexrabeprazole (most potent), Ilaprazole, Lansoprazole, Rabeprazole, Omeprazole, Pantoprazole (least potent).
- Dexlansoprazole: PPI taken with food.
- Metabolized by CYP2C19.
- Maximum CYP inhibition: Omeprazole; least: Rabeprazole/pantoprazole.
- Uses:
  - DOC for peptic ulcer disease (NSAID or H. pylori-induced).
  - DOC for GERD: PPI + prokinetic.
  - Aspiration pneumonia: PPI + prokinetic.
- Prodrugs with 2-5 hr half-life, 2-5 days action.
- Fastest acting: Omeprazole.
- Acid-labile; taken on an empty stomach.

Q1.3: What is the interaction between PPIs and clopidogrel?

PYQ: NEET PG 2023

Answer:

- Clopidogrel is a prodrug activated by CYP2C19.
- Omeprazole inhibits CYP2C19 → avoid with clopidogrel.
- Rabeprazole/pantoprazole preferred with clopidogrel.

Q1.4: What are the adverse effects and other types of PPIs?

Answer:

- Tenatoprazole - reversible.
- Revaprazan, Vonoprazan - block K^+ site of H^+K^+ ATPase.

Q1.5: How do H2 blockers work and what are their features?

PYQ: FMGE 2023

Answer:

- Decrease HCl; similar uses as PPI.
- Drugs:
  - Cimetidine: maximum CYP inhibition, causes gynecomastia, impotence, menstrual irregularities, galactorrhea.
  - Famotidine: non-competitive.
  - Nizatidine: no CYP effect.
  - Lafutidine: ↑ somatostatin →↓ gastric acid.
- Other: Ranitidine, Nizatidine.

Q1.6: What is Misoprostol and when is it used?

Answer:

- Prostaglandin E1 analog.
- Used when NSAIDs cause ulcers.
- PPI remains DOC.

Q1.7: What are antacids and how are they classified?

Answer:

- Basic salts that neutralize HCl for quick relief.
- Chronic suppression effects:
  - Fe deficiency (anemia), Ca deficiency (osteoporosis), Mg deficiency (hypomagnesemia), B12 deficiency (megaloblastic anemia).
  - Infections: CAP, C. difficile, SBP.
  - Other: Hypergastrinemia, gastric polyps, renal failure, Alzheimer's.

Type	Examples	Features
Systemic	Sodium bicarbonate	CO_2 production, ulcer perforation
	Sodium citrate	No CO_2, can cause HTN/heart disease
Calcium salts	Calcium carbonate	Can cause Milk Alkali Syndrome
Magnesium salts	Fast-acting	Diarrhea
Aluminum salts	Slow-acting	Constipation, reduces phosphate absorption
Combo (Mg+Al)		Synergism

Q1.8: What are mucosal protective agents like Sucralfate and Bismuth salts?

Answer:

- Sucralfate = Sucrose + aluminum sulfate.
  - Causes constipation/osteoporosis.
  - Avoid with antacids (pH >4): maintain gaps:

→ 30 min with antacids
→ 60 min with food
→ 120 min with phenytoin/ranitidine

- Bismuth:
  - Effective against H.pylori
  - Can cause black discoloration of tongue and feces.

Q1.9: How do ulcer protective drugs work?

Answer: Polymerize at pH <4 and cover ulcers.

Q1.10: What antibiotics are used against *H. pylori*?

Answer:

- Clarithromycin, Amoxicillin, Metronidazole, Tetracycline, Levofloxacin.
- At least 2 + PPI for 10-14 days.
- Regimens:
  - PCM: PPI + Clarithro + Metronidazole
  - PCA: PPI + Clarithro + Amoxicillin
  - PBMT (India): PPI + Bismuth + Metro + Tetra (due to clarithro resistance)

Q1.11: What are some miscellaneous drugs for acid peptic disorders?

Answer:

- Antifoaming: Alginic acid (GERD).
- Antiflatulence: Simethicone (bursts bubbles).

Q1.12: What is the efficacy comparison of acid suppressant drug classes?

Answer:

- Anti-Muscarinic (Block M1): Pirenzepine, Telenzepine
  Efficacy: 40-60%
- H2 Blockers: Cimetidine, Ranitidine
  Efficacy: 60-80%
- Proton Pump Inhibitors: Omeprazole, Pantoprazole
  Efficacy: 80-99%

BIG QUESTION 2: What are the major classes and mechanisms of drugs used for treating constipation and related disorders?

Broad Answer: Constipation is treated by increasing gastrointestinal motility, bulk, or fluid content in the colon. The main categories include bulk-forming agents, stimulant laxatives, osmotic laxatives, stool softeners, chloride and sodium secretors, and others including motilin agonists and disease-specific laxatives.

DETAILED QUESTIONS

Q2.1: What are bulk-forming laxatives and when are they used?

PYQ: FMGE 2023

Answer:

- Increase bulk → colon stretching → nerve stimulation → muscle contraction → defecation.

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- Examples: Psyllium (Metamucil), Ispaghula (Isabgol), Bran, Husk, Methylcellulose.
- DOC: Idiopathic constipation, IBS, pregnancy.
- Contraindications: Paralytic ileus (megacolon), spastic colon.

Q2.2: What are stimulant laxatives and when are they indicated?

Answer:

- Used to treat paralytic ileus or when bulk forming agents fail.
- Contraindicated in pregnancy.
- Drugs: Bisacodyl, Senna, Cascara, Prucalopride (5HT4 receptor agonist).

Q2.3: What are osmotic laxatives and their indications?

Answer:

- Increase luminal osmolarity to draw water.
- Indications: Constipation, colonoscopy prep.
- Types:
  - Saline purgatives: Sodium phosphate.
  - Sugars: Mannitol, urea.
  - Magnesium salts.
  - Polyethylene glycol.
  - Lactulose: Also used in hepatic encephalopathy.

Q2.4: What are stool softeners and when are they used?

Answer:

- Emulsify hard stool to reduce strain during defecation.
- Given in: Pregnancy, abdominal/GIT surgery, hernia, rectal prolapse.
- Drugs: Docusate (DOSS) in pregnancy, paraffin wax, mineral oil.

Q2.5: What are chloride and sodium secretors and how do they help?

PYQ: AIIMS 2019

Answer:

- Chloride secretors increase chloride secretion:
  - Lubiprostone (PGE1 analog).
  - Linaclotide and Plecanatide: Stimulate guanylyl cyclase.
- Sodium secretors:
  - Tenapanor: Inhibits Na^+/H^+ antiporter.

Q2.6: What are important adverse effects and special cases in constipation treatment?

Answer:

- Senna: Can cause melanosis coli (colon blackening).
- Antibiotic with laxative effect: Erythromycin (motilin receptor agonist).
- DOC in pregnancy: Bulk laxatives.
- DOC in liver disease: Lactulose.

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Q2.7: What drugs are used for dissolving gallstones?

Answer:

- Bile acids: Chenodeoxycholic acid, Ursodeoxycholic acid, Obeticholic acid.
- Obeticholic and ursodeoxycholic acid also used in primary biliary cirrhosis.

Q2.8: What are the drugs for short bowel syndrome?

PYQ: NEET PG 2024

Answer:

- Aim: Reduce malabsorption by increasing small intestinal cell growth.
- Drugs: Growth hormone, Octreotide, Teduglutide (GLP-2 analog).

8. ENDOCRINE SYSTEM

BIG QUESTION -1: What are the types, uses, administration routes, and side effects of insulin therapy in Diabetes Mellitus?

Broad Answer:

- Insulin is the drug of choice for Type 1 Diabetes Mellitus and Gestational Diabetes. Acarbose & pramlintide are approved add-on drugs.
- In Type 2 DM, metformin is the drug of choice. If not controlled, all other OHAs & insulin can be given.
- In Gestational Diabetes, insulin is the drug of choice. Metformin & glyburide are approved add-on drugs.
- Insulins are classified into:
  - Oral:

Drugs For Type -1 DM	• (Beta (β) cell destruction: No insulin) PYQ: FMGE 2021 • Insulin (DOC), • Acarbose and Pramlintide are approved addon drugs
Drugs For Type - 2 DM (Peripheral resistance to Insulin)	• DOC: Metformin • Add: All other OHAs and Insulin if not controlled
Gestational DM (Pregnancy)	• DOC: Insulin • Metformin and Glyburide are approved addon drugs

  - Injectable insulin:

Ultrashort (Rapid)- 3 hrs	• LISPRO • ASPART • GLULISINE • Bolus insulin • Before meals to control PPH	
Short: REGULAR- 6 hrs	• Bolus insulin • Before meals to control PPH • Basal insulin	

Intermediate- 12 to 18 hrs	• LENTE INSULIN
	  o Amorphous + Crystalline
	  o 30:70
	  o Basal insulin
	• NPH (Neutral Protamine Hagedorn)
	  o Basal insulin
		

Long- 18 hrs	• Detemir • Glargine (24 hrs) • Basal insulin	
Ultralong	• Degludec(42 hrs) - Longest acting	

DETAILED QUESTIONS

Q1.1: Which insulin is the DOC for Diabetic Ketoacidosis (DKA)?

Answer: Regular insulin (IV route)

Q1.2: Which insulins have the least risk of hypoglycaemia?

Answer:

- Glargine & Degludec
  - Peak less insulin
  - Least risk of hypoglycaemia
  - Never mix with other insulins in the same injection

Q1.3: Name the bolus insulins and their timing of administration.

Answer:

- Bolus insulins are ultra-short-acting insulins given before meals to control postprandial hyperglycemia (PPH)
- They include:
  - Lispro
  - Aspart
  - Glulisine
- Regular insulin can also be given as bolus insulin

Q1.4: What are the approved add-on drugs in Type 1 DM?

Answer:

- Acarbose
- Pramlintide

Q1.5: What are the features and contraindications of nasal insulin (Afrezza)?

Answer:

- Dry powder inhalation
- Shortest-acting bolus insulin
- Must be combined with long-acting injectable insulin
- **Contraindicated in:**
  - Smokers
  - COPD
  - Asthma
- Associated with the risk of lung cancer

Q1.6: What are the adverse effects of insulin therapy?

Answer:

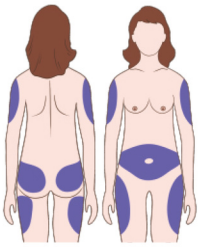
- Hypoglycemia
- Lipodystrophy at subcutaneous fat sites
- Weight gain



Q1.7: What are the common insulin injection sites, and which area should be avoided?

Answer:

- Sites:
  - Abdomen
  - Lateral thighs
  - Upper arms
  - Buttocks
- Avoid: 2 cm around the umbilicus



Insulin Injection Site

Q1.8: What are the 1st and 2nd generation sulfonylureas and their major side effects?

PYQ: FMGE 2021

Answer:

1st generation Drugs: AMIDE	2nd generation drugs: GLI (more potent)
• Chlorpropamide • Acetohexamide • Tolbutamide • Dorzolamide	• Glimepiride • Glipizide • Gliclazide • Glyburide

- **Side effects:**
  - Sulfa allergy
  - Hypoglycemia
  - Chlorpropamide:
    - → ↑ADH secretion → SIADH
    - → Treatment of diabetes insipidus
    - → Disulfiram-like reaction
    - → Avoided in alcoholics

Q1.9: What are Meglitinides and their unique features?

Answer:

- **Drugs:** Repaglinide, Nateglinide (end with -glinide)
- Act as insulin secretagogues
- **Mechanism of action:**

Close ATP-sensitive K^+ channel on the beta (β) cell of the pancreas
↓
Depolarisation of beta (β) cells
↓
Insulin secretion

- **Side effect:** Flu-like syndrome
- Can cause hypoglycemia and weight gain if given with sulfonylureas

Q1.10: Which agents mimic the function of amylin, and what are their features?

Answer:

- Drug: Pramlintide
- Secreted by ß-cells
- Mechanism of action: ↓Glucagon & ↓Appetite (acts on hindbrain)

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- S/C route
- Side effects:
  - Weight loss
  - Gastroparesis
- It does not cause hypoglycemia

Q1.11: List GLP-1 analogues and their key clinical uses.

Answer:

- Drugs:
  - Exenatide
  - Liraglutide
  - Lixisenatide
  - Albiglutide
  - Dulaglutide
  - Semaglutide (Only oral)
- Features:
  - ↑Insulin, ↓Glucagon, ↓Appetite
  - S/C route, except Semaglutide (oral)
  - Weight loss, no hypoglycemia
  - Liraglutide & Semaglutide: Approved as anti-obesity drugs
  - Hepatic & Renal safe: Dulaglutide, Semaglutide
- ADRs:
  - Pancreatitis
  - ↑Risk of pancreatic & thyroid cancers

Q1.12: What are Dipeptidyl Peptidase-4 (DPP4) Inhibitors and their adverse effects?

Answer:

- Drugs:
  - Sitagliptin
  - Vildagliptin
  - Alogliptin
  - Linagliptin
  - Saxagliptin
- Oral, weight-neutral, and do not cause hypoglycemia
- Mechanism: Increases endogenous incretin (GLP-1)
- Side effects:
  - Pancreatitis
  - Pancreatic cancer
  - Nasopharyngitis
  - Arthritis
  - Saxagliptin: ↑Risk of heart failure (metabolized by CYP3A4)
  - Vildagliptin: Hepatotoxic

Q1.13: Which drug is the first-line agent for Type 2 DM, Impaired glucose tolerance, clozapine induced type 2 DM and PCOD? What are its limitations?

Answer:

- Drug: Metformin (Biguanide)
- Mechanism: Inhibit hepatic gluconeogenesis
- Given orally, causes mild weight loss, no hypoglycemia
- Side effects:
  - GIT upset (unexplained diarrhea)
  - Reduced B12 absorption → megaloblastic anemia
  - Lactic acidosis (C/I in renal failure, GFR < 30 ml/min)
- Max daily dose: 2550 mg/day

Q1.14: Which drug is a dual GLP-1 + GIP agonist? Which drug is a GLP-2 analogue?

Answer:

- Tirzepatide: Dual GLP-1 + GIP agonist (injectable)
- Teduglutide: GLP-2 analogue → Used in Short Bowel Syndrome
- Semaglutide: Only oral GLP-1 analogue

Q1.15: Is phenformin still used in clinical practice?

Answer: Phenformin is banned → Deaths due to lactic acidosis

Q1.16: What are the clinical uses of insulin?

Answer:

- Type 1 DM and Type 2 DM: all are given as S.C. insulins
- DKA, HHS: IV Regular insulin is given
- Hyperkalemia: IV Regular insulin + 50% dextrose

BIG QUESTION 2: What are the oral antidiabetic drug classes safe in renal failure?

Broad Answer:

- Drugs safe in renal failure - Mnemonic: "Lina PTSD"
  - Linagliptin
  - Pioglitazone
  - Teneligliptin
  - Saroglitazar
  - Dulaglutide
- No dose reduction is required for these drugs

DETAILED QUESTIONS

Q2.1. What are the key features of Alpha-glucosidase inhibitors?

Answer:

- Drugs: Acarbose, Voglibose, Miglitol
- Mechanism: Inhibits intestinal enzyme α-glucosidase → inhibits breakdown of complex carbohydrates into glucose

- Route: Oral
- Risk of Hypoglycemia: No
- Side Effects:
  - Malabsorption
  - GIT infections
- If hypoglycemia occurs in a patient on Acarbose, Sucrose (table sugar) won't help
  - Treat with pure glucose or fructose (e.g., honey)

Q2.2. What are Thiazolidinediones (TZDs), and what are their clinical concerns?

Answer:

- Drugs:
  - Pioglitazone: ↑ Risk of urinary bladder cancer
  - Troglitazone: Banned due to hepatotoxicity
  - Rosiglitazone: Banned due to CHF/MI
- Mechanism: PPAR-γ agonists →↑ lipogenesis, insulin sensitivity
- Causes weight gain
- No risk of hypoglycemia
- Antidiuretic effect: Contraindicated in CHF
- Dual PPAR-γ + α agonist: Saroglitazar - for diabetic dyslipidemia
- PPAR-α only: Fibrates - used for hyperlipidemia

Q2.3. What are the characteristics and adverse effects of SGLT-2 inhibitors?

PYQ: INICET 2023

Answer:

- Drugs:
  - Canagliflozin
  - Dapagliflozin
  - Empagliflozin
  - Remogliflozin
  - Ertugliflozin
  - Sotagliflozin (acts on SGLT-1 & 2)
- Mechanism: Inhibit sodium-glucose co-transporter in the proximal tubule of the nephron → ↑ urinary glucose excretion
- Benefits:
  - Weight loss
  - No hypoglycemia
  - Diuretic effect
    - → Dapagliflozin and Empagliflozin are approved for CHF
  - Antidiuretic effect
    - → Pioglitazone/Rosiglitazone
    - → C/I in Chronic Heart Failure
- Side Effects:
  - UTI, Cystitis, Candida infection

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- Fournier's gangrene
- DKA
- Osteoporosis (due to calcium loss)
- Lower limb amputation

Q2.4: Which classes of oral antidiabetic drugs target the pancreas and which target peripheral tissues?
Answer:

Acting on Pancreas (Mnemonic: Sundar-MAID)	Acting on Peripheral Organs (Mnemonic: BATS)
• **S** - Sulfonylureas: Insulin secretagogue • **M** - Meglitinides: Insulin secretagogue • **A** - Amylin Analogue: Decreases glucagon production and appetite • **I** - Incretins (GLP-1 analogue): Increase insulin, Decreases glucagon production and appetite • **D** - DPP-4 Inhibitors: Increase insulin, Decreases glucagon production and appetite.	• **B** - Biguanides: Acts on liver • **A** - Alpha (a) Glucosidase Inhibitors: On Intestines • **T** - Thiazolidinediones: On adipose tissue • **S** - SGLT - 2 Inhibitors: In kidneys

BIG QUESTION 3: What are the additional drugs used in Diabetes Mellitus beyond traditional hypoglycemics, their mechanisms, and the pharmacological management of diabetic complications?

Broad Answer: Several non-traditional drugs and specific therapies are used in diabetes mellitus to target complications or complement glycemic control:

- Colesevelam
- Bromocriptine
- Epalrestat
- Imeglimin

DETAILED QUESTIONS

Q3.1. What are the additional oral drugs used in diabetes and their mechanisms?

PYQ: NEET PG 2022

Answer:

Drug	Class/Mechanism	Notes
Colesevelam	Bile acid-binding resin → ↓ glucose absorption from GIT	Also used for hyperlipidemia
Bromocriptine	Dopamine D2 receptor agonist (hypothalamic-pituitary axis)	Taken early morning (< 3 hrs of waking)
Epalrestat	Aldose reductase inhibitor → ↓ conversion of glucose to sorbitol	• Used in diabetic neuropathy • DOC: Pregabalin
Imeglimin	Inhibits hepatic gluconeogenesis	Newer agent

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Q3.2. What are the drug treatments for specific diabetic complications?

Answer:

Diabetic Complication	Treatment Drug	Mechanism / Use
Diabetic Gastroparesis	Erythromycin	Stimulates motilin receptors in the stomach
Diabetic diarrhea	Clonidine	Stimulates α2a receptors in intestine
Diabetic retinopathy	Anti-VEGF agents: Bevacizumab, Ranibizumab, Aflibercept, Pegaptanib	Inhibit neovascularization via intravitreal injection
Diabetic neuropathy	Pregabalin	DOC for neuropathic pain
Anti-obesity in DM	Liraglutide, Semaglutide, Tirzepatide	GLP-1 analogues or dual agonists (GLP-1 + GIP)

Q3.3. Which antidiabetic drugs are associated with an increased risk of fractures?

Answer:

- Canagliflozin
- Dapagliflozin
- Pioglitazone

Q3.4. Which drugs used in diabetes mellitus are known to cause hypoglycaemia?

Answer:

- Insulin
- Sulfonylureas
- Meglitinides

Q3.5. Which antidiabetic drug is associated with megaloblastic anaemia and lactic acidosis?

Answer:

- Metformin
  - Causes ↓ Vitamin B12 absorption → Megaloblastic anemia
  - Risk of lactic acidosis, especially in renal failure

BIG QUESTION 4: Describe the types, mechanisms, and clinical use of thyroid hormones and antithyroid drugs. Include inhibitors of thyroid hormone synthesis, secretion, peripheral conversion, and drugs used in specific thyroid conditions.

Broad Answer: Thyroid hormone therapy and antithyroid drugs include a variety of agents targeting different levels of hormone synthesis, secretion, and conversion. These drugs are used in conditions like hyperthyroidism, thyroid storm, and thyroid cancers, with some specific for pregnancy or emergencies.

DETAILED QUESTIONS

Q4.1. What are the differences between T3 and T4 thyroid hormones?

Answer:

PYQ: NEET PG 2020 PYQ: FMGE 2021

- T4 (Levothyroxine): Prohormone
- T3 (Liothyronine): Active form, Fast acting
- T4 is converted to T3 in peripheral tissues by 5' deiodinase.

Q4.2. What anti-thyroid drugs are inhibitors of the Na^+-I^- symporter?

Answer:

- Drugs:
  - Thiocyanate
  - Perchlorate
  - Pertechnetate
  - Fluoroborate (Not used clinically)
- **Mechanism: Block iodine uptake into thyroid follicular cells**

Q4.3. Which drugs inhibit thyroid peroxidase, and how do they work?

Answer:

Thionamides	• Inhibit the synthesis of T3/T4 • Oxidation, organification, and coupling of iodine
Ethionamide:	• Anti-TB drug - Derivative of methimazole • S/E: Hypothyroidism

Propylthiouracil	• Inhibits peripheral T4-T3 conversion • Used in hyperthyroidism in pregnancy (1st Trimester) • Thyroid storm • Highly hepatotoxic
Carbimazole (pro drug)	• Methimazole(active form) • Graves disease • Used in 2nd and 3rd trimester of pregnancy o Highly teratogenic in 1st trimester o Produce Aplasia cutis o Sulfa containing → Causes Rash and Agranulocytosis



Q4.4. What oral iodides are used, and what is their role?

Answer:

- Drugs:
  - Na^+-iodide
  - Saturated Solution of Potassium Iodide (SSKI)
  - Lugol's Iodine (5% Iodine + 10% KI)
    - → Uses:
      - Rapid action prior to thyroid surgery to reduce size of thyroid
      - Fastest acting antithyroid drug
    - → Side Effects:
      - Sialorrhea
      - Sialadenitis (Mumps-like)

Q4.5. Which drugs inhibit the peripheral conversion of T4 to T3?

Answer:

- Mnemonic: PPIDA
  - Propranolol
  - PTU
  - Iodides
  - Dexamethasone
  - Amiodarone (contains 37% iodine; also causes hypothyroidism)

Given in thyroid storm (PPID)

Q4.6. What are the key features of radioactive iodine therapy?

Answer:

- Drug: Iodine-131
- Mechanism: Destroys thyroid via beta rays
- Half-life: 8 days
- Indication: Inoperable hyperthyroidism, especially in elderly/heart disease patients
- Contraindications:
  - Pregnancy
  - Age < 35 years
- Side effect: Permanent hypothyroidism

Q4.7. What is the treatment of thyroid storm, especially in asthmatics?

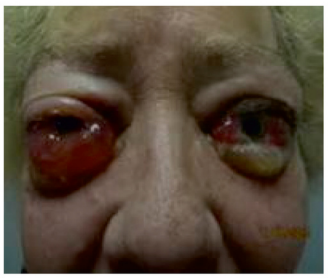
Answer:

- Management of thyroid storm:

Propranolol ●-▶ PTU ●-▶ Iodides ●-▶ Dexamethasone

- In asthmatics: Avoid propranolol → Use Verapamil or Diltiazem

Q4.8. What is Teprotumumab, and what is its use?



Answer:

- Monoclonal antibody against IGF-1
- Used in: Thyroid Eye Disease (Proptosis)

Q4.9. What drug is approved for medullary thyroid carcinoma?

Answer: Vandetanib

BIG QUESTION 5: Describe the pharmacological agents used in the management of osteoporosis, hypercalcemia, and hyperphosphatemia. Include their mechanisms, indications, adverse effects, and contraindications.

Broad Answer: A variety of drugs act either by stimulating bone formation or inhibiting bone resorption. These agents are used in conditions like osteoporosis, Paget's disease, hypercalcemia, and CKD-related hyperphosphatemia. The choice of drug depends on renal safety, severity, and patient tolerance.

DETAILED QUESTIONS

Q5.1. Which drug is used to stimulate osteoblast activity in osteoporosis?

Answer:

- Teriparatide (PTH analogue):
  - Intermittent S/C injection stimulates osteoblasts
  - Indications: Bisphosphonate-resistant osteoporosis
  - C/I:
    - → Hypercalcemia
    - → Paget's disease of bone
  - Adverse Effects:
    - → Renal stones
    - → Osteosarcoma
  - Increase the risk of osteosarcoma

Q5.2. Which drugs inhibit bone resorption by acting on osteoclasts?

Answer:

- Bisphosphonates
  - Drugs: Alendronate, Ibandronate, Zoledronate
  - Longest acting: Given once a year (most potent)
  - MOA: Inhibits ATP production, FPPS synthetase (Farnesyl pyrophosphate synthase) → Kills Osteoblast.
  - DOC: Hypercalcemia, Osteoporosis (Cushing syndrome, Post menopausal osteoporosis) and Paget's disease
  - ADR: Reflux esophagitis, Osteonecrosis of mandible
  - C/I: Renal diseases
- Calcitonin
  - Fastest calcium-lowering agent for Hypercalcemia
- Denosumab (anti- RANK)
  - Blocks rank receptor on osteoclast
  - Renal safe drug
  - Contraindicated: Hypocalcemia
- Cinacalcet
  - Suppress PTH secretion
  - Used in hyperparathyroidism
- Gallium Nitrate
- Oestrogen/Raloxifene

Q5.3. What is the DOC for various types of osteoporosis?

Answer:

- Postmenopausal & Cushing's Osteoporosis: Bisphosphonates (DOC)
- Paget's Disease: Bisphosphonates
- Bisphosphonate-resistant osteoporosis: Teriparatide
- Renal failure: Denosumab (safe option)

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Q5.4. How is acute hypercalcemia treated?

Answer:

- Saline 6-8 L/day
- Loop Diuretics: Promote calcium excretion
  - o C/I: Thiazide diuretics
- Bisphosphonates: Zoledronate, Pamidronate
- Calcitonin: Fastest acting
- Denosumab: Most effective
- Corticosteroids: Especially for granulomatous conditions (Increase Vitamin D)
- Cinacalcet: Used in hyperparathyroidism

Q5.5. What drugs are used for hyperphosphatemia, especially in CKD?

Answer:

- Sevelamer (DOC)
- Lanthanum carbonate
- Calcium carbonate
- Aluminum hydroxide
- Iron salts
- Niacin (Nicotinic acid)

Q5.6. What are some key differences between bisphosphonates and denosumab?

Feature	Bisphosphonates	Denosumab
Mechanism	Inhibits FPPS →↓ osteoclasts	Anti-RANKL → inhibits osteoclasts
Route	Oral/IV	S/C injection
Renal Safety	Not safe	Safe in renal failure
Frequency	Zoledronate: Once yearly	Every 6 months
Side Effects	• Reflux esophagitis • Osteonecrosis of the mandible • High risk of subtrochanteric femur fracture	Hypocalcemia

Q5.7 What are Selective Estrogen Receptor Modulators (SERMs), and where are they used?

Answer: SERMs act as estrogen receptor agonists or antagonists depending on the tissue.

Drug	Indications	Adverse Effects
Tamoxifen	Breast cancer (Tx & prevention) Osteoporosis	• Increase risk of endometrial cancer • Cataracts • Hepatotoxicity • Hot flushes • Thromboembolism

Raloxifene	Postmenopausal osteoporosis Breast cancer prevention	• Hot flushes • Thromboembolism
Clomiphene	Ovulation induction PCOS	-
Ormeloxifene	Contraceptive (India)	-
Bazedoxifene	• HRT for postmenopausal hot flushes (DOC: HRT) • Often combined with estrogens	-
Ospemifene	Senile/atrophic vaginitis	Vaginal discharge, hot flushes

Q5.8. Which drugs are used in tamoxifen-resistant breast cancer?

PYQ: NEET PG 2020

Answer:

- **Fulvestrant, Elacestrant:** SERDs (Selective Estrogen Receptor Downregulators)
  - o DOC for tamoxifen-resistant cases

Q5.9. What are Aromatase Inhibitors and their clinical uses?

Answer:

- Inhibit aromatase enzyme, blocking conversion of testosterone to estrogen
- DOC for postmenopausal breast cancer

Drugs	Other Uses
Letrozole	Ovulation induction in PCOD
Exemestane	Postmenopausal breast cancer
Anastrozole	
Vorozole	
Formestane Exemestane	

Q5.10. What is the types & doses of glucocorticoids and mineralocorticoids used in clinical practice?

Answer:

		Drug	Gluco (GC)	Mineralo (MC)	Equivalent. Dose
Glucocorticoids	Short acting ($t^{1/2}$ <12hr)	1. Hydrocortisone (cortisol)	1	1	20 mg
		2. Cortisone	0.8	0.8	24 mg
	Intermediate acting ($t^{1/2}$ 12-36 hr)	3. Prednisolone	4	0.8	5 mg
		4. Methyl-prednisolone	5	0.5	4 mg
		5. Triamcinolone	5	0	4 mg
		6. Deflazacort	3-4	0	6 mg
	Long acting ($t^{1/2}$ >36hr)	7. Dexamethasone	25	0	0.75 mg
		8. Betamethasone	25	0	0.75 mg

	Compound	Gluco (GC)	Mineralo (MC)	Equivalent dose
Mineralocorticoids	Desoxycorticosterone acetate (DOCA)	0	100	2.5 mg (sublingual)
	Fludrocortisone	10	150	0.2 mg (oral or I.V.)
	Aldosterone	0.3	3000	Not used clinically

GC with max MC activity	Hydrocortisone
Least potent GC	Cortisone
Most potent GC	Dexamethasone and betamethasone
Pure GC with no MC activity	Dexamethasone and betamethasone
Pure MC	DOCA
Most potent MC	Aldosterone
MC with maximum GC activity	Fludrocortisone
Only oral and IV preparation	
Most potent topical glucocorticoid	Beclomethasone dipropionate (0.5% in vehicle) Clobetasole propionate (0.5%)
Adrenal insufficiency	Hydrocortisone
Foetal lung maturation	Dexamethasone IM Betamethasone IM

Q5.11 Which glucocorticoids are used in MTP (Medical Termination of Pregnancy)?

Answer:

- Mifepristone: Antagonist at progesterone and GC receptors.
- Use: Cushing disease, abortion and MTP

Q5.12 What is Ulipristal and its use?

Answer:

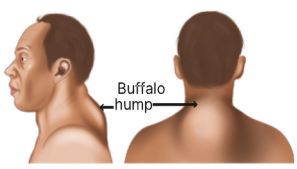
- Selective progesterone receptor modulator (SPRM)
- Used as an emergency contraceptive
- 30 mg single dose within 5 days of intercourse

Q5.13 What are the clinical manifestations of Cushing's syndrome?

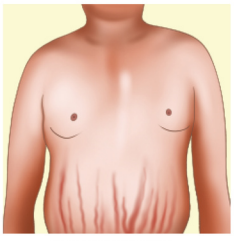
Answer:

- Classical cushingoid features:
  - Moon-like facies
  - Buffalo hump
  - Central obesity
  - Eye complications:
    → Oral steroids → Posterior subcapsular cataract
    → Steroid eye drops → Glaucoma


Moon like facies



Buffalo hump


Central obesity

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BIG QUESTION 6: What is medical adrenalectomy, and which drugs are used?

Broad Answer: Medical adrenalectomy refers to the pharmacological suppression of corticosteroid synthesis from the adrenal glands.

Drug	Mechanism
Mitotane	Inhibits 11β-hydroxylase
Osilodrostat	
Metyrapone	

- Other drugs:

Drug	Mechanism
Ketoconazole	Inhibits steroid synthesis (can cause adrenal insufficiency)
Etomidate	GA agent; inhibits cortisol synthesis at low doses

DETAILED QUESTIONS

PYQ: INICET 2020 PYQ: FMGE 2021

Q6.1. How is androgen synthesis and action pharmacologically targeted?

Answer: Androgen production and effects are targeted at 3 levels:

• Synthesis inhibitor	• Ketoconazole • Abiraterone
• 5 - alpha (α) reductase inhibitors	• Finasteride • Dutasteride
• Androgen receptor antagonist	• Flutamide • Bicalutamide • Enzalutamide • Nilutamide • Spironolactone • Cyproterone • Drosperinone

Q6.2 What are the common indications of anti-androgens?

Answer:

- All are used in:
  - Prostate cancer in males
  - Hirsutism in females
- BPH:
  - Finasteride
  - Dutasteride
- Alopecia:
  - Finasteride + Dutasteride
  - Minoxidil (2-5% cream)
- ADR: Gynaecomastia, impotence

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BIG QUESTION 7: Discuss the drugs acting on the pituitary hormone axis, including growth hormone-related disorders, prolactinomas, and GnRH analogues.

Broad Answer:

- Hypothalamus → GHrH → Stimulates pituitary → Growth Hormone → Liver → IGF-1
- Drugs for GH disorders include Somatropin for dwarfism and Octreotide/Pegvisomant for acromegaly. Prolactinomas are treated with dopamine agonists like Cabergoline or Bromocriptine. GnRH analogues (e.g., Leuprolide) suppress FSH/LH on continuous use, while GnRH antagonists (e.g., Cetrorelix) directly block receptors without an initial flare.

DETAILED QUESTIONS

Q7.1. Which hormone is mainly inhibited by somatostatin and dopamine?

Answer:

- Somatostatin: Inhibits growth hormone (GH)
- Dopamine: Inhibits prolactin

Q7.2. What is the drug of choice (DOC) for dwarfism due to GH deficiency?

Answer:

- DOC: Somatropin (Recombinant GH)
  - ADR: Hyperglycemia
- In GH-resistant cases: Mecasermin (Recombinant IGF-1)
  - ADR: Hypoglycemia

Q7.3. How is acromegaly (excess GH) managed pharmacologically?

Answer:

- First-line treatment: Pituitary removal
- If the patient is not fit for surgery: DOC - Somatostatin
  - Octreotide
  - Lanreotide
- In resistant cases: Pegvisomant (GH receptor antagonist)

Q7.4. What are the drugs used for treating prolactinomas?

Answer:

- DOC: Cabergoline (Dopamine D2 agonist)
- In pregnancy: Bromocriptine
- If resistant to drugs: Surgical pituitary tumor removal

Q7.5. What is Lu-Dotatate, and where is it used?

Answer:

- Lu-Dotatate is a Lutetium-labeled octreotide (radioactive)
- Used in PNET tumors (Pancreatic neuroendocrine tumors)

Q7.6. Name the drugs used in short bowel syndrome.

Answer:

- GH (Somatropin)
- Octreotide
- Teduglutide: Recombinant GLP-2 analogue

Q7.7. Name GnRH agonist drugs and their side effects.

Answer:

- Drugs:
  - Leuprolide
  - Gonadorelin
  - Buserelin
  - Histrelin
  - Triptorelin
  - Nafarelin (Nasal spray)
- Side Effect: Initial flare-up reaction (Initial increase in FSH/LH on continuous injection)

Q7.8 What are the indications of intermittent & continuous injection of GnRH agonists?

PYQ: NEET PG 2021

Answer:

Intermittent injection	Continuous injection
• Increase FSH/ LH o Female Infertility- anovulation o Male Infertility- azoospermia o Delayed Puberty (DOC)	• Decrease FSH/LH o Prostate Cancer (DOC) o Breast Cancer/Endometriosis, Leiomyoma o Precocious puberty

Q7.9 Name some GnRH receptor antagonists and their advantages.

Answer:

- Drugs:
  - Cetrorelix, Degarelix, Abarelix, Ganirelix: Used in prostate cancer
  - Elagolix: Used in endometriosis
- Advantage: No initial rise in LH/FSH

Q7.10: What are the clinical uses of octreotide?

Answer: Mnemonic: **IDEAS**

I - Insulinoma/ glucagonoma/ gastrinoma (PNET tumors)
D - Diarrhoea-due to carcinoid tumor
E - Esophageal varices (Terlipressin > Octreotide)
A - Acromegaly
S - Short bowel syndrome

9. BLOOD DISORDERS

BIG QUESTION 1: What are the types and mechanisms of antiplatelet drugs?

Broad Answer: Antiplatelet drugs inhibit platelet aggregation by targeting various pathways such as COX enzymes, ADP receptors, PDE3 inhibition, and GPIIb/IIIa receptors. These agents play a vital role in treating and preventing cardiovascular events such as myocardial infarction (MI), stroke, and Buerger's disease.

DETAILED QUESTIONS

Q1.1: What are the key features of aspirin as an antiplatelet agent?

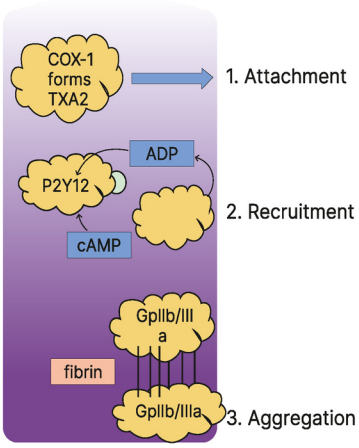
Answer:

- Irreversible COX inhibitor (COX-1)
- Suicide inhibitor; "hit and run" action
- Reduces thromboxane A2 (TXA2) production in platelets
- Drug of choice (DOC) for:
  - Myocardial infarction (MI)
  - Stroke
  - Buerger's disease
- Dosing:
  - Acute MI and stroke: 325 mg (maximum dose)
  - Secondary prophylaxis: 75–100 mg
- Reduces mortality
- Side effects:
  - Increases bleeding time
  - Peptic ulcers (DOC: PPI > Misoprostol)
- Should be stopped 7 days before surgery
- Contraindications:
  - Risk of Reye syndrome (in children)
  - Lactation

Q1.2: How do platelets aggregate physiologically?

Answer:

- Platelets attach via COX-1 enzymes
- ADP release recruits more platelets
- cAMP inhibits recruitment
- Fibrin helps aggregation through GPIIb/IIIa receptors



Q1.3: What are the characteristics and side effects of ADP (P2Y12) receptor blockers?

Answer:

- Often combined with aspirin for synergistic effect and better mortality reduction

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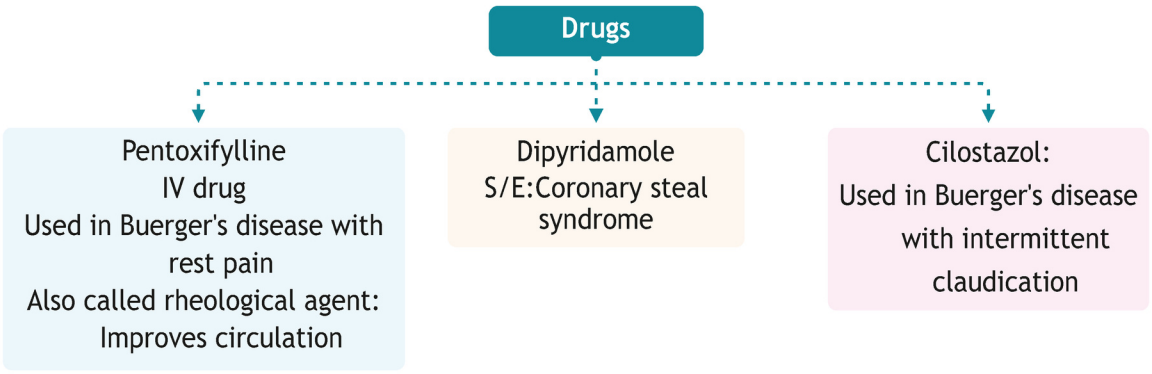
- Clopidogrel:
  - Prodrug, activated by CYP2C19
  - Omeprazole (strong CYP2C19 inhibitor) reduces efficacy
  - Safe alternatives: Rabeprazole > Pantoprazole
  - Side effects: Diarrhea, thrombotic thrombocytopenic purpura (TTP)
- Ticlopidine:
  - Causes agranulocytosis

PYQ: INICET 2021

Q1.4: What are PDE3 inhibitors and their clinical considerations?

Answer:

- Increase cAMP levels
- Uses:
  - Stroke
  - Buerger's disease
- Contraindicated in MI (increases oxygen demand)



Q1.5: What are the features of GPIIb/IIIa inhibitors?

Answer:

- Act as antiaggregant and anti-integrin drugs
- Drugs include:
  - Eptifibatide
  - Abciximab:
    - → Safe in renal disease (not excreted in urine)
    - → Has immunosuppressive action
    - → Half-life: 30 minutes
  - Tirofiban
- Administered intravenously
- Indications: Acute MI and percutaneous transluminal coronary angioplasty (PTCA)

Q1.6: Which drugs are contraindicated or indicated in MI vs stroke?

Answer:

- Ticlopidine and clopidogrel: Indicated in both MI and stroke
- Prasugrel, ticagrelor, cangrelor: Contraindicated in stroke

Q1.7: What is the classification of P2Y12 blockers based on reversibility?

Answer:

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- Irreversible blockers (prodrugs):
  - Ticlopidine
  - Clopidogrel
  - Prasugrel
- Reversible blockers (active drugs):
  - Ticagrelor
  - Cangrelor

Q1.8: What are the other antiplatelet drug classes and examples?

Answer:

- Vorapaxar:
  - PAR-1 (Platelet Activating Receptor-1) antagonist
  - Used with aspirin in MI
- Dazoxiben:
  - Thromboxane synthase inhibitor
  - Currently under trial

BIG QUESTION 2: What are the classes and clinical uses of anticoagulants?

Broad Answer: Anticoagulants prevent fibrin deposition and are used in thromboembolic conditions like DVT, PE, atrial fibrillation, and during/after surgeries. They are classified into oral and parenteral types, with various mechanisms targeting vitamin K, thrombin, or factor Xa.

DETAILED QUESTIONS

Q2.1: What are the uses and classifications of anticoagulants?

Answer:

<table>
<tr><th colspan="3">Anticoagulants</th></tr>
<tr><th colspan="3">Uses</th></tr>
<tr><th>DVT/Pulmonary embolism</th><th>Atrial fibrillation and Mitral stenosis</th><th>DIC: Occurs in</th></tr>
<tr><td>• Immobility
• ICU patients: s/c heparin
• After knee and hip surgery: Oral drug</td><td>• Can lead to TIA or ischemic stroke
• Oral drug: Warfarin</td><td>• Sepsis: IV heparin
• Abruptio placentae: IV heparin
• Mechanical heart valves: Long-term Oral warfarin</td></tr>
<tr><th colspan="3">Classification</th></tr>
<tr><th colspan="2">Oral Anticoagulants</th><th>Parenteral Anticoagulants</th></tr>
<tr><td colspan="2">• Vitamin K antagonists
o Warfarin
o Coumarin
• Factor Xa inhibitor: Direct inhibitors (Apixaban)
• Direct thrombin inhibitor: Dabigatran</td><td>• Indirect thrombin inhibitors
o Activates antithrombin 3
o Drug: Heparin
• Direct thrombin inhibitor
o Hirudin
o Lepirudin</td></tr>
</table>

Q2.2: What are key indications for warfarin therapy?

PYQ: NEET PG 2019
PYQ: INICET 2022
PYQ: FMGE 2021

Answer:

- DOC for:
  - Mechanical heart valve
  - DVT/PE
  - AF with mitral stenosis
- Used in DIC, ICU patients, sepsis, and after surgeries

Q2.3: How does warfarin work and what are its pharmacokinetics?

Answer: Name from Wisconsin Alumni Research Foundation + Coumarin

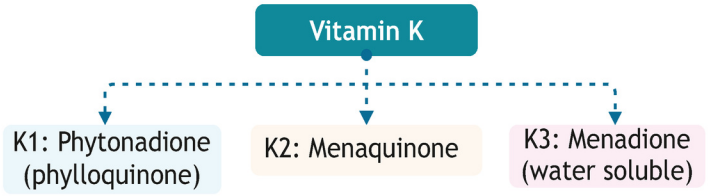
- Inhibits vitamin K epoxide reductase (VKOR-C1) in the liver
- Leads to deficiency of clotting factors: 2, 7, 9, 10 and anti-clotting factors: Protein C and S
  - Deficiency takes > 5 days
  - < 5 days: Deficiency of anti-clotting factor protein C and S
- Initial 5 days:
  - Imbalance: Excess clotting factors, deficiency of anti-clotting factors
  - Can cause hypercoagulation and dermal vascular necrosis
- Heparin is co-administered for first 5 days, then stopped
- Pharmacokinetics:
  - 99% protein-bound
  - Low volume of distribution (no role of hemodialysis)
  - Racemic mixture (S-warfarin is active, metabolized by CYP2C9)
  - Genetic testing: VKOR-C1 and CYP2C9



Q2.4: How is warfarin therapy monitored and adjusted?

Answer:

- Monitoring via PT and INR
  - INR = Patient PT / Mean normal PT
  - Normal INR: 0.8-1.1
  - Therapeutic INR for warfarin: 2-3
- Interactions:
  - Increased INR (warfarin toxicity): CYP inhibitors, aspirin, antibiotics, cefoperazone
  - Decreased INR: CYP inducers, estrogen, nephrotic syndrome, CKD
- Raised INR interventions:
  - <5: Stop warfarin
  - 5-9: Oral Vitamin K1 (2.5 mg)
  - 9-20: Oral Vitamin K1 (5 mg)
  - 20: IM Vitamin K1 (10 mg)
  - Bleeding at any INR:
    - → FFP (15 mg/kg)
    - → 4 factor PCC (prothrombin complex conjugate) → Factors 2,7,9 and 10 (best option).



Q2.5: What are the antidotes for different anticoagulants?

Answer:

- Warfarin: Vitamin K1
- Rivaroxaban, Apixaban: Andexanet alpha
- Dabigatran: Idarucizumab
- Heparin (HMW/LMW): Protamine sulfate
- Ciraparantag: Common antidote for apixaban, rivaroxaban, dabigatran, and heparins
- No antidote: Fondaparinux, Idraparinux, Hirudin, Bivalirudin
- Idrabiotaparinux: Contains biotin; antidote is avidin

Q2.6: What are the uses of vitamin K?

Answer:

- Warfarin overdose
- Extended antibiotic therapy
- Aspirin toxicity
- Phenytoin induced Osteoporosis
- Obstructive jaundice
- Newborn

Q2.7: How are parenteral anticoagulants classified?

Answer: Parenteral Anticoagulants

- Never given IM: Causes hematoma formation
- IV drugs require aPTT monitoring

Direct thrombin inhibitors	Indirect thrombin inhibitors
• Drugs o Hirudin: Obtained from saliva of leeches o Lepirudin: Liver safe o Desirudin o Bivalirudin o Argatroban: Renal Safe • **DOC:** Heparin-induced Thrombocytopenia • No Antidote available • Requires aPTT monitoring	• Heparin o Activates antithrombin 3 o Inhibits clotting factors

Q2.8: What are the various forms of heparin used clinically?

Answer:

High molecular weight Heparin /unfractionated/ crude heparin	Low Molecular weight Heparin/ fractionated heparin	Ultra-low Molecular weight Heparin /synthetic heparin
• DOC in renal failure • Drug: Heparin • Inhibits factor 10 and 2 • Route: IV • Requires aPTT monitoring	• Drugs o Enoxaparin o Dalteparin o Tinzaparin • Renal unsafe	• Drugs o Fondaparinux o Idraparinux • Inhibits only factor 10 • Route: SC

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• Natural crude (from ox lung) • RE cells • Antidote: Protamine sulfate	• Inhibits factor 10 > 2 • Route: SC • No monitoring required • Natural but filtered • Less risk of HIT • Renal excretion • Protamine sulfate is less effective	• No monitoring required • Synthetic pentasaccharide • No risk of HIT • Renal excretion • Protein sulfate is not effective

Q2.9: Which anticoagulants are safe to use during pregnancy?

Answer:

- **DOC:** LMW or VLMW heparins
  - Safe in all trimesters
  - Should be stopped 1 day before delivery
- **Warfarin:** Contraindicated in 1st trimester (up to 12 weeks)
  - Inhibits Vitamin K
  - Leads to bone and cartilage defects in the fetus (chondrodysplasia punctata)
  - Called Fetal warfarin syndrome
  - **Symptoms:** ***Mnemonic: SLiMS***
    - → **S -** Saddle nose
    - → **Li -** Limb hypoplasia
    - → **M -** Microcephaly
    - → **S -** Stippled epiphysis.

BIG QUESTION 3: What are fibrinolytic agents and how are they used clinically?

Broad Answer: Fibrinolytics (thrombolytics) dissolve clots by converting plasminogen to plasmin, which breaks down fibrin. These drugs are used in emergencies like STEMI, ischemic stroke, and massive pulmonary embolism, but come with risks like internal bleeding.

DETAILED QUESTIONS

Q3.1: What is the mechanism of action and primary use of fibrinolytics?

PYQ: NEET PG 2023

Answer: Fibrinolytics/Thrombolytics

- MOA: Plasminogen → plasmin → degrades fibrin
- Uses:
  - STEMI (contraindicated in NSTEMI)
  - Ischemic stroke (contraindicated in hemorrhagic stroke)
  - Massive pulmonary embolism causing right heart failure (hypotension or shock)

Q3.2: What are the main fibrinolytic agents and their characteristics?

Answer:

- Streptokinase:
  - From Group C Beta Hemolytic Streptococci
  - Antibodies form post-use → single lifetime dose

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- Dose: 1.5 million IU/hr; Half-life: 80 mins
- Urokinase:
  - From cultured human kidney cells
  - Can be used after streptokinase
- Alteplase:
  - Recombinant human TPA
- Reteplase:
  - Modified TPA; long-acting; bolus dose
- Tenecteplase:
  - Mutant TPA; long-acting; bolus dose
  - Dose: 0.5 mg/kg
  - Most preferred agent

Q3.3: What are the side effects and reversal options for fibrinolytics?

Answer:

- Major risk: Acute fatal internal bleeding
- Antifibrinolytics/Antithrombotics:
  - Tranexamic acid: Control active internal bleeding; Used in menorrhagia and esophageal varices
  - Epsilon aminocaproic acid: Antidote of fibrinolytic (Streptokinase, Urokinase, Alteplase); More potent and longer-acting drug.

Q3.4: Which fibrinolytic agents are preferred for specific situations?

Answer:

- Tenecteplase: Most preferred overall
- Urokinase: Preferred if patient has received streptokinase before

Q3.5: How are fibrinolytic drugs classified?

Answer:

- Natural:
  - Streptokinase
  - Urokinase

- Recombinants, TPA (Tissue plasminogen activator)
  - Alteplase
  - Reteplase
  - Tenecteplase

BIG QUESTION 4: What are the mechanisms and indications of hypolipidemic drugs?

Broad Answer: Hypolipidemic drugs are used to reduce levels of cholesterol and triglycerides, thus managing dyslipidemia and preventing atherosclerotic cardiovascular disease. These include statins, fibrates, niacin, resins, and newer agents, each targeting different aspects of lipid metabolism.

DETAILED QUESTIONS

Q4.1: What is the mechanism and clinical utility of statins?

Answer:

- Inhibit HMG-CoA reductase (rate-limiting step in cholesterol synthesis)
- Increase LDL receptors in liver → enhance LDL clearance
- DOC for hypercholesterolemia, especially in:
  - Metabolic syndrome
  - Nephrotic syndrome
  - Drug-induced hyperlipidemia (Loop, thiazide, beta-blockers)
  - Alcohol-related dyslipidemia
- Pleiotropic effects:
  - Anti-atherosclerotic
  - Uric acid reduction
- Drugs:
  - Rosuvastatin > Atorvastatin (longest-acting, most effective)
  - Lovastatin, Simvastatin (prodrugs)
  - Pitavastatin (most potent, least dose)
- Metabolism:
  - Most via CYP3A4 except:
    - → Rosuvastatin, Pravastatin (not via CYP)
    - → Fluvastatin (CYP2C9)
- Side effects:
  - Hepatotoxicity
  - Myopathy, rhabdomyolysis (↑CPK, myoglobinuria, cola-colored urine)
  - Women > men
- Contraindications: Pregnancy, children <12 years

Q4.2: What are the properties and uses of bile acid sequestrants (resins)?

Answer:

- Bind bile acids in GIT and prevent their reabsorption
- Liver increases LDL receptor expression to compensate → ↓LDL in blood
- Drugs:
  - Cholestyramine
  - Colestipol
  - Colesevelam
- DOC: Hypercholesterolemia during pregnancy
- Side effects:
  - Malabsorption of fat-soluble vitamins
  - Interfere with absorption of:
    - → Digoxin
    - → Propranolol
    - → Thyroxine (Mnemonic: DPT)

Q4.3: What are the effects and cautions of fibrates?

Answer:

- Act on PPAR-alpha receptors → ↑LPL activity → ↓triglycerides

- DOC: Hypertriglyceridemia >500 mg/dL
- Drugs (end in -fibrate):
  - Clofibrate: Banned (↑MI risk)
  - Fenofibrate: Most used; no CYP action; often with statins
  - Bezafibrate
  - Gemfibrozil: CYP inhibitor → avoid with statins (↑myopathy risk)
- Side effects:
  - Myopathy
  - Gallstones (↓gallbladder motility)

Q4.4: How does niacin (vitamin B3) act as a lipid-lowering agent?

Answer:

- High dose: 2-6 grams/day
- Acts on liver and adipose tissue
- ↓ TG synthesis, ↓ Lipoprotein(a), ↑ HDL
- Side effects:
  - Flushing (↑PGD2 → vasodilation)
    → Treatment: Aspirin or Laropiprant (PGD2 receptor blocker)
  - Hepatotoxicity
  - Hyperuricemia (bad for gout)
  - Hyperglycemia (worsens diabetes)
- Not commonly used now due to toxicity



Flushing

Q4.5: What are the newer hypolipidemic agents and their mechanisms?

Answer:

- Ezetimibe:
  - Inhibits NPC1L1 transporter in intestine → ↓cholesterol absorption
- Evolocumab, Alirocumab:
  - Monoclonal antibodies against PCSK-9 → ↑LDL receptor recycling
- Inclisiran:
  - siRNA → ↓PCSK-9 production in liver
- Bempedoic acid:
  - Inhibits ATP citrate lyase → ↓cholesterol synthesis
- Lomitapide:
  - Inhibits microsomal TG transfer protein → ↓VLDL
- Omega-3 fatty acids (EPA/DHA from fish):
  - ↓VLDL
- CETP inhibitors (Anacetrapib, Torcetrapib):
  - ↑HDL via cholesteryl ester transfer protein inhibition

BIG QUESTION 5: What are hematinics and how are they used in clinical practice?

Broad Answer: Hematinics are agents that increase the production of red blood cells, white blood cells, and platelets. They are used in the treatment of various types of anemia, especially iron-deficiency anemia (IDA), and are administered either orally or parenterally depending on tolerance and severity.

DETAILED QUESTIONS

Q5.1: What are the key features of iron therapy in IDA?

Answer:

- Used to treat microcytic hypochromic anemia
- **Preparations:**
  - Oral iron (DOC: Ferrous sulfate)
  - Parenteral iron (if oral not tolerated)
- Ferrous ascorbate: Best oral absorption
- Vitamin C increases iron absorption
- **Side effects:**
  - GI irritation, severe nausea, vomiting
  - Black stools
- IM iron: Z-track technique to avoid skin staining
- Earliest response: Increase in reticulocyte count

Q5.2: What are the different oral iron preparations and their content?

Answer:

Oral Iron Preparation	Iron Content (per 60 mg tablet)
Ferrous sulfate	32%
Ferrous gluconate	12%
Ferrous fumarate	33% (maximum iron content)

Q5.3: What are the types and safety of parenteral iron formulations?

Answer:

Parenteral Iron	Route	Anaphylaxis Risk (allergic testing)
Iron dextran	IV, IM	Yes
Iron sorbitol nitrate	IM	Yes
Iron sucrose	IV	No
Ferric gluconate	IV	No

Q5.4: What factors influence iron absorption positively and negatively?

Answer:

- **Increases absorption:**
  - Lemon juice (Vitamin C), Amla, Acidic pH
- **Decreases absorption:**
  - PPIs (↓HCl)
  - Food, tea, coffee (contain phytate/tannate)
  - Tetracyclines (chelate iron and calcium)

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Q5.5: What are the RBC growth factors and their indications?

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Answer:

- **Erythropoietin (EPO):** DOC for:
  - Anemia in CKD
  - Anemia in cancer
  - Zidovudine-induced anemia
- Injection forms:
  - Darbepoetin (Long acting: Darbepoetin>epoetin)
  - Epoetin
  - Peginesatide (PEG-attached, longest-acting)
- Oral HIF-prolyl hydroxylase inhibitors:
  - Daprodustat
  - Roxadustat
  - Molidustat
  - Increase endogenous EPO by reducing its degradation

Q5.6: What are the WBC growth factors and their uses?

PYQ: FMGE 2021

Answer:

- Given IV only
- **Filgrastim:**
  - Recombinant G-CSF (granulocyte colony-stimulating factor)
  - Used for leukopenia due to anticancer drugs
- **Sargramostim, Molgramostim:**
  - Recombinant GM-CSF (granulocyte-monocyte colony-stimulating factor)
  - Also for chemotherapy-induced leukopenia

Q5.7: What is the treatment for thrombocytopenia in ITP?

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Answer:

- Mnemonic: FEAR (for Idiopathic Thrombocytopenic Purpura)
- Drug:
  - **Oprelvekin:**
    → Recombinant IL-11
    → Increases platelet count
    → Given via injection

F- Fostamatinib	E- Eltrombopag	A- Avatrombopag	R- Romiplostim
Tyrosine kinase inhibitor	Thrombopoietin agonist	Thrombopoietin agonist	• Platelet stimulator
Oral drug	Oral drug	Oral drug	• I/v drug

BIG QUESTION 6: What are chelators and their roles in heavy metal poisoning?

Broad Answer: Chelating agents bind to heavy metals in the body to form non-toxic complexes that can be excreted. They are essential in managing acute and chronic metal toxicities such as lead, arsenic, iron, and copper poisoning.

DETAILED QUESTIONS

Q6.1: What is BAL (dimercaprol) and when is it used?

Answer:

- Full form: British Anti Lewisite
- Mnemonic for use: BArHANS
  - B - Bismuth
  - Ar - Arsenic
  - H - Mercury (Hg)
  - A - Gold (Au)
  - N - Nickel (Ni)
  - S - Antimony (Sb)
- Contraindicated in:
  - Cadmium poisoning (forms toxic complex)
  - Iron poisoning

Q6.2: What are the uses and features of Ca-2Na-EDTA?

Answer:

- DOC for:
  - Manganese poisoning
  - Lead poisoning
  - Cadmium poisoning

Q6.3: What is penicillamine used for?

Answer:

- DOC for copper poisoning
- DOC for Wilson's disease

Q6.4: What are the iron-chelating agents and their characteristics?

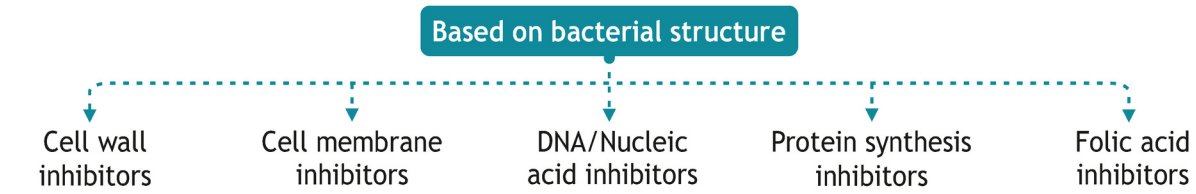
Answer:

- **Deferoxamine:**
  - IV route
  - DOC for iron poisoning
- **Deferiprone:**
  - Oral route
  - DOC for iron poisoning

10. ANTI-MICROBIALS PART-1

BIG QUESTION 1: What are the mechanisms and uses of cell wall inhibitor antimicrobials? How are anti-microbials classified?

Broad Answer: Cell wall inhibitors prevent bacterial growth by interfering with peptidoglycan synthesis. Most of these are bactericidal, except cycloserine (static). They are ineffective against atypical bacteria (Mycoplasma, Chlamydia, Rickettsia) that lack cell walls.

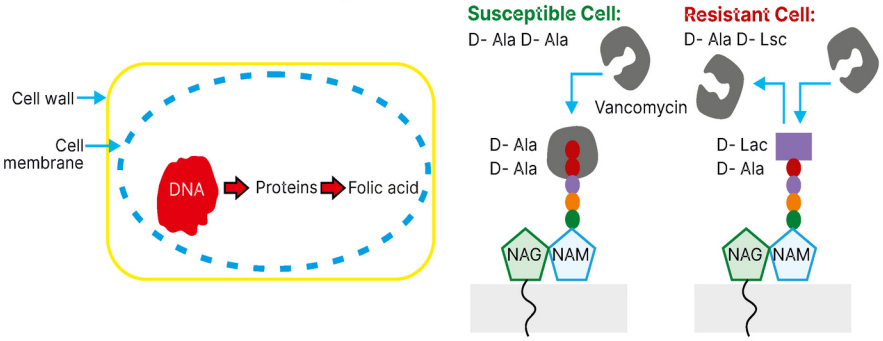


DETAILED QUESTIONS

Q1.1: What are the types and key features of cell wall inhibitors?

Answer: Mnemonic: BBC Very Famous

- **B**eta-lactams: Inhibits transpeptidase enzyme
- **B**acitracin: Topical drug for gram positive infections for staph/streptococcus which can cause impetigo, folliculitis (not effective for MRSA)
- **C**ycloserine: used in MDR TB
- **V**ancomycin: inhibits transglycosylase and binds to D-alanine/D-amine
- **F**osfomycin: given as 3g single oral dose for UTI
- Note: Only Cycloserine is a bacteriostatic drug, rest all are bactericidal drugs



Q1.2: Why are beta-lactam antibiotics ineffective against atypical bacteria?

Answer: Because these atypical bacteria lack cell walls, and beta-lactam antibiotics (like penicillins and cephalosporins) act by inhibiting cell wall synthesis

Q1.3: What are the subtypes of beta-lactams?

Answer:

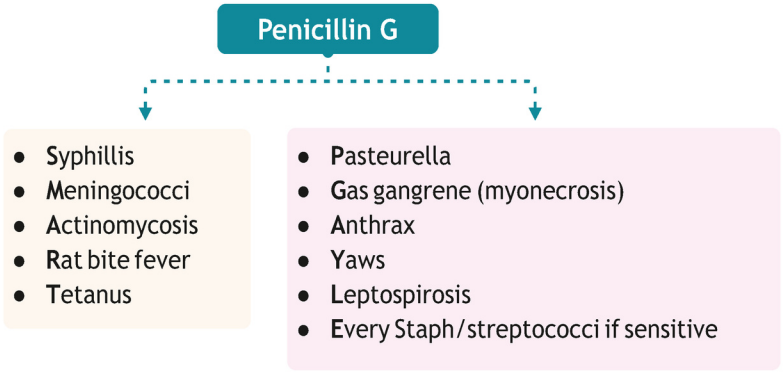
- Penicillin
- Cephalosporin
- Carbapenem
- Monobactam

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Q1.4: What are the clinical uses of Penicillin G?

PYQ: FMGE 2021

Answer: Mnemonic: SMART Player GAYLE



Q1.5: What is the treatment and prophylaxis for meningococcal infection?

Answer:

- Treatment: Ceftriaxone (IV) > Penicillin G
- Prophylaxis to eliminate nasal carrier state:
  - Ciprofloxacin > Rifampicin
  - Pregnancy/children: Ceftriaxone (IV)
- DOC for prevention of meningococci: Ciprofloxacin

Q1.6: From where is Penicillin G obtained?

Answer: Penicillin G is a natural product obtained from the penicillium

Q1.7: What are the major drawbacks of Penicillin G, and how have new synthetic penicillins been developed to overcome them?

Answer:

Drawbacks of Penicillin G	New synthetic Penicillin
• Acid labile (poor Oral absorption)	• Acid-stable penicillin (given orally)
• Short acting	• Long-acting
• Narrow spectrum	• Extended spectrum
• Acquired resistance	• Penicillinase resistance to penicillin • Beta-lactamase inhibitors

Q1.8: What are the oral and long-acting penicillin options?

PYQ: FMGE 2020

Answer:

- Oral: Penicillin V, Oxacillin, Dicloxacillin, Cloxacillin, Amoxicillin, Ampicillin
- Long-acting:
  - Penicillin G + Probenecid (IV)
  - Procaine penicillin
  - Benzathine penicillin (IM)
    - → 1.2 million IU (>20 kg)
    - → 0.6 million IU (<20 kg)
    - → Once/month for rheumatic fever prophylaxis

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Q1.9: What are the types of hypersensitivity reactions seen with penicillin, and what is the drug of choice in penicillin allergy?

Answer:

- All 4 types of hypersensitivity seen:
  - Type I: Anaphylaxis
  - Type II: Hemolytic anemia (Coombs +)
- Cross-allergy with cephalosporins and carbapenems (not with monobactams)
- DOC for penicillin allergy: Erythromycin/Azithromycin

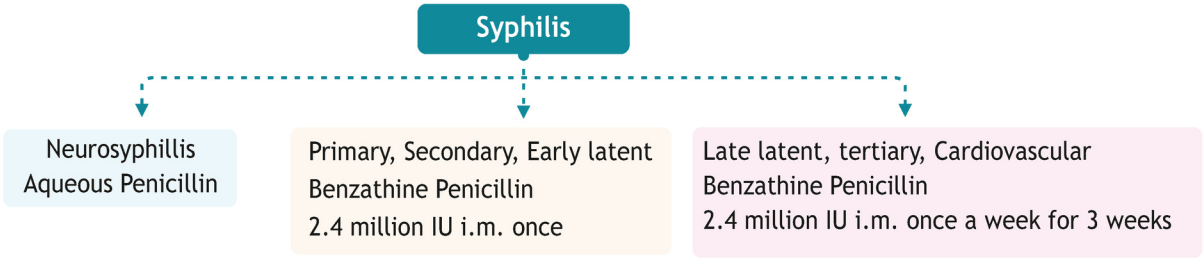
Q1.10: What are disease-specific DOCs involving penicillins?

Answer:

- ENT or community pneumonia: Amoxicillin (Strep pneumoniae)
- Listeria: Ampicillin (CI in EBV allergy)
- Penicillin hypersensitivity (syphilis): Doxycycline

Q1.11: What are the recommended penicillin treatment regimens for different stages of syphilis?

Answer:



Q1.12: What is the Jarisch-Herxheimer reaction, and when does it occur in the context of syphilis treatment?

Answer: Jarisch-Herxheimer reaction occurs due to Penicillin hypersensitivity during treatment of syphilis



Jarisch herxheimer reaction
Penicillin Hypersensitivity in syphilis

BIG QUESTION 2: How is resistance manifested in various bacteria and how is it managed?

Broad Answer: Resistance in bacteria can occur through target mutation, enzyme production, or efflux mechanisms. It varies across organisms like Staphylococcus, Enterobacteriaceae, and Gram-negative pathogens.

DETAILED QUESTIONS

Q2.1: What are the extended spectrum penicillins and their targets?

Answer:

- Amoxicillin, Ampicillin, Carbenicillin, Ticarcillin, Mezlocillin, Azlocillin, Piperacillin
- Targets:
  - E. coli: ACT MAP
  - Pseudomonas: CT, MAP
  - Klebsiella: MAP only

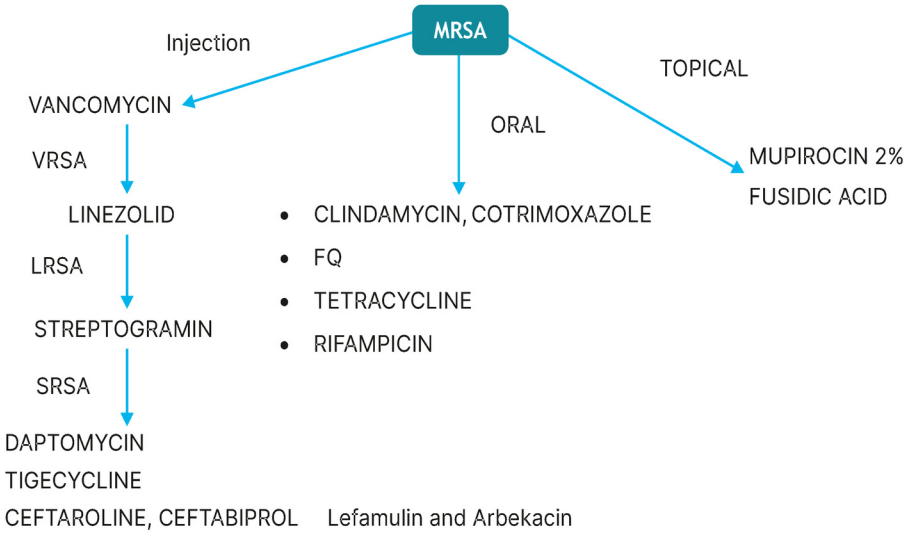
Q2.2: What are the drugs ineffective in Methicillin-sensitive and Methicillin-resistant Staphylococcus aureus?

Answer:

Methicillin-sensitive Staphylococcus aureus	Methicillin-resistant Staphylococcus aureus
• Mnemonic: **CONDM** • **C**loxacillin → Clotting abnormalities or bleeding • **O**xacillin and dicloxacillin → Hepatotoxic. • **N**aficillin → Neutropenia • **D**icloxacillin → Hepatotoxic • **M**ethicillin → Interstitial nephritis.	• Reason: Mutations in transpeptidase enzymes (PBP-2A). • Drugs not effective are **PCCMM** o **P**enicillins (All) o **C**ephalosporin, except 5th generation o **C**arbapenem o **M**onobactam o **M**acrolides (Azithromycin)

Q2.3:What are the different treatment options for MRSA, categorized by their route of administration and resistance profiles?

Answer:



Q2.4: What is the DOC for MRSA causing various types of infections?

Answer: Vancomycin

Q2.5: What is the drug of choice for treating Vancomycin-resistant Staphylococcus aureus?

Answer: DOC for VRSA: Daptomycin (Not effective in pneumonia) > Linezolid (Effective in pneumonia)

Q2.6: What are the common bacteria that show resistance in community-acquired vs hospital-acquired infections?

Answer:

Resistance in Enterobacteriaceae and Gram-negative bacteria's	
Community acquired	**Hospital acquired**
• E.Coli (diarrhea, UTI) • H influenzae • Typhoid • Shigella	• Klebsiella • Pseudomonas • Proteus • Acinetobacter • Burkholderia • Proteus • Serratia

Q2.7: What are some examples of extended-spectrum penicillins and third-generation cephalosporins?

Answer:

- Amoxicillin
- Ticarcillin
- Ampicillin
- Cefoperazone
- Piperacillin

Q2.8: What are some common examples of beta-lactamase inhibitors?

Answer:

- Clavulanic acid
- Sulbactam
- Tazobactam

Q2.9: What is the drug of choice (DOC) for community-acquired infections, and how is resistance via ESBL managed?

Answer:

- **DOC for community-acquired infections:**
  - **3rd generation cephalosporins:**
    - → Inj. Ceftriaxone
    - → Oral Cefixime
  - **Extended-release spectrum of Penicillin G**
    - → These drugs can be degraded by ESBL (Extended-Spectrum Beta-Lactamase) enzymes. To overcome this resistance, beta-lactamase inhibitors are used in combination

Q2.10: What is the DOC for hospital-acquired infections and bacteria producing the ESBL enzyme?

Answer: Carbapenem

Q2.11: What are carbapenemase-producing bacteria and their types?

Answer:

- Enzymes that degrade carbapenems:
  - NDM-1: E. coli, Klebsiella
  - CRAB: Acinetobacter baumannii
  - CRKP: Klebsiella pneumonia
  - CRPA: Pseudomonas aeruginosa

Q2.12: What is the drug of choice (DOC) in cases resistant to Carbapenems?

Answer: Colistin

Q2.13: What are some examples of combinations of beta-lactamase inhibitors and carbapenems?

Answer:

Vaborbactam	Meropenem
Relebactam	Imipenem

BIG QUESTION 3: What is the role of cephalosporins, their classification, and clinical applications?

Broad Answer: Cephalosporins are beta-lactam antibiotics grouped by generations (1st to 5th) with varying spectrum. They inhibit bacterial cell wall synthesis and are used based on gram-stain profile, resistance, and clinical infection type.

DETAILED QUESTIONS

Q3.1: How are cephalosporins classified by generation and spectrum?

Answer:

Generation	Spectrum	Use	Drugs
1st	Gram-positive	Surgical prophylaxis (>30 min before incision)	Cefazolin (IV), Cephalexin, Cefadroxil
2nd	Anaerobes (e.g., Bacteroides)	Not DOC; metronidazole preferred	Cefaclor, Cefuroxime, Cefamandole
3rd	Gram-negative (Community-acquired)	Meningococci, Gonococci, H. influenza, Typhoid	**Not effective for pseudomonas:** • Cefixime - Oral • Cefpodoxime - Oral • Ceftriaxone (Injection) • Cefotaxime (Injection) **Effective for pseudomonas:** • Cefoperazone • Ceftazidime • Ceftolozane
4th	Gram-negative (Hospital-acquired, ESBL-resistant)	–	Cefepime, Cefpirome
5th	Effective against MRSA (only beta-lactams that are)	–	Ceftaroline, Ceftobiprole

Q3.2: What are cephalosporins with special features or warnings?

Answer:

- Disulfiram-like reaction: Avoid with alcohol
  - Cefoperazone
  - Cefamandole
  - Cefotetan
  - Cefazolin
- Bleeding (↓ fibrin): Cefoperazone
- Biliary excretion (renal safe):
  - Cefoperazone
  - Ceftriaxone
- Neonatal risk: Jaundice/kernicterus with ceftriaxone

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Q3.3: What are the new or special cephalosporins?

Answer:

- Cefiderocol: New drug with siderophore group
- CefopERAzone mnemonic:
  - E = Excessive bleeding
  - R = Renal safe
  - A = Alcohol avoid

Q 3.4: What are the key side effects and precautions associated with the use of Cefoperazone?

Answer:

- Mnemonic: **ERA**
  - **E**- Excessive bleeding
  - **R**- Renal safety
  - **A-** Alcoholics avoid

Q3.5: What organisms are cephalosporins not effective against?

Answer:

- Listeria
- Atypicals (Mycoplasma, Chlamydia)
- MRSA (except 5th gen)
- Enterococci

BIG QUESTION 4: What are the characteristics, uses, and side effects of carbapenems and glycopeptide antibiotics?

Broad Answer: Carbapenems are broad-spectrum beta-lactam antibiotics used for severe hospital-acquired infections, particularly ESBL-producing organisms. Glycopeptides like vancomycin are used for resistant gram-positive infections, including MRSA. Both classes have specific toxicities and unique pharmacokinetics.

DETAILED QUESTIONS

Q4.1: What are the key features of carbapenems?

Answer:

- Resistant to ESBL enzymes
- Reserved for hospital-acquired infections
- Side effects: Neurotoxicity, seizures, nephrotoxicity
- Most toxic: Imipenem
- Combined with Cilastatin (DHP-1 inhibitor) to reduce toxicity

Q4.2: Which Carbepenems are administered via oral and IV?

Answer:

IV	• Imipenem • Meropenem • Doripenem • Ertapenem
Oral	• Faropenem

Q4.3: Name the antibiotics that belong to the Glycopeptide group.

PYQ: NEET PG 2021

Answer:

- Drugs:
  - Vancomycin
  - Teicoplanin
  - Oritavancin
  - Dalbavancin
  - Telavancin

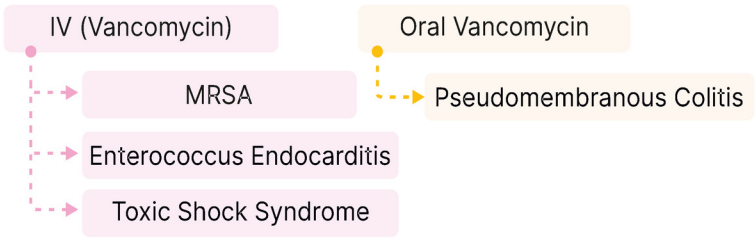
Q4.4: What is Vancomycin used for, and against which organisms is it ineffective?

Answer:

- Vancomycin is given in resistant cases of gram-positive infections
- It is not effective against gram-negative infections (e.g., Typhoid)

Q4.5: In what conditions is Vancomycin used as a drug of choice?

Answer:



Q4.6: What is the drug of choice (DOC) for toxic shock syndrome and why?



Answer:

- To kill bacteria: IV Vancomycin
- To inhibit toxin production: Clindamycin
- Caused by: Superantigens from Staphylococcus and Streptococcus

Q4.7: What are the side effects of vancomycin?

PYQ: FMGE 2020



Answer:

- Ototoxicity
- Nephrotoxicity
- Red Man Syndrome:
  - Caused by rapid IV infusion
  - Due to histamine release → vasodilation and flushing

BIG QUESTION 5: What are the causes, drugs, and treatment strategies for Clostridium difficile diarrhea and membrane-active agents?

Broad Answer: Clostridium difficile infection (CDI) occurs after antibiotics disrupt gut flora. High-risk drugs can trigger it. Treatment includes specific antibiotics and supportive therapies. Membrane-active agents like polymyxins and daptomycin target resistant organisms but have specific limitations.

DETAILED QUESTIONS

Q5.1: What are the high-risk drugs for CDI and why?

Answer:

- Kill normal gut bacteria → allow *C. difficile* overgrowth
- High-risk:
  - Clindamycin (highest)
  - 3rd gen cephalosporins
  - Ampicillin
  - Fluoroquinolones

Q5.2: What are the treatment options for CDI?

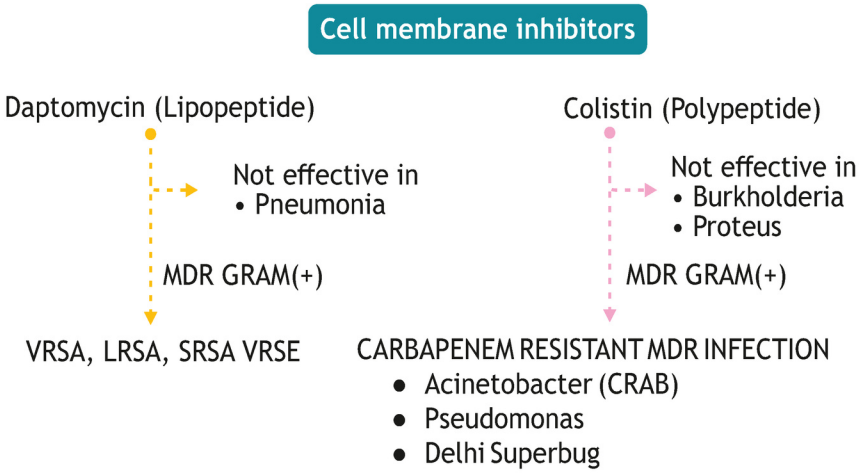
Answer:

- DOC (India): Oral Vancomycin
- Overall DOC (global): Fidaxomicin (not available in India)
- Other options:
  - Metronidazole
  - Fecal microbiota transplant (for recurrent cases)
  - Bezlotoxumab: Monoclonal antibody against toxin B

Q5.3: What are important membrane-active agents and their features?

Answer:

- Colistin (aka polymyxin): Not effective against BSP (Burkholderia, Serratia, Proteus)
- Daptomycin:
  - Reserve drug for MDR gram-positives
  - Not effective in pneumonia (inactivated by surfactant)



BIG QUESTION 6: What are the types, mechanisms, and clinical uses of DNA/nucleic acid synthesis inhibitors?

Broad Answer: These antibiotics inhibit bacterial DNA synthesis by interfering with DNA gyrase, topoisomerase, or through nitric oxide-induced DNA damage. They are used for anaerobic infections, diarrheal diseases, UTIs, and certain STDs.

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DETAILED QUESTIONS

Q6.1: What is the mechanism and classification of nitroimidazoles?

Answer:

- MOA: Donate nitric oxide → cause DNA damage
- Drugs end in -nidazole:
  - Metronidazole
  - Tinidazole
  - Ornidazole
  - Secnidazole (longest acting)
  - Satranidazole (no disulfiram reaction)
  - Benznidazole (DOC: Chagas disease)
  - Nitazoxanide (DOC: HIV-related diarrhea by Cryptosporidium parvum)

Q6.2: In what conditions is Metronidazole the drug of choice?

Answer:

- Mnemonic: **GUPTAA**
  - **G**- Giardiasis
  - **U-** Ulcers by H Pylori
  - **P**- Pseudomembranous Colitis
  - **T**- Trichomonas
  - **A**- Amebiasis
  - **A**- Anaerobes

Q6.3: What are common side effects of Metronidazole?

PYQ: NEET PG 2022

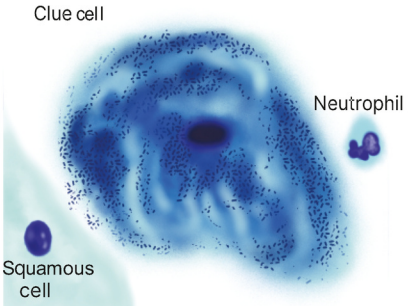
Answer:

- Disulfiram-like reaction: avoid alcohol

Q6.4: What is the DOC in a patient whose vaginal discharge showed Clue cells on histopathology?

Answer:

- Clue cells in vaginal discharge is the case of Gardnerella or bacterial vaginosis
- DOC: Metronidazole



Presence of Clue cell indicated Bacterial vaginosis

Q6.5: A female presents with yellow-green vaginal discharge and a "strawberry cervix." What is the most likely diagnosis and treatment?

Answer:

- **Diagnosis:** Trichomonas vaginalis infection
- **Key features:**
  - Yellow-green, frothy vaginal discharge
  - Unpleasant fishy odor
  - "Strawberry cervix" (punctate hemorrhages on cervix)
- **Treatment:**
- **Drug of Choice (DOC):** Metronidazole
- **Important:** Treat the sexual partner as well to prevent reinfection

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BIG QUESTION 7: What are the features and uses of fluoroquinolones?

Broad Answer: Fluoroquinolones inhibit DNA gyrase and topoisomerase IV, showing broad activity against gram-negative bacteria. They're used for UTIs, diarrhea, typhoid, and respiratory infections. Some are renal safe but hepatotoxic.

DETAILED QUESTIONS

Q7.1: What is the mechanism and key drugs of fluoroquinolones?

Answer:

- MOA: Inhibit DNA gyrase and topoisomerase IV
- Drugs end in -floxacin:
  - Norfloxacin (DOC: spontaneous bacterial peritonitis)
  - Ciprofloxacin (diarrhea, UTI)
  - Levofloxacin (no CYP interaction)
  - Sparfloxacin, Moxifloxacin (longest acting; photosensitivity, QT prolongation)

Q7.2: Which fluoroquinolones are hepatotoxic but renal safe?

Answer:

- P: Pefloxacin
- M: Moxifloxacin
- T: Trovafloxacin

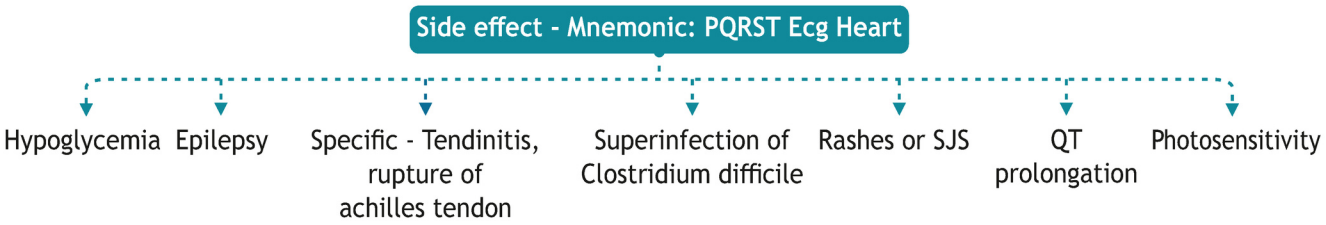
Q7.3: What are fluoroquinolone-related drug interactions and risks?

Answer:

- Ciprofloxacin: CYP inhibitor
  - ↑ Theophylline → seizures
  - ↑ Warfarin → bleeding
- Gatifloxacin: hypoglycemia risk (banned, re-approved for TB)
- Levofloxacin has no CYP interactions and has 100% oral bioavailability

Q7.4: What are the side effects of Fluoroquinolones?

Answer:



Q7.5: What are the drugs of choice (DOC) for treating urinary tract infections (UTIs) in different clinical scenarios, including pregnancy?

Answer:

- **Mild UTI (Non-pregnant):**
  - Trimethoprim-Sulfamethoxazole (Cotrimoxazole)
  - Ciprofloxacin

    Note: These are not safe in pregnancy (contraindicated)

- **UTI in Pregnancy:**
  - Drugs of choice:
    - → Beta-lactams (e.g., Penicillins)
    - → Cephalosporins
- **Severe UTI:**
  - IV Beta-lactams or Cephalosporins

BIG QUESTION 8: What are the different classes of protein synthesis inhibitors and their clinical roles?

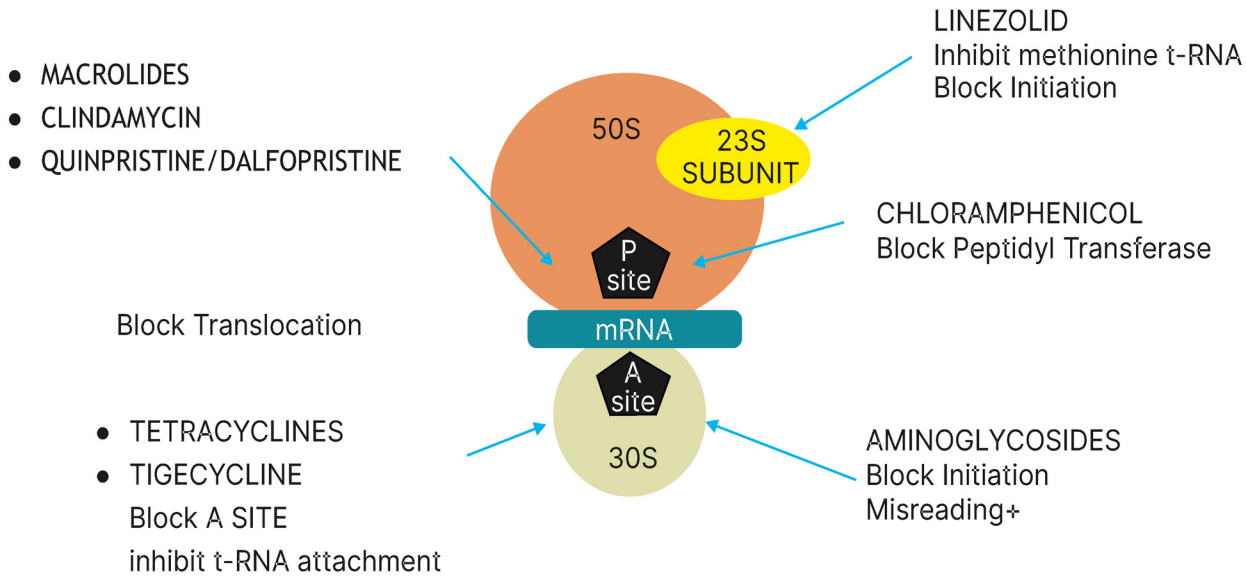
Broad Answer: Protein synthesis inhibitors target the bacterial ribosome, acting on either the 30S or 50S subunit. Their spectrum, toxicity, and bactericidal/static nature vary widely. Some are safe in renal failure, others not.

DETAILED QUESTIONS

Q8.1: Which drugs act on the 30S subunit and what are their features?

Answer:

- Tetracyclines, aminoglycosides, tigecycline: act at A site of 30S
- Aminoglycosides, streptogramins (Quinupristin + Dalfopristin = 30:70): bactericidal



Q8.2: Write briefly about Chloramphenicol.

Answer:

- Chloramphenicol crosses BBB
- It is a Broadspectrum antibiotic
- It causes BM suppression/Aplastic anaemia
- Contraindicated in neonates as it causes Grey baby syndrome



Q8.3: What is Tetracycline used for and what's its adverse effect?

Answer:

- Tetracycline is used to H. pylori infection
- It causes tooth damage by chelating calcium


Mottling of teeth

Q8.4: What conditions are treated with Minocycline?

Answer:

- Leprosy
- Acne

Q8.5: Write briefly about MOA, uses and side effects of Demeclocycline.

Answer:

- MOA: Blocks ADH on Kidney
- Uses: Used in SIADH
- Side effect: Diabetes insipidus

Q8.6: Elaborate on the uses, and contraidications of Doxycycline.

Answer:

- Doxycycline is DOC in:
  - Rickettsia
  - Cholera
  - Chlamydia (LGV, Trachoma)
  - Leptospira
  - Brucella
  - Borrelia (Lyme's disease)
- Contraindications:
  - Contraindicated in pregnancy; bone and cartilage defects may occur as it chelates with calcium
  - Contraindicated in children <8 years Stunting

Q8.7: Which antibiotic is the drug of choice in pregnancy and children?

Answer:

- DOC in pregnancy and children: Azithromycin

Q8.8: What are the newer tetracyclines and their indications?

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Answer:

- Sarecycline: severe acne
- Omadacycline, Eravacycline, Tigecycline:
  - Use: MRSA, abdominal infections, skin/soft tissue infections
  - Renal safe, reserve drug for hospital infections
  - Resistance is uncommon, if occurs it is due to efflux of drugs out of the cell

BIG QUESTION 9: What are the uses and precautions associated with macrolides and other 50S-targeting antibiotics?

Broad Answer: Macrolides act on the 50S ribosomal subunit and are used in respiratory, sexually transmitted, and intracellular infections. Other 50S-targeting drugs include linezolid, clindamycin, and streptogramins. CYP interactions, QT prolongation, and safety in neonates vary.

DETAILED QUESTIONS

Q9.1: What are key uses of macrolides?

Answer:

- Tacrolimus: Used as immunosuppressive, which inhibits calcineurin
- Diphtheria: Erythromycin/Azithromycin
- STDs:
  - Gonorrhea: Ceftriaxone + Azithromycin (2g)
  - Chlamydia (LGV, trachoma): Doxycycline + Azithromycin (1g)
- Others: Leptospira, Brucella, Borrelia
- Used in **BLACS**

Bordetella pertussis or whooping cough

Legionella pneumonia

Atypical or Mycoplasma pneumonia

Chancroid

STD

Q9.2: What are macrolide side effects and pharmacokinetics?

Answer:

Drug	Duration	CYP Inhibition	QT Prolongation	IHPS Risk
Erythromycin	Shortest	Max	Max risk	Yes
Clarithromycin	Medium	Yes	Medium risk	Yes
Azithromycin	Longest	Least	Least risk	Safe

- IHPS: Infantile hypertrophic pyloric stenosis
  - C/I in neonates: Erythro, Clarithro

Q9.3: What are additional 50S inhibitors and their clinical relevance?

Answer:

- Linezolid:
  - MOA: Blocks 23S subunit of 50S ribosome, and inhibits protein synthesis
  - DOC in VRSA, VRE
  - 100% oral bioavailability
  - Renal safe
  - S/E: **COMB** = **C**horioretinitis, **O**ptic neuritis, **M**AO-I, **B**M suppression
- Streptogramins: 30% Quinpristine + 70% Dalfopristin. Used in treating LRSA as IV only

BIG QUESTION 10: What are the features, side effects, and uses of aminoglycosides?

Broad Answer: Aminoglycosides are bactericidal 30S ribosomal inhibitors used for serious gram-negative infections. They are given parenterally and are known for nephrotoxicity, ototoxicity, and neuromuscular blockade.

DETAILED QUESTIONS

Q10.1:What are the drug of choice (DOC) for tuberculosis, examples of topical creams, and the common treatments for Pseudomonas infections?

Answer:

- Given in injection form only (Not absorbed orally)

DOC for TB	Topical creams	T/t of pseudomonas
• Streptomycin o Also, used in plague, and tularemia • Amikacin • Capreomycin • Kanamycin	• Neomycin → Neosporin • Framycetin → Soframycin	• Gentamicin • Amikacin • Tobramycin (Eye drops)

Q10.2: What are the major side effects of aminoglycosides and what is the antidote for aminoglycoside toxicity?

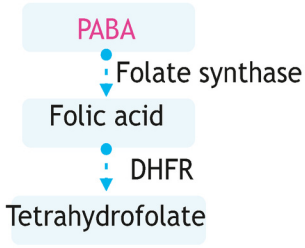
Answer:

- Ototoxicity (high-frequency hearing loss)
- Nephrotoxicity → Renal tubular acidosis (RTA)
- Neuromuscular blockade → contraindicated in myasthenia gravis
- Antidote for toxicity: Calcium gluconate

BIG QUESTION 11: What are antifolate drugs, their mechanisms, and clinical relevance?

Broad Answer: Antifolate drugs inhibit folate metabolism at different steps, either by blocking synthesis (sulfonamides) or DHFR (trimethoprim and others). They are used in burns, UTIs, toxoplasmosis, and certain pneumonias.

DETAILED QUESTIONS



Q11.1: What are folate synthase inhibitors?

Answer:

- Sulfonamides
- Dapsone (used in leprosy, dermatitis herpetiformis)

Q11.2: What are DHFR inhibitors?

Answer:

- Trimethoprim
- Pyrimethamine
- Proguanil
- Combine it with folic acid: Tetrahydrofolate

Q11.3:What is the mechanism of action for the drug combinations Sulfadiazine + Pyrimethamine and Cotrimoxazole, and what are their primary uses?

Answer: Combination of folate synthesis Inhibitors + Dihydrofolate reductase enzyme inhibitors: Bactericidal action

Sulfadiazine + Pyrimethamine	Cotrimoxazole: Trimethoprim + Sulfamethoxazole (1:5)
• DOC: Toxoplasma gondii • In Pregnancy: Spiramycin is given to present placental transmission	• DOC: Pneumocystis, burkholderia

Q11.4: What is the DOC in a burns patient?

Answer:

- Silver sulfadiazine (1%) and Mafenide used as topical creams in burns patient

Q11.5: Which antibiotics are avoided in children?

Answer:

- Grey baby syndrome: Chloramphenicol
- Kernicterus: Sulphonamides, Cotrimoxazole
- Infantile hypertrophic pyloric stenosis: Erythromycin, Clarithromycin (not Azithromycin)

Q11.6: Which antibiotics are safe in renal failure?

Answer:

- Do not require dose reduction & excreted in bile
- Mnemonic: Contra Indicated REnAL Failure Disease o
  - o **C**efoperazone
  - o **I**soniazid
  - o **R**ifampicin
  - o **E**rythromycin
  - o **A**zithromycin
  - o **L**inezolid
  - o 3**FQ**
    - → Pefloxacin
    - → Moxifloxacin
    - → Trovafloxacin
  - o Doxycycline
- Penicillins + Aminoglycosides: Require dose reduction in renal failure cases
  - o Excreted in urine

BIG QUESTION 12: What are the key mechanisms of bacterial resistance and antimicrobial killing kinetics?

Broad Answer: Resistance arises through enzymatic degradation, efflux pumps, or mutation of drug targets. Killing efficacy of antibiotics also varies by concentration, time, and post-antibiotic effect (PAE).

DETAILED QUESTIONS

Q12.1: What is the difference between CDK, TDK, and PAE?

Answer:

- CDK (Concentration Dependent Killing): once daily high dose
- TDK (Time Dependent Killing): multiple daily doses
- PAE: continued killing after drug discontinuation

CDK + LONG PAE	CDK + SHORT PAE	TDK + LONG PAE	TDK + SHORT PAE
Metronidazole	Daptomycin	Azithromycin	Clindamycin
Aminoglycoside		Vancomycin	Penicillin
Rifampicin		FQ	Erythromycin
Streptogramin		Tetracycline	Cephalosporin

Q12.2: What are examples of acquired antibiotic resistance mechanisms?

Answer:

Drug efflux	• Example: **ATT** o Anti-malarial: Chloroquine o Tetracycline o Tigecycline
Enzymatic degradation	• Degrades the antibiotics • Example **ABC** o Aminoglycosides o Beta lactams o Chloramphenicol
Mutation in target	• MRSA: Penicillins can't bind to penicillin-binding proteins-2A • Macrolides (50s ribosome) • FQ **(DNA gyrase)**

Q12.3: What is inherent resistance and examples?

Answer:

Aminoglycosides are never effective against	Colistin is not effective against
• Mnemonic: BATA o Burkholderia o Anaerobes o Typhoid o Acinetobacter	• Mnemonic: BSP o Burkholderia o Serratia o Proteus

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11. ANTIMICROBIALS PART-2

BIG QUESTION 1: What are the pharmacological agents used in the treatment of tuberculosis, and what are their features?

Broad Answer: Tuberculosis is treated using a combination of first-line and second-line anti-tubercular drugs based on disease severity, resistance, and patient tolerance. First-line drugs are the core of standard therapy, while second-line agents are used in resistant TB. Newer drugs are reserved for MDR and XDR TB cases.

DETAILED QUESTIONS

Q1.1: What is the national health program for the treatment of TB?

Answer: National Tuberculosis Elimination Program Guidelines (NTEP)

Q1.2: What are the first-line drugs used in TB treatment?

Answer: First-line drugs: New case of TB

Drugs	ROA	Cidal/Static
H: Isoniazid	Oral	Cidal
R: Rifampicin		
Z: Pyrazinamide		
E: Ethambutol		Static

Q1.3: What are the second-line drugs, and how are they grouped?

Answer: Second-line drugs: Drug-resistant TB

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Group A	• Most effective drugs o Mnemonic: **Be LL** → Be: Bedaquiline → L: Linezolid → L: Levofloxacin/Moxifloxacin
Group B	• Added to complete the regimen o Clofazimine o Cycloserine
Group C	• Additional drugs o Delamanid o Ethambutol o PAS o Thioacetazone

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Q1.4: How is drug-resistant TB classified?

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Answer:

Multi drug resistant TB (MDR)	Resistant to isoniazid and rifampicin
Extensive drug-resistant TB (XDR TB)	Resistant to MDR + BeLL (Bedaquiline Linezolid Levofloxacin/Moxifloxacin)
Pre-extensive drug-resistant TB (Pre XDR TB)	MDR TB with fluoroquinolone resistance

Q1.5: What is the mechanism of action of Isonazid?

Answer:

Prodrug
↓
Enters into the bacteria
↓
Converted to the active form by catalase-peroxidase
↓
Inhibits the mycolic acid synthesis

Q1.6: What is the mechanism of Isoniazid resistance?

Answer: Resistance is due to the mutation of the KATg gene that produces catalase peroxidase.

Q1.7: What is the role of acetylation in the metabolism and resistance of isoniazid?

Answer:

Fast acetylators	Slow acetylators
Risk of resistance to isoniazid	Risk of toxicity to isoniazid

Q1.8: What are the toxic effects of isoniazid?

Answer:

- Insanity: Seizures, hallucinations, and transient memory loss in the brain
  - o Treatment: Vitamin B6
- Neurotoxic: Peripheral neuropathy
  - o Treatment: Vitamin B6
- Hepatotoxic

Q1.9: What is the mechanism of action of Rifampicin?

Answer: Inhibits the RNA polymerase enzyme

Q1.10: What is the basis of resistance to rifampicin, and how is it detected?

Answer:

- Resistance to rifampicin is due to the mutation rpo-B gene
- Detection by: CBNAAT test (Cartridge-based nucleic acid amplification test)

Q1.11: What is the effect of rifampicin on drug metabolism, and how does it alter the efficacy of other drugs?

Answer:

CYP inducer	• Increases the metabolism of other drugs • Contraceptive failure: Degradation of oestrogen
Pglycoprotein inducer	• Increases the excretion of digoxin o Digoxin failure

Q1.12: What are the side effects of rifamipicin?

Answer:

- Hepatotoxic
- Hypersensitivity
  - o Flu-like syndrome
  - o Cutaneous syndrome
  - o Pulmonary Syndrome
- Rifamycin Group (Rifampicin, Rifapentin, Rifabutin, Rifaximin): Orange colour drugs
  - o Orange color skin
  - o Lead to pseudo-jaundice



Q1.13: What are he uses of Rifamycin group of drugs?

Answer:

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Rifampicin	• Recommended in Mnemonic: TB LAMBS o TB o Leprosy o Anthrax o Meningitis prophylaxis o Brucelosis o Staphylococcus aureus: MRSA
Rifapentine	• Approved for the prophylaxis of TB
Rifabutin	• Recommended for mycobacterium avium complex (MAC) infection
Rifaximin	• Recommended for gut sterilisation • DOC o Hepatic encephalopathy o Travellers diarrhoea o Irritable bowel syndrome

Q1.14: What are the features of Pyrazinamide?

Answer:

- Prodrug
- MOA: Inhibits protein synthesis
- The most toxic drug
- Causes gout or hyperuricemia
  - o Lead to gouty arthritis

Q1.15: What is the relative order of side effects caused by anti-tubercular drugs? PYQ: NEET PG 2021

Answer:

- Hepatotoxic: Z>H>R
- Gouty arthritis: Z>E

Q1.16: What is the mechanism of action and the side effects of ethambutol?

Answer:

- MOA: Inhibits Arabinogalactan synthesis
- Side effects
  - Red-green colorblindness
  - Retrobulbar optic neuritis: Reduced visual acuity

Q1.17: How is anti-tubercular treatment modified in special clinical situations? PYQ: INICET 2020, 2022

Answer:

TB in liver disease	• More hepatotoxic: Z>H>R o These drugs are stopped • Start treatment with: Streptomycin + Levofloxacin + Ethambutol
TB in Gout	• Gout: Z>E o Continue the drugs • Treat with Anti-gout medication like allopurinol
TB in HIV	• Most common opportunistic infection in India • 1st treatment: Antitubercular therapy o HIV Treatment: After 2 weeks (ART) • Rifampicin: CYP inducer o Increase the degradation of ART like: 1. Nevirapine 2. Dolutegravir o Dose is increased for the above drugs o Or can replace the rifampicin with rifabutin
Corticosteroids in TB	• Inhibits fibrosis and reduces edema • Recommended in o Meningeal TB o Pleural TB o Spinal TB • Contraindicated in: Intestinal TB o Causes perforation of intestine
TB in Pregnancy	• All are safe drugs: HRZE • Contraindicated: Aminoglycosides o Streptomycin o Amikacin o Kanamycin

Q1.18: What are the drugs approved for the prophylaxis of TB?

Answer:

Four combinations are approved

- Isoniazid
- Rifampicin
- Isoniazid + Rifampicin

} Recommended daily

- Isoniazid + Rifapentine: Once a weekly

Q1.19: What are the newer drugs for drug-resistant TB, and their features?

Answer:

Bedaquiline	• Reduces ATP production by inhibiting the ATP synthase enzyme • Side effect: QT prolongation • Treatment: MDR TB • Duration: 24 weeks only • Food increases the absorption • Given in all age groups • Shows cross-resistance with clofazimine
Clofazimine	• Recommended for TB and leprosy • Side effects: Ichthyosis • Shows cross-resistance to bedaquiline
Cycloserine	• Resistant to alanine racemase enzyme • Side effect: CNS problems o Psychosis o Depression o Increase the risk of suicides
Delamanid and Pretomanid	• MOA: Inhibits mycolic acid synthesis • Side effect: o Delamanid: QT prolongation o Pretomanid: Peripheral neuropathy
Ethionamide	• Side effects: o Erectile dysfunction o Thyroid abnormality → Hypothyroid goiter
Thioacetazone	• Contraindicated in HIV o Causes allergic reaction • Bacteriostatic drug

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Q1.20: Which drug causes the given skin condition?



Answer: Side effects of Clofazime- Ichthyosis and hyperpigmentation.

Q1.21: Which drug causes the given condition?



Answer: Side effects of Ethinamide- Hypothyroid goiter

BIG QUESTION 2: What is the treatment of leprosy, and what are its important clinical and pharmacological features?

Broad Answer: Leprosy is a chronic infectious disease caused by Mycobacterium leprae, primarily affecting skin and peripheral nerves. It is treated under the NLEP (National Leprosy Eradication Programme) using Multidrug Therapy (MDT). Cases are classified as paucibacillary (PB) or multibacillary (MB) based on skin lesion count. MDT may lead to leprosy reactions like Type I (reversal) and Type II (ENL), which require prompt management.

DETAILED QUESTIONS

Q2.1: What is the national plan for leprosy?

Answer:

- National Leprosy Eradication Program (NLEP)
- Treatment uses multidrug therapy (MDT) according to the program

Q2.2: How is leprosy classified, and what are its features?

Answer: Leprosy is divided into 2 groups:

Paucibacillary leprosy	• Skin lesions: 1-6
	• Nerve thickening: 0-1
	• Treatment: RDC for 6 months
	  o Rifampicin: Once a month (Supervised)
	  o Dapsone: Daily (Unsupervised)
	  o Clofazimine: Both supervised and unsupervised

Multibacillary leprosy	• Skin lesions: >6 • Nerve thickening: ≥2 • Treatment: RDC for 12 months

Q2.3: What are the first-line drugs used in the management of leprosy under MDT?

Answer:

- Dapsone
- Rifampicin
- Clofazimine

Q2.4: What is the mechanism of action, other uses, and side effects of Dapsone?

Answer:

- MOA: Antifolate drug
- It is the DOC for: Dermatitis herpetiformis (Seen in Celiac disease)
- Side effect: Hemolytic Anaemia (Most common)



Dermatitis herpetiformis

Q2.5: What are the 2nd line drugs used in the treatment of leprosy?

Answer:

- New drugs include
  - Clarithromycin
  - Ofloxacin
  - Minocycline
  - Ethionamide
- Bactericidal drugs
  - Rifampicin
  - Ofloxacin

Q2.6: What are the hypersensitivity reactions associated with MDT? How is it managed?

Answer:

Type 1 lepra reaction	• Reversal reaction o Type 4 hypersensitivity
Type 2 lepra reaction	• Erythema nodosum leprosum (ENL) o Type 3 hypersensitivity

- Continue the MDT and add prednisolone.
- Type 2 ENL: Add thalidomide in Prednisolone-resistant cases

BIG QUESTION 3: What are the different classes of antifungal drugs, their mechanisms of action, and clinical significance?

Broad Answer: Antifungal drugs are classified based on their target in the fungal cell: some disrupt the cell membrane (e.g., polyenes, azoles), others inhibit cell wall synthesis (e.g., echinocandins), nucleic acid synthesis (e.g., flucytosine), or mitosis (e.g., griseofulvin). These agents are used based on fungal species, infection site, and resistance patterns. Broad- and narrow-spectrum drugs are chosen accordingly for superficial or systemic fungal infections.

DETAILED QUESTIONS

Q3.1: What is the fungal cell wall made of?

Answer: Beta-glucan

Q3.2: What is the composition of the fungal cell membrane?

Answer:

- The fungal cell membrane is made of ergosterol
- Antifungal drugs acting on cell membranes inhibit ergosterol

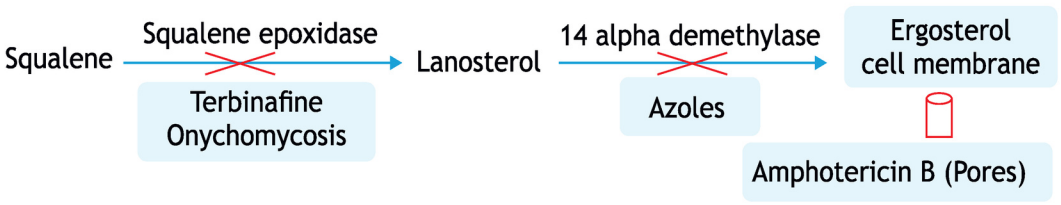
Q3.3: How are Antifungal drugs grouped?

Answer: Based on the target, antifungals are grouped into:

Cell wall Inhibitors	• MOA: Inhibits beta glucan synthase o Caspofungin o Anidulafungin o Micafungin • ROA: IV • Recommended in invasive cases of Candida and Aspergillosis • Advantage: Renal safe
DNA synthesis Inhibitors	• Drug: Flucytosine • MOA: Decreases thymidine synthesis o Causes thymidine-deficient cell death
Microtubule inhibitors	• ROA: Oral • Drug: Griseofulvin PYQ: FMGE 2021 • DOC: Tinea capitis o Used in all types except Tinea Versicolor

Q3.4: Describe the synthesis of ergosterol. What are the drugs inhibiting ergosterol synthesis?

Answer:



- Terbinafine: Inhibits squalene epoxidase
  - o DOC: Onychomycosis
- Azoles: Inhibit the 14 alpha demethylase enzyme
- Amphotericin B: Creates pores on the cell membrane

Q3.5: How are azole antifungal drugs classified based on their route of use?

Answer:

Topical only: Treat candidiasis	Topical + Systemic	Systemic only
Clotrimazole: Vulvovaginal Candidiasis (VVC) ROA: Pessary, Suppository	Ketoconazole: DOC for dandruff	Voriconazole
Luliconazole		Itraconazole
Osteoconazole		Posaconazole
Sertaconazole: Has antipruritic effect	Fluconazole	Isavuconazole
Efinaconazole		
Miconazole		

Q3.6: Azole antifungals are metabolized by which hepatic enzyme?
Answer: CYP2C19

Q3.7: Which azole drug has the maximum CYP inhibiting action?
Answer: Ketoconazole

Q3.8: What are the adverse effects of ketoconazole?
Answer:

- Adrenal insufficiency
- Gynecomastia
- Menstrual abnormality

Q3.9: What are some important side effects and contraindications of azole antifungals?
Answer:

- Fluconazole undergoes renal excretion
  - o Contraindicated in Renal disease
- Voriconazole:
  - o Visual disturbances
  - o QT prolongation
- Itraconazole: Skin cancer

Q3.10: What are the different groups of fungi and the types of infections they cause?
Answer:

Yeast like fungi	Dimorphic fungi	Molds	Mucormycosis
• Candida • Cryptococcal • Coccidioidomycosis	• Histoplasmosis • Blastomycosis • Sporotrichosis • Para coccidioidomycosis	• Aspergillosis	

YOURWISH

Q3.11: What is the DOC for systemic fungal infections?

Answer: Amphotericin B

Q3.12: What class of antifungals are preferred for maintenance therapy?

Answer: Azoles

Q3.13: What are the preferred antifungal agents for specific fungal pathogens?

Answer:

Yeast like fungi	• Fluconazole
Dimorphic fungi	• Iraconazole
Moulds	• DOC: Voriconazole
Mucormycosis/Aspergillosis	• DOC: Amphotericin B o Azoles → Posaconazole → Isavuconazole

Q3.14: What is the mechanism of action and the side effects of Amphotericin B?

Answer:

- Most effective and broad-spectrum drug
- **MOA:** Creates pores on the ergosterol cell membrane
- **Side effects:** IV Amphotericin B-
  - o Allergy/infusion reaction
    - → Treatment: Antihistamines
    - → Pethidine: Opioid
  - o Azotemia: Nephrotoxic
  - o Anaemia: Injections of erythropoietin

Q3.15: What are topical antifungals and their uses?

Answer:

- Natamycin: Eye drops
  - o DOC: Fungal Keratitis
- Nystatin: Oral paint
  - o DOC: Oral thrush or candida infection

Q3.16: What is the treatment of Cryptococcal meningitis?

Answer: L-AMB + Flucytosine

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Q3.17: What are the different formulations of Amphotericin B?

Answer:

C-AMB	Conventional Amphotericin B
AMB-CD	Amphotericin B colloid Dispersion

AMB-LC	Amphotericin B lipid complex
L-AMB	• Liposomal amphotericin B • Longest-acting and safest drug

Q3.18: What are the different nail lacquers used in onychomycosis?

Answer:

- Ciclopirox olamine
- Amorolfine

Q3.19: Which antifungal is safe in pregnancy?

Answer:

- Safest: Amphotericin B
- Contraindicated: Azoles

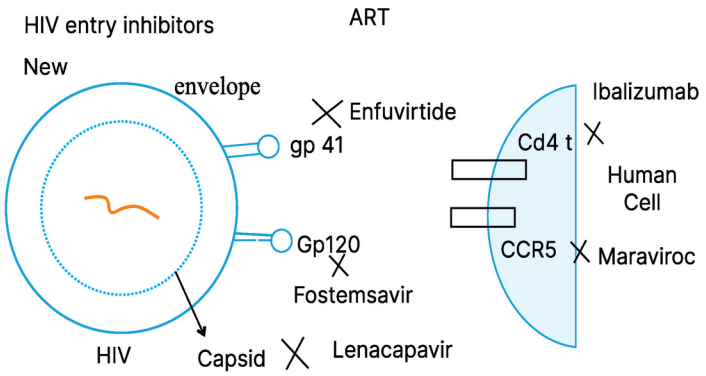
BIG QUESTION 4: What are the different classes of antiretroviral drugs used in HIV treatment, and how do they target various stages of the viral life cycle?

Broad Answer: HIV treatment involves the use of combination antiretroviral therapy (cART) that includes drugs acting at multiple stages of the HIV life cycle. These classes include entry inhibitors, reverse transcriptase inhibitors (NRTIs & NNRTIs), integrase inhibitors, and protease inhibitors. Each class targets a specific step, such as viral entry, reverse transcription, integration into host DNA, or viral protein processing. Drug selection depends on viral load, resistance profile, and patient factors.

DETAILED QUESTIONS

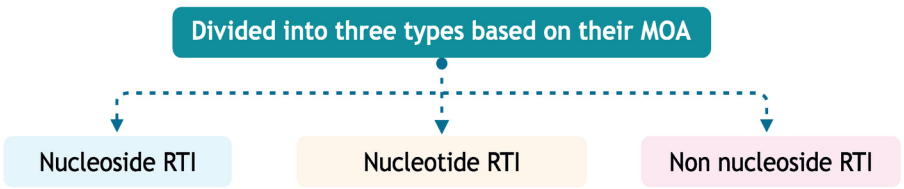
Q4.1: What are the HIV entry inhibitors, and at which stage of the viral life cycle do they act?

Answer:



Q4.2: What are reverse transcriptase inhibitors (RTIs), and how are they classified?

Answer: Inhibits the conversion of single-stranded RNA to dsDNA



Q4.3: How are RTIs classified, and what are their features?

Answer:

Nucleoside RTI (NRTI)	• Drugs PYQ: NEET PG 2021 o Z: Zidovudine o A: Abacavir o D: Didanosine o S: Stavudine • Zidovudine: Bone marrow suppression, myopathy o Contraindicated in: Severe anemia → Hb: <9 gm/dl o Treatment: Erythropoietin injections
	• Pancreatitis: Didanosine (Maximum risk) • Abacavir o Test HLA B 5701 before the administration (Positive: Severe allergy) • Stavudine: Causes lactic acidosis, lipodystrophy syndrome PYQ: FMGE 2022
Nucleotide RTI (Nt-RTI)	• Drug: Tenofovir o Main drug to treat HIV o DOC: Hepatitis B virus o Side effect: Nephrotoxic o C/I: Renal disease (high creatinine), Children o Causes damage to PCT of nephron → Syndrome: Fanconi syndrome → Leads to phosphate loss → Hypophosphatemic rickets, osteoporosis • Renal failure + Children: Replace tenofovir with zidovudine
Non nucleoside RTI (NNRTI)	• Nevirapine: DOC in neonates o Neonatal prophylaxis from HIV mother (PTCT) • Efavirenz: Neurotoxic o Causes peripheral neuropathy and depression • Etravirine • Doravirine: All side effects of rashes and Steven Johnson syndrome

Q4.4: What are the mechanisms of action and uses of protease inhibitors?

Answer:

- Ends with the word -navir
- MOA: Inhibits the assembly of viral proteins
  - o Other Name: Packaging of viral proteins
- Drugs:
  - o Ritonavir: Maximum CYP3A4 inhibiting action PYQ: NEET PG 2019
  - o Indinavir
  - o Saquinavir
  - o Tipranavir
  - o Atazanavir: Causes jaundice or an increase in bilirubin level

YOURWISH

Q4.5: What is lipodystrophy syndrome?



Answer:

It is a side effect of protease inhibitors

- Obesity
- Type 2 DM: Insulin resistance
- Dyslipidemia
- Breast hypertrophy

Q4.6: What are the specific side effects of protease inhibitors?

Answer:

- Renal stone (Nephrolithiasis): Indinavir
- Hyperbilirubinemia: Atazanavir
  - Causes jaundice
- QT prolongation: Saquinavir
- Hypertension and intracranial hemorrhage: Tipranavir

Q4.7: What are boosted protease inhibitors?

Answer:

- Low-dose ritonavir is combined with other protease inhibitors
  - Lopinavir
  - Darunavir
  - Not with nelfinavir

Q4.8: Give examples of integrase inhibitors and their side effects.

Answer:

- Ends with the word -gravir
  - Bictegravir
  - Cabotegravir
  - Dolutegravir
  - Raltegravir
- **Side effects**
  - Rashes
  - Stevens-Johnson syndrome
- Dolutegravir + Rifampicin: Increase the dose of dolutegravir

Q4.9: What is the ART regimen of choice?

Answer:

- TLD regimen
  - Tenofovir: Contraindicated in children <10 years of age and renal disease
  - Replaced with zidovudine
  - Lamivudine
  - Dolutegravir

Q4.10: What is the post-exposure prophylaxis (PEP) for HIV?

Answer:

- Accidental contact with HIV-positive secretions

YOURWISH

- Post-exposure Prophylaxis: Within 72 hrs
- Duration: 28 days or 1 month
- Same 3 drug combination: TLD

Q4.11: What is the protocol for prophylaxis in a newborn born to an HIV-positive mother?

Answer:

Low risk infants	• Maternal HIV after 32 weeks • Having <1000 copies of HIV	• Syrups of nevirapine to neonate o Duration: 6 weeks
High risk infants	• Maternal HIV after 32 weeks • Having > 1000 copies of HIV	• Syrups of nevirapine + Zidovudine o Duration: 6 weeks

BIG QUESTION 5: What are the drugs used in the treatment of Hepatitis B and C, and how are treatment regimens selected based on viral type and genotype?

Broad Answer: Hepatitis B is treated using nucleos(t)ide analogues and pegylated interferon, while Hepatitis C therapy includes direct-acting antivirals (DAAs) targeting viral enzymes. Pangenotypic regimens for HCV allow genotype-independent treatment using fixed-dose combinations.

DETAILED QUESTIONS

Q5.1: What is the treatment protocol for hepatitis B virus (HBV)?

Answer:

- DOC: Reverse transcriptase inhibitors
- Tenofovir: First line
- Entecavir: First line
- Lamivudine: Second line
- Route: Oral

Q5.2: How is hepatitis C virus (HCV) infection treated?

Answer:

- DOC: NS inhibitors
- Second-line drugs: Ribavirin
- Route: Oral

Q5.3: Which antiviral drugs are used in the treatment of more than one viral infection?

Answer:

- Common drug for both HBV and HCV: Interferon alpha
  - o Interferon beta: DOC in multiple sclerosis
- Common drugs for both HIV and HBV: Tenofovir, Lamivudine
- Common drug for respiratory syncytial virus and HCV: Ribavirin
  - o Treatment: Aerosols of Ribavirin
  - o Prophylaxis: Palivizumab

Q5.4: What is the pan-genotyping treatment regimen used in HCV?

Answer:

- Sofosbuvir + Velpatasvir
- Sofosbuvir + Velpatasvir + Voxilaprevir
- Glecaprevir + Pibrentasvir

Q5.5: How can antiviral drugs be classified based on common suffixes in their names?

Answer:

- Buvir: NS-5B inhibitor
- Asvir: NS-5A inhibitor
- Previr: NS3/4 inhibitor

BIG QUESTION 6: What are the drugs used in the treatment of herpes group viruses, and how is drug resistance managed?

Broad Answer: Herpes viruses are DNA viruses treated primarily with Acyclovir. Other antivirals like valacyclovir, famciclovir, and ganciclovir are also used. In cases of resistance to Acyclovir or Ganciclovir, Foscarnet is the drug of choice.

DETAILED QUESTIONS

Q6.1: What type of virus is the herpes group classified as?

Answer: Herpes viruses are DNA viruses

Q6.2: What is the drug of choice for the herpes virus infections?

Answer: Acyclovir

Q6.3: What are the other drugs used in the treatment of the herpes virus infections?

Answer:

- Valaciclovir
- Penciclovir
- Famciclovir

Q6.4: Which drug is used to treat HSV-1, HSV-2, and VZV infections?

Answer: Acyclovir is used to treat HSV-1, HSV-2, and VZV.

Q6.5: What are the side effects of Acyclovir?

Answer:

- Nephrotoxic
- Neurotoxic
  - Not myelotoxic

Q6.6: What drug is used when there is resistance to Acyclovir and Ganciclovir?

Answer:

- Foscarnet
  - Not myelotoxic

- Cidofovir
  - DOC: Respiratory papillomatosis

Q6.7: What is the DOC for cytomegalovirus infection?

Answer:

- DOC: Ganciclovir and Valganciclovir
- Side effect: Myelotoxic

Q6.8: What is Bell's palsy, and how is it treated?

Answer:

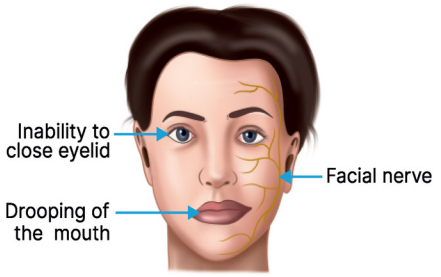
- The facial nerve is paralyzed
- DOC: Prednisolone (Corticosteroids)
- Exact cause: Suspect the herpes virus
  - Acyclovir
  - Valaciclovir

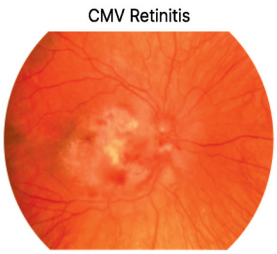
Q6.9: What is cytomegalovirus retinitis, and its treatment recommendations?

PYQ: FMGE 2022

Answer:

- Hemorrhage in the retina
- DOC: Ganciclovir
  - Route: Intravitreal
  - Resistant
    - → Foscarnet
    - → Fomivirsen: Another drug





Q6.10: What are the drugs used for the treatment of smallpox and monkeypox?

Answer:

- DOC: Brencidofovir
- Another drug for monkeypox: Tecovirimat

BIG QUESTION 7: What are the drugs used in the treatment and prevention of influenza virus infection?

Broad Answer: Influenza is an RNA virus. Neuraminidase inhibitors such as oseltamivir and zanamivir are used in the treatment and prophylaxis of influenza A and B. These drugs act by inhibiting the release of new viral particles. M2 ion channel blockers like amantadine and rimantadine were previously used for influenza A. However, due to widespread resistance, they are now considered obsolete.

DETAILED QUESTIONS

Q7.1: What is another name for the influenza virus?

Answer: The influenza virus is also known as the flu virus.

Q7.2: What are the two major drug classes used against the influenza virus?

Answer:

- M2 Proton Channel Inhibitors
- Neuraminidase Inhibitors

Q7.3: What are M2 proton channel inhibitors, and how do they act?

Answer:

- M2 proton channel inhibitors act by inhibiting the entry of the virus.
- The M2 protein is present on the envelope of the influenza virus.
- Examples:
  - Amantadine (also used in Parkinson's disease)
  - Rimantadine
- They are effective against Influenza A.

Q7.4: What are neuraminidase inhibitors, and how do they act?

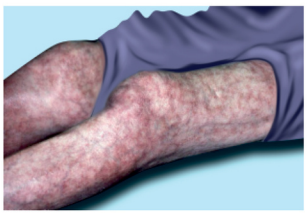
Answer:

- Neuraminidase inhibitors act by inhibiting the exit of the virus from infected cells.
- Examples and routes:
  - Oseltamivir (oral)
  - Zanamivir (nasal drops)
  - Peramivir (parenteral)
- These drugs are the drug of choice for influenza, swine flu, and avian flu.

Q7.5: What is the drug that is used for both influenza and Parkinson's disease, and what are its side effects?

Answer:

- Amantadine is used for both influenza and Parkinson's disease.
- Side effect: Livedo reticularis (vasodilation)



BIG QUESTION 8: What are the drugs used in the treatment of helminthic infections?

Broad Answer: Albendazole is the drug of choice for most helminthic infections, including cestodes and nematodes. Niclosamide is used as a second-line agent for cestodes. Specific helminths such as Echinococcus, Neurocysticercosis, Fasciola hepatica, Strongyloides, Onchocerca, Loa loa, and Dracunculus have their preferred treatments. Additional agents like ivermectin, permethrin, and diethylcarbamazine are used for selected conditions.

DETAILED QUESTIONS

Q8.1: What are cestodes and trematodes?

Answer:

Cestodes	Trematodes
• Other Name: Tapeworms • It includes o Taenia solium: Pork tapeworm o Taenia saginata: Beef tapeworm o Hymenolepsis Nana: Dwarf tapeworm o Diphyllobothrium latum: Fish tapeworm	• Other Name: Flukes • It includes o Paragonimus o Schistosoma

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Q8.2: What is the drug of choice for both cestodes and trematodes?
Answer: Praziquantel

Q8.3: What is the second-line drug for cestodes?
Answer: Niclosamide

Q8.4: What is the drug of choice for Echinococcus?
Answer: Albendazole

Q8.5: What is the drug of choice for Neurocysticercosis?
Answer: Albendazole + Corticosteroids + Phenytoin

Q8.6: What is the drug of choice for Fasciola hepatica?
Answer: Triclabendazole

Q8.7: What is the drug of choice for nematodes?
Answer: Albendazole or Mebendazole

Q8.8: What is the drug of choice for mass deworming in children?
Answer: Albendazole

Q8.9: What are the common names of various nematodes?
Answer:

Ascariasis	Roundworm
Necator	Hookworm
Ancylostoma	Hookworm
Enterobius	Pinworm
Trichuris	Whipworm
Trichinella	-

Q8.10: What are the exceptions to the standard treatment of helminthic infections? PYQ: FMGE 2021
Answer:

- DOC for Strongyloides, Onchocerca volvulus: Ivermectin
  - Treatment of Scabies (DOC: 5% Permethrin)
- DOC for Lymphatic filariasis, Loa-Loa: Diethylcarbamazine
- DOC for Dracunculus: Metronidazole

BIG QUESTION 9: What is the pharmacological treatment of malaria and its special considerations?
Broad Answer: Antimalarial drugs are used based on the species of Plasmodium, chloroquine sensitivity, and clinical setting. Chloroquine and ACT are the primary treatments, with primaquine added for radical cure or to prevent transmission. Drug choices also vary for complicated malaria, pregnancy, G6PD deficiency, and prophylaxis in travelers. Artemisinin-based combinations are recommended for resistant falciparum, and special regimens exist for different patient categories.

DETAILED QUESTIONS

PYQ: FMGE 2020, 2021, 2022
PYQ: NEET PG 2020
PYQ: INICET 2023

Q9.1: What is the national program for the treatment and control of malaria?

Answer: Treatment guideline: National vector-borne disease control program

Q9.2: How is P.vivax/ovale malaria treated?

Answer:

- P.vivax/ovale: Chloroquine + Primaquine
  - Primaquine: Radical cure (Hypnozoite & Gametocidal)
  - Chloroquine: Clinical Cure (Erythrocyte)

Q9.3: What is the treatment for P.falciparum malaria?

Answer:

- P.falciparum: Chloroquine resistant
- Treatment: ACT + Primaquine (Gametocidal agent)

Q9.4: What are the main drugs used in Artemisinin combination therapy (ACT)?

Answer:

- All states of India: Artesunate + Sulfadoxine/pyrimethamine
- North-eastern states: Artemether + Lumifantrine

Q9.5: What are the mechanisms of action of primaquine?

Answer:

- Gametocidal agent: Against all the species of Plasmodium
- Hypnozoitocidal

Q9.6: What is Tafenoquine?

Answer:

- Tafenoquine is a Hypnozoitocidal agent
- Recommended in case of P.vivax/ovale

Q9.7: What is the prophylaxis protocol for malaria in travelers?

Answer:

Country: Non-endemic	• DOC: Chloroquine o Dose: 600 mg weekly
Country: Endemic	• DOC: Mefloquine (250 mg weekly) or Doxycycline (100 mg daily)

Q9.8: What antimalarials are used in patients with G6PD patients?

Answer:

- Antimalarials cause hemolysis of RBCs
- Unsafe: Mnemonic PPQ
  - Primaquine
  - Proguanil
  - Quinine

- Safer: Chloroquine
- Safest: Mefloquine

Q9.9: What is the treatment protocol for complicated malaria?

Answer:

- Other Name: Acute severe malaria
- Injectable drugs are recommended
- DOC: IV Artesunate
  - Allergy: IV quinine + 5% dextrose solution (Hypoglycemia)

Q9.10: How is malaria treated during pregnancy?

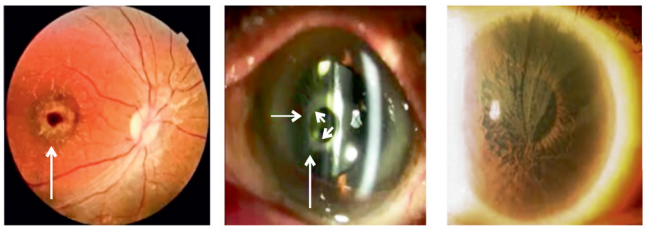
Answer:

- Safest drug: Chloroquine or Quinine + Clindamycin
- C/I in the first trimester: Artemisinin combination therapy
- C/I in all trimesters: Primaquine
- **P.vivax/ovale:**
  - Only chloroquine is given
  - Do not give radical cure (Primaquine)
- **P.falciparum:**
  - First trimester: Quinine + Clindamycin
  - 2nd /3rd trimester: Artesunate combination therapy
- DOC for complicated Malaria: IV Artesunate
  - Recommended in all trimesters

Q9.11: What are the ocular side effects of Chloroquine?

Answer:

- Bull's-eye retinopathy
- Lens: It causes anterior subcapsular cataract
- Cornea: It causes vortex keratopathy
  - Also seen with amiodarone



Q9.12: What are the side effects and contraindications of antimalarial drugs?

Answer:

- Hypoglycemia, cinchonism/Ototoxicity: Quinine
  - Obtained from cinchona
- QT prolongation: Quinine, Lumefantrine
- C/I in cerebral malaria: Mefloquine

BIG QUESTION 10: What are the drugs used in the treatment of Entamoeba histolytica infections and their clinical applications?

Broad Answer: Entamoeba histolytica causes amoebiasis, which includes luminal infections, intestinal dysentery, and liver abscesses. Treatment is based on the site of infection. Luminal agents like paromomycin are used for asymptomatic carriers, while metronidazole is preferred for invasive disease. In liver abscess, a combination of metronidazole and chloroquine is used. Certain drugs, like iodoquinol, can have specific adverse effects.

DETAILED QUESTIONS

Q10.1: What condition is caused by Entamoeba histolytica?

Answer: It causes Amoebiasis.

Q10.2: What is the drug of choice for Luminal Amoebiasis?

Answer

- **Paromomycin** (DOC)
- Diloxanide furoate
- Quiniodochlor
  - S/E: Subacute myelo-optic neuritis
- Iodoquinol

Q10.3: What is the pathology seen in Amoebic dysentery, and how is it treated?

Answer

- Damage to the intestine: Flask-shaped ulcer
- DOC: Metronidazole

Q10.4: What is the treatment of Amoebic liver abscess?

Answer: DOC: Metronidazole + Chloroquine

BIG QUESTION 11: What are the clinical types and drug treatments of African and South American Trypanosomiasis (Sleeping Sickness)?

Broad Answer: African Trypanosomiasis, also known as Sleeping Sickness, is classified into West and East African types, while a separate form exists in South America. Each type is caused by a specific subspecies of Trypanosoma and has its drug of choice. The classification and treatment are summarized in a comparative table.

DETAILED QUESTIONS

Q11.1: What are the types of Trypanosomiasis and their respective drugs of choice?

Answer:

West African type	• Causative organism: Trypanosoma brucei gambiense • Early stage: Pentamidine • Late stage: Eflornithine + Nifurtimox • Fexinidazole: Effective in both state • Eflornithine: Treat hirsutism
East African type	• Causative organism: Trypanosoma brucei rhodesiense • Early stage: Suramin • Late stage: Melarsoprol
South American type	• Other Name: Chagas disease • Causative organism: Trypanosoma cruzi • DOC: Benznidazole o Nifurtimox

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BIG QUESTION 12: What is Pneumocystis jirovecii pneumonia, and how is it treated?

Broad Answer: Pneumocystis jirovecii is a serious respiratory infection seen in immunocompromised individuals. Early diagnosis and appropriate prophylaxis or treatment are essential. Management typically includes antimicrobial drugs suited to the immune status of the patient.

DETAILED QUESTIONS

Q12.1: What type of infection is caused by Pneumocystis jirovecii?

Answer: It causes opportunistic pneumonia.

Q12.2: In which patients does Pneumocystis pneumonia most commonly occur?

Answer: In HIV-positive individuals with a CD4 count <200/mm^3.

Q12.3: What is the drug of choice for both treatment and prophylaxis of Pneumocystis pneumonia?

Answer: Cotrimoxazole

Q12.4: What is the second-line treatment for resistant Pneumocystis infections?

Answer: Pentamidine (given as IV or aerosol)

BIG QUESTION 13: What is kala-azar, and how is it treated?

Broad Answer: Kala-azar is a parasitic disease seen in certain endemic regions. Diagnosis involves rapid testing methods, and pharmacological treatment includes specific antileishmanial agents. Drug selection may vary based on patient factors like age or comorbidities

DETAILED QUESTIONS

Q13.1: What is the other name for Kala-azar?

Answer: Visceral Leishmaniasis

Q13.2: What is the causative agent of Kala-azar?

Answer:

- Leishmania donovani
- Endemic to India

Q13.3: What test is used for the diagnosis of Kala-azar?

Answer: K39 (recombinant K39 antigen) Rapid Diagnostic Test

Q13.4: What are the drugs used in Kala-azar?

Answer: Mnemonic: LAMPAS

LA	• Liposomal amphotericin B o Dose: 10 mg/kg IV once
M	• Miltefosine: Oral
P	• Paromomycin

A	• Amphotericin B (Older preparations)
S	• S: Sodium stibogluconate o Least preferred o Dose: 20 mg/kg IV for 1 month o Have antimony

Q13.5: What is the treatment of post-kala-azar dermal leishmaniasis (PKLD)? PYQ: FMGE 2019

Answer: DOC: Oral Miltefosine



Q13.6: What are the contraindications of Miltefosine?

Answer:

- Highly teratogenic drug
- C/I:
  - o Pregnancy
  - o Children
    - → DOC in children: Liposomal amphotericin B (L-AMB)

12. ANTICANCER AND IMMUNOMODULATORS

BIG QUESTION 1: Explain the classification and core mechanisms of anticancer drugs, including their major types, key examples, and common toxicities.

PYQ: INICET 2023

Broad Answer:

- Anticancer drugs include cytotoxic agents (cell cycle-specific or nonspecific), targeted therapies (TKIs, monoclonal antibodies), and immunomodulators. Cytotoxics kill rapidly dividing cells, causing toxicities like bone marrow suppression (except VABC), mucositis, alopecia, and infertility
- Targeted therapies act on specific molecules (e.g., imatinib, rituximab) with fewer off-target effects. Supportive care uses growth factors, antidotes, and tumor lysis management

DETAILED QUESTIONS

Q1.1: List the main types of anticancer drugs.

Answer

- Cytotoxic drugs
- Targeted therapy
  - Tyrosine kinase inhibitors and New drugs
  - Monoclonal antibodies
- Immunosuppressant and Thalidomide

Q1.2: What is the MOA of cytotoxic drugs?

Answer : Cytotoxic drugs kill any rapidly dividing cells in our body

Q1.3: What are the common toxicities of cytotoxic drugs?

Answer:

PYQ: AIIMS 2020

- Bone marrow suppression
- Mucosal ulcer in the GIT
- Alopecia
- Teratogenic
- Azoospermia/anovulation → Infertility

Q1.4: Which cytotoxic drugs do not cause bone marrow suppression?

Answer:

- All cytotoxic drugs except Mnemonic: **VABC**
  - **V**incristine
  - **A**sparaginase enzyme
  - **B**leomycin
  - **C**hlorambucil

YOURWISH

Q1.5: What are the main consequences of bone marrow suppression and their treatments?

Answer:

Anemia	• Decreased RBC PYQ: INICET 2019 • Treatment: Recombinant form of Erythropoietin injections
Leucopenia	• Decreased WBC PYQ: FMGE 2023 • Treatment: Filgrastim o Recombinant form of G-CSF (Granulocyte colony stimulating factor) injection
Thrombocytopenia	• Decrease in platelet count PYQ: NEET PG 2023 • Treatment: Oprelvekin, (Rec. IL-11) injection

Q1.6: All the drugs given for the treatment of bone marrow suppression are administered by which route?

Answer: Injections

Q1.7: What do mucosal ulcers cause in the GIT, and how are they treated?

Answer:

- Causes diarrhea
- Treatment: Palifermin injection (Recombinant form of Keratinocyte Growth Factor)

Q1.8: What are the electrolyte changes in Tumor lysis syndrome and their treatments?

Answer:

- ↑ Uric acid: Gout
  - o Treatment: Allopurinol
  - o Allopurinol-resistant cases: Rasburicase (Degrades uric acid)
- ↑ Potassium & ↑ Phosphate
  - o Hemodialysis
- ↓ Calcium
  - o Hypocalcemia
  - o Treatment: Calcium gluconate

Big Question 2: How are cytotoxic agents classified, and what is their MOA?

Broad Answer:

- **Cytotoxic agents are classified into:**
  - o Cycle non-specific (CCNS) drugs kill cancer cells at any phase of the cell cycle
  - o Cell cycle-specific (CCS) drugs kill cancer cells at a specific phase of the cell cycle

DETAILED QUESTIONS

Q2.1: What is the MOA of cell cycle non-specific drugs?

Answer:

- Cycle non-specific (CCNS) drugs kill cancer cells at any phase of the cell cycle
- Causes direct DNA damage to cancer cells

Q2.2: Give examples of cell cycle nonspecific anticancer drugs.

Answer:

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Alkylating agents	• Donate alkyl group
Platinum compounds	• Donate platinum ion • Cisplatin • Carboplatin • Oxaliplatin

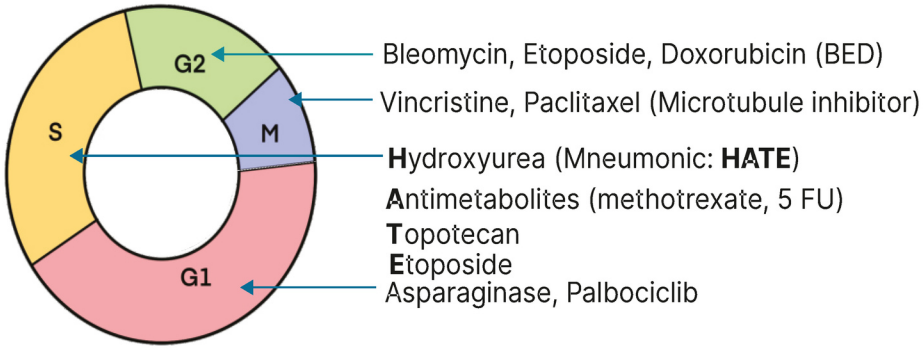
Q2.3: What is the MOA of cell cycle-specific drugs?

Answer: Cell cycle-specific (CCS) drugs kill cancer cells at a specific phase of the cell cycle

Q2.4: What are the drugs classified under cell cycle-specific drugs?

Answer:

PYQ: FMGE 2020



Q2.5: What is the mechanism of action of alkylating agents in cancer treatment Q1.1: List the main types of anticancer drugs.

Answer:

Donate alkyl group inside the cancer cell
↓
Attaches to N7 guanine of DNA
↓
Causes DNA damage

Q2.6: Name the drugs classified under alkylating agents in cancer treatment.

Answer:

- Mechlorethamine
- Dacarbazine
- Procarbazine
- Melphalan
- Cyclophosphamide
- Chlorambucil
- Busulfan

Q2.7: Which was the first anticancer drug developed, and what is its use?

Answer:

- Mechlorethamine
- Given in Hodgkin's lymphoma

Q2.8: What are the main chemotherapy regimens for Hodgkin's lymphoma?

Answer:

MOPP	ABVD (Most Preferred Regimen)
• Mechlorethamine • Oncovin (Vincristine) • Procarbazine • Prednisolone	• Adriamycin • Bleomycin • Vinblastine • Dacarbazine

Q2.9: Name two alkylating agents used in Hodgkin's lymphoma.

Answer:

- Dacarbazine
- Procarbazine

Q2.10: What are the adverse effects caused by Procarbazine?

Answer:

- Azoospermia → Male infertility
- Depression
- Disulfiram-like reaction → avoid in alcoholics

Q2.11: Which alkylating agent is used in Multiple myeloma?

Answer: Melphalan

Q2.12: What are the main uses of cyclophosphamide?

Answer: Used in Non-Hodgkin's lymphoma, Burkitt's Lymphoma, Wegner's granulomatosis

Q2.13: What is the R-CHOP regimen for Non-Hodgkin's lymphoma?

Answer:

- **R**ituximab - Blocks CD20 receptor
- **C**yclophosphamide
- **H**ydroxy Daunorubicin
- **O**ncovin - AKA: Vincristine
- **P**rednisolone

Q2.14: What drugs are used in Chronic Lymphocytic Leukemia?

Answer:

Mnemonic: FCR

- **F**ludarabine
- **C**yclophosphamide
- **R**ituximab

Q2.15: Which are the toxic byproducts of cyclophosphamide?

Answer:

Cyclophosphamide
↓
4-Hydroxycyclophosphamide
↓
Aldophosphamide (Anticancer) + Acrolein (toxin)

Q2.16: Which drug toxicity causes hemorrhagic cystitis, and how is it prevented?

Answer:

- Acrolein damages the urinary bladder, leading to Hemorrhagic cystitis → Painful hematuria
- Ifosfamide has an even higher risk of causing Hemorrhagic cystitis
- Antidote for Hemorrhagic Cystitis: MESNA
  - Oral and IV

Q2.17: Which alkylating agent is used in CLL and ALL?

Answer: Chlorambucil

Q2.18: What is the MOA of Chlorambucil?

Answer:

- Kills peripheral lymphocytes
- Spare myelocyte/Bone marrow cells
  - Immature cells
- No Bone marrow suppression

Q2.19: Which drug is used in CML and AML that causes maximum bone marrow suppression?

Answer: Busulfan

Q2.20: What is the MOA of Busulfan?

Answer:

- Kills myelocyte/BM cells
- Spare peripheral lymphocyte

Q2.21: Which anticancer drug can cause Budd-Chiari syndrome/Veno-occlusive disease of the liver?

Answer: Busulfan

Q2.22: What is the antidote for Budd-Chiari syndrome/Veno-occlusive disease caused by Busulfan?

Answer: Defibrotide

Q2.23: What is the most common brain tumor?

Answer: Astrocytoma

Q2.24: Name two dangerous varieties of brain tumors.

Answer: Malignant glioma, Glioblastoma multiforme

Q2.25: What is the drug of choice for brain tumors?

Answer: Temozolomide: Has a good BBB entry

Q2.26: Name the drugs used in Temozolomide-resistant brain tumors.

Answer: Carmustine, Lomustine, Semustine

Q2.27: What are the main side effects of mustine-like drugs?

Answer: Delayed neutropenia (bone marrow suppression lasting for years after stopping the drug)

Big Question 3: What is the MOA of platinum compounds in CCNS?

Broad Answer:

Donate platinum ions inside cancer cells
↓
Attach to N7 guanine position of DNA
↓
DNA damage

DETAILED QUESTIONS

Q3.1: Name three platinum compounds that are cell cycle nonspecific (CCNS).

Answer: Cisplatin, Carboplatin, and Oxaliplatin

Q3.2: What are the conditions in which Cisplatin is used?

Answer:

- Mnemonic: **LOGHUR**
  - **L:** Lung cancer (DOC)
  - **O:** Osteosarcoma
  - **G:** GIT cancer
  - **H:** Head and neck cancer
  - **U:** Urogenital cancer (Testicular, cervical cancer)
  - **R:** Retinoblastoma

Q3.3: Which is the DOC for testicular, cervical cancer, and retinoblastoma, and what are its side effects?

Answer: Cisplatin

Q3.4: What are the side effects of Platinum compounds?

Answer:

- Side effects of Platinum compounds
  - Most emetogenic: Cisplatin
  - Ototoxic: Maximum by Cisplatin

Q3.5: Which anticancer drug causes maximum nephrotoxicity, what is its antidote, and which drug causes maximum neurotoxicity?

Answer:

- **Maximum nephrotoxicity:** Cisplatin
  - Effect: Kidney damage
  - Antidote: Amifostine
  - Prevention: Mannitol + chloride ions → diuresis → removes platinum compounds in urine
- **Maximum neurotoxicity:** Oxaliplatin

Q3.6: Name drugs that act as radiosensitizers in cancer therapy.

Answer:

- **GIT, Head & Neck cancers:** 5-Fluorouracil (5-FU), Cisplatin → make tumors more radiosensitive
- **Pancreatic cancer:** Gemcitabine → increases radiosensitivity

YOURWISH

YOURWISH

Q3.7: What are the side effects of radiotherapy?

Answer: Radiotherapy also damages normal cells, not just cancer cells

Q3.8: Which drug is used as a radioprotector, and what other protective effect does it have?

Answer:

- **Radioprotector:** Amifostine
- **Other effect:** Nephroprotective against Cisplatin-induced kidney damage
- **Note:** Not a neuroprotector

Big Question 4: What are S-phase drugs in chemotherapy, and why are cancer cells particularly vulnerable to them?

Broad Answer:

- S-phase drugs are chemotherapy agents that specifically target and kill cancer cells during the S-phase (DNA synthesis phase) of the cell cycle
- Cancer cells divide more rapidly than normal cells, so they spend more time in S-phase → increased susceptibility to S-phase drugs

DETAILED QUESTIONS

Q4.1: What is the MOA of drugs acting on the S phase?

Answer: Inhibit DNA synthesis

Q4.2: What are the main types of drugs acting on the S phase?

Answer:

- Hydroxyurea
- Antimetabolites

Q4.3: What is the MOA of hydroxyurea?

Answer: Inhibit Ribonucleotide reductase required for DNA synthesis

Q4.4: What are the uses of hydroxyurea?

Answer:

- Used for the treatment of tumors of
  - RBC: Polycythemia
  - Platelets: Essential Thrombocytosis
  - Bone marrow tumors: Myelofibrosis

Q4.5: What is the drug of choice for Sickle cell disease?

Answer: Hydroxyurea: Due to its non-cancerous effect

Q4.6: What is the defect in sickle cell disease?

Answer: **Defect**: Mutation in the β-globin chain of hemoglobin (HbS formation)

Q4.7: What is the mechanism by which Hydroxyurea benefits Sickle cell disease?

Answer: Hydroxyurea increases fetal hemoglobin (HbF) synthesis

Q4.8: What chains does fetal hemoglobin contain?
Answer: Alpha and gamma chains

Q4.9: Which drug in Sickle cell disease inhibits veno-occlusion?
Answer: Voxelotor

Q4.10: Which drug inhibits P-selectin and prevents RBC sickling?
Answer: Crizanlizumab

Big Question 5: What is the mechanism of action of antimetabolites, and how are they classified?

Broad Answer:

- Metabolites are required for DNA synthesis
- Antimetabolites are fake substrates required for DNA synthesis

Folate analogue --▶ Purine analogue --▶ Pyrimidine analogue

DETAILED QUESTIONS

Q5.1: Name examples of folate analogues.

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Answer:

- Has (-trex) word
  - Methotrexate
  - Pemetrexed
  - Pralatrexate
  - Trimetrexate

Q5.2: What is the mechanism of folate analogues?
Answer:

- Inhibits DHFR (Dihydrofolate reductase)
- DHFR converts folic acid to tetrahydrofolate (active form)
- Tetrahydrofolate is a cofactor for Thymidylate synthase
- These drugs indirectly inhibit Thymidylate synthase
- This enzyme converts UMP (Uridine monophosphate) to TMP (Thymidine Monophosphate)
- Reduce DNA synthesis

Q5.3: What is the antidote for Methotrexate poisoning?
Answer:

- THF
- Folinic acid
- Folic acid + Vitamin B12 (can also be given)

Q5.4: Pemetrexed is a DOC for which cancer?
Answer: Tumor of the pleura of the lungs (Mesothelioma)

Q5.5: Which drug is used for the treatment of cutaneous T-cell lymphoma?
Answer: Pralatrexate

Q5.6: Trimetrexate is an antibiotic used to treat which infection?
Answer: Pneumocystis jirovecii infection

Q5.7: What are the causes of Methotrexate toxicity?
Answer:

- Megaloblastic anemia - Complete blood count
- Hepatotoxic - LFT (AST)
- Pneumonia - Chest X-ray

Q5.8: What is the drug of choice for Choriocarcinoma?
Answer: Methotrexate

Q5.9: Name three antidotes or management options for Methotrexate toxicity.
Answer:

- Folinic acid
- Enzyme: Glucarpidase use of
  - If Folinic acid is not effective
  - Directly degrades methotrexate
- Forced alkaline diuresis

Q5.10: What are the uses of folinic acid?
Answer:

- AKA, Leucovorin & Citrovorum factor (an active form of folic acid)
- Uses:
  - Given with Methotrexate to reduce toxicity (Leucovorin rescue)
  - Given with 5-fluorouracil (5FU) to increase the anticancer effect

Q5.11: What are the uses of 5-Fluorouracil (5-FU)?
Answer:

- IV form: GIT cancer, head & neck cancer, breast cancer
- Topical form: Mycosis fungoides (cutaneous T-cell carcinoma), basal cell carcinoma

Q5.12: What is the mechanism of action of 5-FU?
Answer:

- Inhibits thymidylate synthase, blocking DNA synthesis
- Leads to thymidine-deficient cell death

Q5.13: What is the oral prodrug of 5-Fluorouracil?
Answer: Capecitabine

Q5.14: For which cancer is Capecitabine specifically approved?
Answer: Breast cancer

Q5.15: Which drug causes hand-foot syndrome more frequently?
Answer: Capacitabine > 5-FU

Q5.16: Why does Capecitabine cause hand-foot syndrome?

Answer: It is excreted in sweat, leading to toxicity in palms and soles.



Hand Foot Syndrome

Q5.17: What is the regimen used in colorectal cancer?

PYQ: FMGE 2023

Answer:

- FOLFOX/FOLFIRI + Bevacizumab regimen
  - Folinic acid
  - 5-Flurouracil
  - Oxaliplatin/Irinotecan
  - Bevacizumab inhibits the formation of blood vessels
    - → Inhibition of VEGF (Vascular Endothelial Growth Factor)
    - → Inhibition of angiogenesis (Angiogenesis is the hallmark of cancer)

Q5.18: Cytosine arabinoside is the drug of choice for which leukemia?

Answer: Cytosine arabinoside, also known as Cytarabine (fake pyrimidine), is the DOC in Acute Myeloid Leukemia (AML)

Q5.19: What are the side effects of Cytosine arabinoside?

Answer:

- Cerebellar toxicity
  - Ataxia
  - Nystagmus
  - Slurred speech

Q5.20: Gemcitabine is the drug of choice for which cancer?

Answer: Gemcitabine, a cytosine analogue and radiosensitizer, is DOC in Pancreatic cancer

Q5.21: What is the DOC for Myelodysplastic syndrome?

Answer: Azacitidine and Decitabine

Q5.22: What is the MOA of Azacitidine and Decitabine?

Answer:

- These drugs inhibit the methylation of DNA
- AKA: Hypomethylating agents

Q5.23: What is the mechanism of action of 6-thioguanine and 6-mercaptopurine, and what are they used for?

Answer:

- **Type:** Fake purine analogues → converted into fake nucleotides
- **Activation:** By HGPRTase (Hypoxanthine-guanine phosphoribosyltransferase)
- **Mechanism:** Inhibit DNA synthesis
- **Use:** Treatment of resistant lymphomas

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Q5.25: What is the active form of Azathioprine?

Answer: Azathioprine is a prodrug, and its active form is 6-Mercaptopurine

Q5.26: What are the uses of mercaptopurine?

Answer:

- Used as an immunosuppressant in:
  - o Inflammatory bowel disease
    - → Ulcerative colitis
    - → Crohn's disease

Q5.27: Which enzyme degrades 6-mercaptopurine and Azathioprine?

Answer: Xanthine oxidase

Q5.28: Which drug inhibits xanthine oxidase?

Answer: Allopurinol

Q5.29: What are the main toxicities associated with 6-mercaptopurine?

Answer: Bone marrow suppression, hepatotoxicity

Q5.30: Why is TPMT (Thiopurine methyltransferase) testing important before starting 6-mercaptopurine therapy?

Answer: To prevent toxicity (Pharmacogenetics)

Q5.31: Which drug is the drug of choice for Chronic Lymphocytic Leukemia (CLL), and what regimen is used for it?

Answer:

- Fludarabine
- FCR regime

Q5.32: In which condition is Cladribine used as a DOC?

Answer: Cladribine,a fake adenine analogue and is the drug of choice for hairy cell leukemia and histiocytosis

Q5.33: What is the MOA and use of Pentostatin?

Answer: Pentostatin inhibits adenosine deaminase and was formerly used to treat hairy-cell leukemia

Big Question 6: What are microtubule inhibitors, and how do they work in cancer chemotherapy?

Broad Answer: Microtubule inhibitors are a class of drugs that interfere with the function of microtubules, which are essential components of the cell's cytoskeleton. By disrupting the normal function of microtubules, these drugs can inhibit cell division (mitosis), making them a key part of cancer chemotherapy

DETAILED QUESTIONS

Q6.1: What are microtubule inhibitors, and at which phase of the cell cycle do they act?

Answer: Microtubule inhibitors, also called spindle poisons, are plant-derived drugs that act specifically at the M phase of the cell cycle

Q6.2: What are the side effects of Fludarabine, Cladribine, Pentostatin, and what prophylaxis is given for it?

Answer:

- Side effects
  - o Severe immunodeficiency
  - o Lead to opportunistic infection
    - → Pneumocystis
- Prophylaxis: Cotrimoxazole

Q6.3: What are the main differences between Vinca alkaloids and Taxanes?

Answer:

Vinca alkaloids	Taxanes
• **Drugs:** o **Vincristine**: Cannot penetrate bone cells, hence no bone marrow suppression o **Vinblastine**: Causes bone marrow suppression • Inhibit polymerisation of microtubules • Inhibit the formation of spindles	• **Drugs**: Paclitaxel, Docetaxel, Cabazitaxel • Inhibit the depolymerisation of microtubules • Inhibit the movement of spindles

Q6.4: What are the side effects of microtubule inhibitors?

Answer:

- Neurotoxicity
  - o Maximum: Vincristine
- In the brain: SIADH (Syndrome of inappropriate ADH secretion)
- In GIT: Paralytic ileus
  - o Constipation
- Specific side effects of Vincristine
  - o Foot drops- Damage to the Common peroneal nerve
- Taxanes
  - o Glove stock neuropathy

Q6.5: Name the other microtubule inhibitors and their uses.

Answers:

Eribulin	• Treatment of breast cancer
Ixabepilone	• Treatment of breast cancer
Estramustine	• Contain estrogen • Treatment of prostate cancer
Colchicine	• Treatment of acute attack of gout o Inhibition of movement of WBC o Prevent inflammation • DOC: Karyotyping o Causes arrest of cell cycle at mitotic phase

Big Question 7: What are topoisomerase inhibitors, and what is their role in cancer treatment?

Broad Answer: Topoisomerase inhibitors are a class of chemotherapy drugs that are widely used to treat various types of cancer. They work by targeting and disrupting the function of enzymes called topoisomerases, which are essential for DNA replication, transcription, and repair

DETAILED QUESTIONS

Q7.1: What is the role of topoisomerase in cells, and during which cell cycle phases do topoisomerase inhibitors act?

Answer:

- Topoisomerase is required for DNA replication
- These act during the G2 and S phases of the cell cycle

Q7.2: Enumerate types of topoisomerase inhibitors.

Answer:

Topoisomerase-1 inhibitor	• Irinotecan o SE: Diarrhea • Overall DOC for diarrhea is Loperamide o Opioid drug o Contraindicated in Crigler Najjar syndrome • Topotecan
Topoisomerase-2 inhibitor	• Etoposide • Teniposide

Q7.3: Which bacterial enzyme is inhibited by Fluoroquinolones?

Answer: Top-4 is inhibited by Fluoroquinolones

BIG QUESTION 8: Explain the core concepts, uses, and key side effects of antitumor antibiotics and related cancer drug classes, including anthracyclines, vinca alkaloids, taxanes, topoisomerase inhibitors, and targeted therapies such as tyrosine kinase inhibitors and monoclonal antibodies.

Broad Answer:

- Antitumor antibiotics (e.g., doxorubicin) damage DNA but may cause cardiotoxicity. Vinca alkaloids and taxanes disrupt microtubules, blocking cell division. Topoisomerase inhibitors prevent DNA replication.
- Targeted therapies like tyrosine kinase inhibitors (imatinib) and monoclonal antibodies (trastuzumab) block cancer-specific molecules. These drugs have distinct side effects and are used in combination regimens for cancers like lymphoma and colorectal cancer.

DETAILED QUESTIONS

Q8.1: What is the source of antitumor antibiotics?

Answer: Streptomyces bacteria

Q8.2: Which drugs belong to the Anthracycline class?

Answer:

- End with (-rubicin)
  - Doxorubicin
  - Daunorubicin
  - Epirubicin
  - Idarubicin



Doxorubicin syrup

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Q8.3: What is the MOA of Anthracycline, and which specific phase of the cell cycle does it act on?

Answer:

- MOA: Top-2 inhibitor
- Cell cycle-specific: G2 phase

Q8.4: What are the uses of Anthracyclines?

Answer: DOC for Breast Cancer

Q8.5: What is the commonly used regimen in breast cancer?

Answer:

- Commonly used regimen - **CAT**
  - **C**yclophosphamide
  - **A**driamycin / Doxorubicin
  - **T**axane

Q8.6: What are the side effects of Anthracyclines?

Answer:

- Cardiotoxicity
  - Dilated cardiomyopathy
  - Antidote: Dexrazoxane

Q8.7: What is Mitoxantrone used for, and what is its advantage?

Answer:

- Mitoxantrone is a Top-2 inhibitor used in Multiple sclerosis
- Advantages: Less cardiotoxic

Q8.8: What is the MOA of Bleomycin?

Answer: Bleomycin causes DNA damage in the G2 phase

Q8.9: What are the side effects caused by Bleomycin?

Answer:

- Side effects
  - Lungs: Pulmonary fibrosis
  - Damage type 1 alveolar cells
  - Affect exchange of oxygen
  - Measured by DLCO (Diffusion Lung Capacity for Carbon Monoxide)
- Skin:
  - Flagellate pigmentation
  - Ichthyosis
- Fish like skin
- Increased keratin deposition
  - Raynaud's disease



Flagellate Pigmentation



Ichthyosis

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Q8.9: What is Actinomycin D used to treat?

Answer:

- Actinomycin D, also known as Dactinomycin, is given in childhood tumors
  - o Wilms tumor
  - o Rhabdomyosarcoma

Q8.10: How is Mitomycin administered for the treatment of bladder cancer?

Answer:

- Intravesical injection
  - o Directly injected into the bladder

Q8.11: What is another drug used in bladder treatment?

Answer: The BCG vaccine is also given into the bladder for superficial bladder cancer

Q8.12: Besides cancer treatment, what antifibrotic use does Mitomycin have?

Answer: Mitomycin prevents laryngotracheal stenosis after radiotherapy for laryngeal cancer

Q8.13: What serious side effect is associated with Mitomycin?

Answer: HUS-TTP (Hemolytic Uremic Syndrome Thrombocytopenia purpura)

Q8.14: What is the drug of choice for Acute Promyelocytic Leukemia (APML)?

Answer: All-trans retinoic acid (ATRA), also known as Tretinoin

Q8.15: Which drug is used for ATRA-resistant APML cases?

Answer: Arsenic trioxide

Q8.16: What is the mechanism of action of ATRA in APML?

Answer: It does not kill cancer cells directly but causes rapid maturation and differentiation of cancer cells, including white blood cells, leading to apoptosis

Q8.17: What is a common side effect of ATRA therapy, and how is it managed?

Answer:

- Retinoic acid syndrome, causing lung inflammation and WBC maturation in the lungs
- It is prevented by pretreatment with the corticosteroid, Dexamethasone

Q8.18: What toxicity is associated with Arsenic trioxide?

Answer: Arsenic toxicity can cause a white line on nails (MEES line)

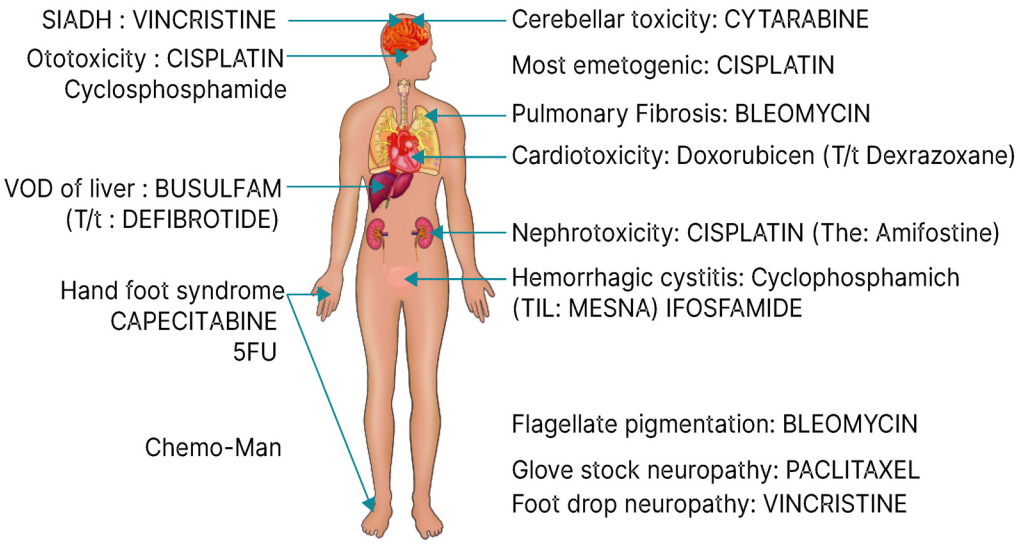
Q8.19: Which enzyme is used in the treatment of acute lymphoblastic leukemia (ALL), and what is its major side effect?

Answer:

- **Drug/Enzyme:** Asparaginase
- **Use:** Treatment of acute lymphoblastic leukemia (ALL)
- **Major side effect:** Pancreatitis → pancreatic damage

Q8.20: According to "Chemo-Man," what are the major organ-specific toxicities of common chemotherapy drugs?

Answer:



Q8.21: Enumerate different regimens used in cancer.

Answer:

- Hodgkin's lymphoma: ABVD (common) > MOPP
- CLL: FCR
- Hairy cell leukemia: Cladribine
- Non-Hodgkin's lymphoma: R-CHOP
- Colorectal cancer: FOLFOX/FOLFIRI + Bevacizumab
- Retinoblastoma: VEC
  - o Carboplatin
- APML: ATRA, Arsenic trioxide
- AML: 7C + 3D

Big Question 9: What are tyrosine kinase inhibitors (TKIs), and how do they differ from traditional chemotherapy?

Broad Answer: Tyrosine kinase inhibitors (TKIs) are a type of targeted therapy that has revolutionized cancer treatment. Unlike traditional chemotherapy, which kills all rapidly dividing cells, TKIs are designed to specifically block the signals that promote cancer cell growth, survival, and division

DETAILED QUESTIONS

Q9.1: What are tyrosine kinase inhibitors (TKIs), how are they administered, and what are their common side effects?

Answer:

- Protein kinase inhibitors/ Tyrosine kinase inhibitors (TKI) are a new targeted therapy used in cancer treatment
- Protein kinase/tyrosine kinase receptor mutation leads to cancer
- Drugs end with (-nib)
- Given orally
- Side effects
  - o Skin rashes
  - o Diarrhea due to GIT damage

Q9.2: Which drugs target the Bcr-Abl tyrosine kinase receptor mutation in CML, and what are their common side effects?

Answer:

- Drugs: Mnemonic - **PIND Balluchi**
  - o **P**onatinib
  - o **I**matinib
    - → DOC: CML
    - → First TKI
  - o **N**ilotinib
  - o **D**asatinib
  - o **B**osutinib
  - o **Note**: Other drugs are given in resistant cases of Imatinib
- Side effects
  - o Diarrhea: Treat with loperamide
  - o Pulmonary artery hypertension

Q9.3: Which drugs are commonly used to treat Gastrointestinal Stromal Tumor (GIST)?

Answer:

- Drugs, Mnemonic: **SIR**
  - o **S**unitinib
  - o **I**matinib
  - o **R**egorafenib

Q9.4: Which VEGFR inhibitors are used to treat renal cell carcinoma, and what is their MOA?

Answer:

- Drugs, Mnemonic: **PASS**
  - o **P**azopanib
  - o **A**xitinib
  - o **S**orafenib
    - → Given in RCC and HCC (Hepatic cell carcinoma)
    - → Lenvatinib is also given in HCC
  - o **S**unitinib: Given in RCC (Renal cell carcinoma) and GIST
- VEGFR (Vascular Endothelial Growth Factor Receptor) inhibitors act by inhibiting angiogenesis

Q9.5: Which EGFR inhibitors (type of TKI) are used in non-small cell lung cancer?

Answer:

- Drugs, Mnemonic: **Everyone to GOA**
  - o **E**rlotinib
    - → Also given in pancreatic cancer
    - → Avoid with food as it increases absorption & leads to toxicity
  - o **G**efitinib
    - → Safe with food
  - o **O**simertinib
    - → Resistant cases
- T790M mutation
- Erlotinib and gefitinib are not effective
  - o **A**fatinib

Q9.6: Which ALK (Anaplastic Lymphoma Kinase) inhibitors are used for non-small cell lung cancer?
Answer: Crizotinib, Certinib, Alectinib

Q9.7: Which drugs are used for HER/Neu-positive Breast Cancer?
Answer:

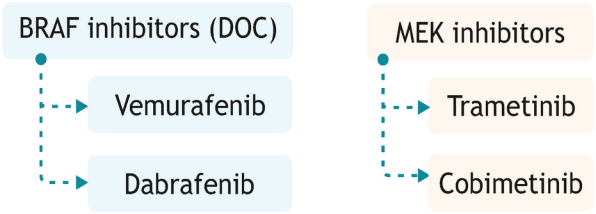
- Lapatinib
  - Blocks HER/Neu receptor
    → Tyrosine kinase receptor causes breast cancer
  - Used in Resistant cases to Trastuzumab (monoclonal antibody)
  - First drug for HER/Neu positive Breast Cancer
- Neratinib

Q9.8: Which drug is used to treat medullary carcinoma of the thyroid?
Answer: Vandetanib (**mnemonic: Vandematram**)

Q9.9: Which two genetic mutations are most commonly associated with malignant melanoma?
Answer:

- BRAF mutation causes malignant melanoma
- MEK is the second most common mutation that leads to malignant melanoma

Q9.10: Which drugs are commonly used for malignant melanoma?
Answer:



Q9.11: Which of Bruton's tyrosine kinase inhibitors are used to treat various lymphomas?
Answer:

- Ibrutinib
- Acalabrutinib
- Zanubrutinib

Q9.12: What lymphomas are treated by Bruton's tyrosine kinase inhibitors?
Answer:

- Mnemonic - **Ma Ma Can Sell Water**
  - **Ma**ntle cell lymphoma
  - **Ma**rginal cell lymphoma
  - **C**LL
  - **S**LL
  - **W**aldenstrom MGG (macro gamma globulinemia)

Q9.13: What is the action of CDK 4,6 inhibitors on the cell cycle?
Answer:

- Inhibit the cell cycle at the G1-S phase
- Cause G1 phase arrest

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Q9.14: Name a few CDK 4,6 inhibitors.

Answer:

- Drugs end with -CICLIB
  - Ribociclib
  - Abemaciclib
  - Palbociclib

Q9.15: Which class of drugs is commonly used in ER-positive breast cancer treatment?

Answer: CDK 4/6 inhibitors

Q9.16: Name a few PARP (Poly ADP Ribose Phosphate) inhibitors.

Answer:

- Drugs end with -PARIB
  - Rucaparib
  - Iniparib
  - Olaparib
  - Talazoparib

Q9.17: What class of drugs targets BRCA-positive breast and ovarian cancers?

Answer: PARP inhibitors

Q9.18: What are epigenetic actions in the context of cancer therapy?

Answer: Drugs that change the histone protein and change the DNA, epigenetic action

Q9.19: Name some drugs with epigenetic actions.

Answer:

Histone Deacetylase inhibitors	• NOSTAT	• Vorinostat • Belinostat • Panobinostat	• Cutaneous T cell carcinoma • Peripheral T-cell lymphoma • Multiple myeloma
Histone methyltransferase inhibitors	• METOSTAT	• Tazemetostat	• Epithelioid sarcoma
Proteasome inhibitor	• ZOMIB	• Bortezomib (DOC) • Carfilzomib • Ixazomib	• Multiple myeloma

Q9.20: . What is the drug of choice for multiple myeloma, and what other drugs are used?

Answer:

- Treatment
  - Bortezomib (DOC)
  - Thalidomide/Lenalidomide/Pomalidomide
  - Dexamethasone

Q9.21: Name some miscellaneous drugs.

Answer:

Sonic Hedgehog pathway inhibitor • Pathway for embryonic development	• DEGIB	• Sonidegib • Vismodegib • Glasdegib	• Basal cell carcinoma • **C/I:** pregnancy
Nuclear export inhibitor (Inhibits XPO 1) • New drug	-	• Selinexor	• Multiple myeloma • DLBCL (diffuse large B cell lymphoma)

BCL-2 inhibitors • BCL 2 is an anti-apoptotic factor • Inhibition of BCL 2 leads to apoptosis of cell	• CLAX	• Venetoclax • Obatoclax	• CLL with 17p deletion

Q9.22: What is the recently approved drug for Von Hippel-Lindau (VHL) cancer?

Answer: Belzutifan

Q9.23: Which chromosome mutation is associated with Von Hippel-Lindau (VHL) disease?

Answer: A mutation in chromosome 3

Q9.24: Name types of cancers or lesions caused by the Von Hippel-Lindau (VHL) mutation

Answer: Renal cell carcinoma (RCC), Pheochromocytoma, Hemangioblastoma, Pancreatic lesions, Eye dysfunction

Q9.25: What is the mechanism of action of Belzutifan in cancer treatment?

Answer: It inhibits hypoxia-inducing factor (HIF)-2 alpha, which reduces erythropoietin production

Q9.26: What is a common side effect of Belzutifan, and what causes it?

Answer: Anaemia: caused by reduced erythropoietin levels due to HIF inhibition

Big Question 10: What is CAR T-cell therapy, and why is it called a "living drug"?

Broad Answer: CAR T-cell therapy, or Chimeric Antigen Receptor T-cell therapy, is a groundbreaking and highly personalized form of cancer immunotherapy. It's often described as a "living drug" because it uses a patient's own genetically modified immune cells to fight their cancer

DETAILED QUESTIONS

Q10.1: What is the MOA of drugs in CART therapy?

Answer: Special T Cells that contain chimeric receptors are made

Chimeric receptors
↓
Identify CD-19 on lymphocytes
↓
T cell goes to lymphocytes and kill them

Q10.2: CART therapy is primarily used to treat which types of cancers?

Answer: All CD-19 containing lymphomas

Q10.3: What are some examples of CD-19 CAR T-cell therapies and their clinical uses?

Answer:

CD-19 CART therapy (Chimeric Antigen Receptor T cell)	• Axicabtagene Ciol**eucel** • Tisageniec **Leucel** • Brexicabtagene Auto**leucel**	• Diffuse large B cell lymphoma • ALL • ALL, Mantle cell lymphoma

Q10.4: Which cancer vaccines use T cells, and what cancers do they treat?

Answer:

- Sipuleucel T: Treatment of prostate cancer
- Lifileucel: Treatment of melanoma

Big Question 11: What are monoclonal antibodies (mAbs) in cancer therapy, and how do they work?

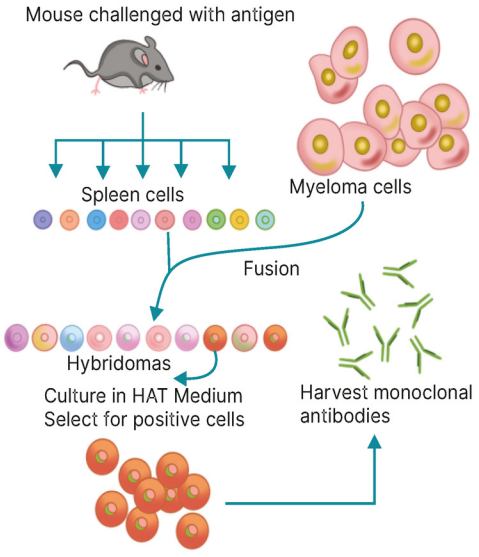
Broad Answer: Monoclonal antibodies (mAbs) are a type of targeted therapy that uses laboratory-produced proteins to mimic the natural antibodies of the immune system. They are produced by the Hybridoma technique. They are designed to specifically recognize and bind to a single target, such as a protein on the surface of a cancer cell or a substance that the cancer cell needs to grow

DETAILED QUESTIONS

Q11.1: What are the different types of monoclonal antibodies based on their source?

Answer:

- Source
  - -mo mab (mouse)
  - -xi mab (chimeric)
    → 50% mouse and 50% human
  - -zu mab (humanized)
    → >90% human
  - -mu mab (fully human)
  - Adalimumab



Q11.2: What is the mechanism, use, and major side effect of Trastuzumab, and how does pertuzumab differ?

Answer:

- **Trastuzumab:**
  - **Mechanism:** HER-2/neu (human epidermal growth factor receptor) blocker
  - **Use:** Drug of choice for **HER2-positive breast cancer**
  - **Side effect:** Cardiotoxicity
  - **Note:** Cardiotoxicity risk increases by 30% when combined with **doxorubicin**
- **Pertuzumab:** Cardio-safe alternative HER-2 blocker

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Q11.3: What is the mechanism of action and clinical uses of Cetuximab? Name two newer drugs with the same target.

Answer:

- **Mechanism:** EGFR (epidermal growth factor receptor) blocker – also called **HER-1**
- **Uses:**
  - Colorectal cancer
  - Head and neck cancer
  - Non-small cell lung cancer
- **Newer drugs:**
  - Panitumumab
  - Necitumumab

Q11.4: What is the mechanism of action and uses of Rituximab, and mention one newer drug with the same target.

Answer:

- **Mechanism:** CD20 blocker on lymphocytes
- **Newer drug:** Obinutuzumab
- **Uses (Mnemonic - ReLIANCe):**
  - **Re**: Rheumatoid arthritis
  - **L**: Lupus erythematosus
  - **I**: ITP (Idiopathic thrombocytopenic purpura)
  - **A**: AIHA (Autoimmune hemolytic anemia)
  - **N**: NHL (Non-Hodgkin's lymphoma)
  - **Ce**: CLL (Chronic lymphocytic leukemia)

Q11.5: What is the MOA and the uses of Aletuzumab?

Answer:

- MOA: CD52 blocker
- Uses: Chronic lymphocytic leukemia(Second line to fludarabine)

Q11.6: What is the MOA and the uses of Daratumumab? Mention one newer drug with the same MOA

Answer:

- MOA: CD38 blocker
- Uses: Multiple myeloma
- Newer drug: Isatuximab

Q11.7: What is the MOA and the uses of Mogamulizumab?

Answer:

- MOA: CCR-4 receptor blocker
- Uses: Mycosis fungoides (Sezary syndrome) - T cell tumor

Q11.8: What is the mechanism of action and the uses of Eculizumab? Name one newer drug with the same target.

Answer:

- **Mechanism:** C5 complement blocker
- **Newer drug:** Ravulizumab
- **Uses (Mnemonic – PHaD):**

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- **P**: PNH (Paroxysmal nocturnal hemoglobinuria)
- **H**: HUS-TTP (Hemolytic uremic syndrome-Thrombotic thrombocytopenic purpura)
- **D**: Devic's syndrome (Neuromyelitis optica)

Big Question 12: What are immune checkpoint inhibitors, and how do they work in cancer therapy?

Broad Answer: Immune checkpoint inhibitors are a type of cancer immunotherapy that essentially "unleash the brakes" on the immune system to allow it to recognize and attack cancer cells. Our immune system has built-in checkpoints-proteins on immune cells that act as a safety mechanism to prevent an overactive immune response from attacking healthy cells. Cancer cells can exploit these checkpoints to "hide" from the immune system

Q12.1: What is the MOA of immune checkpoint inhibitors?

Answer:

- In the body, WBC cells try to kill cancer cells
- But cancer cells escape immunity
- Cancer cells make special proteins

Q12.2: Name some CTLA4 receptor blockers.

Answer:

- Ipilimumab
- Tremelimumab

Q12.3: CTLA4 receptor blockers are used in the treatment of which cancers?

Answer:

- Malignant melanoma
- Non-small cell lung cancer

Q12.4: Name three PD-L1 blockers used as immune checkpoint inhibitors in cancer therapy.

Answer:

- Atezolizumab
- Avelumab
- Durvalumab

Q12.5: Which cancers are commonly treated with PD-L1 blockers?

Answer:

- Urothelial cancer (bladder cancer)
- Anaplastic thyroid cancer
- Nonsmall cell lung cancer
- Endometrial cancer (also Pembrolizumab)

Q12.6: Name three PD-1 receptor blockers used in cancer therapy

Answer:

- Nivolumab
- Cepilimumab
- Pembrolizumab

Q12.7: What are the main cancers treated with Nivolumab, a PD-1 receptor blocker?

Answer:

- Malignant melanoma
- Nonsmall cell lung cancer
- Hodgkin's lymphoma

Q12.8: What drugs block IL-7? Mention their uses.

Answer:

- **Drugs**: Ixekizumab, Secukinumab, and Brodalumab
- **Uses**: Plaque psoriasis

Q12.9: What is the target of Tildrakizumab in the treatment of plaque psoriasis?

Answer: IL-23

Q12.10: Which interleukins does Ustekinumab block, and what conditions does it treat?

Answer: Ustekinumab blocks IL-12 and IL-23 and is used to treat plaque psoriasis and Inflammatory bowel disease (Ulcerative colitis and Crohn's disease)

Q12.11: What receptor does Pembrolizumab block in cancer therapy?

Answer: PD-1 receptor

Q12.12: Name types of cancers for which Pembrolizumab is approved for treatment.

Answer:

- Non-small cell lung cancer
- Endometrial cancer
- Mantle cell lymphoma
- Breast cancer
- Renal cell carcinoma
- Esophageal/stomach/colorectal cancer

Q12.13: Which drug is used to treat endometrial cancer?

Answer:

- Pembrolizumab
- Durvalumab is also used for treatment

Q12.14: Drug that blocks interleukin 17?

Answer: Secukinumab

Q12.15: Which MABs are used in SLE?

Answer:

- Belimumab: BAFF (B cell activating factor) blocker
- Anifrolumab: Interferon-1 blocker
  - Recently approved for SLE

Q12.16: Which MABs are used in hemophilia A and Type 1 DM?

Answer:

- MAB in Hemophilia A
  - o Emicizumab
    - → Inhibits clotting factors 10 and 11
    - → Used in hemophilia A
- MAB in type 1 diabetes mellitus
  - o Teplizumab
    - → Blocks the CD3 receptor on T lymphocytes
    - → Prevents the destruction of beta cells of the pancreas

Q12.17: Name some monoclonal antibodies used against microbial infections

Answer:

Palivizumab	Against - Virus	RSV Virus (respiratory syncytial virus)
Bezlotoxumab	Against - Toxin B of Clostridium difficile	Pseudomembranous Colitis
Raxibacumab	Against - Bacteria	Anthrax

Big Question 13: What is the role of angiogenesis inhibitors in cancer treatment, and how do they help stop tumor growth?

Broad Answer: Angiogenesis inhibitors are a class of drugs that prevent the formation of new blood vessels. In the context of cancer, these medications are designed to starve tumors of the oxygen and nutrients they need to grow and spread

Q13.1: Name some drugs used as angiogenesis inhibitors in cancer treatment.

Answer:

Drugs	Target	Use
• Bevacizumab	• VEGF (vascular endothelial growth factor) • Inhibits the formation of new blood vessels	• Colorectal cancer • Breast cancer
• Ramucirumab	• VEGFR (VEGF receptor)	• Colorectal cancer • Breast cancer
• Bevacizumab • Ranibizumab • Aflibercept • Pegaptanib	• Intravitreal injection in the eye	• Diabetic retinopathy • ARMD-WET type (Age-related macular degeneration)

Q13.2: What is an armed monoclonal antibody?

Answer: Armed antibody is conjugated with a toxin

Q13.3: What is Brentuximab Vedotin, and what types of cancer is it used to treat?

Answer:

- Brentuximab Vedotin is an armed monoclonal antibody where Vedotin acts as the toxin.
- It is used to treat Hodgkin's lymphoma and large B-cell lymphoma.

Q13.4: What is Gemtuzumab Ozogamicin, and what is its primary use in cancer treatment?

Answer:

- Gemtuzumab Ozogamicin is an armed monoclonal antibody conjugated with the toxin Ozogamicin.
- It is primarily used to treat relapsed acute myeloid leukemia (AML)

Q13.5: What is Moxetumomab pasudotox, and its clinical use?

Answer:

- Moxetumomab pasudotox is an armed monoclonal antibody linked to the toxin Pasudotox, which contains Pseudomonas toxin
- It is used to treat hairy-cell leukemia

Big Question 14: What are immunosuppressants, and in what situations are they used?

Broad Answer: Immunosuppressants are a broad class of drugs that inhibit or prevent the activity of the immune system. They are powerful medications used to treat a range of medical conditions where the immune system is either overactive or needs to be suppressed to prevent a harmful reaction

Q14.1: What are immunosuppressants used for, and in which conditions are they commonly applied?

Answer:

- Immunosuppressants are drugs that reduce the immune response.
- Commonly used in
  - Autoimmune diseases
  - Organ transplantation
    - → Graft vs Host Disease (GVHD)

Q14.2: Which drugs are used as DOC for organ transplantation?

Answer: Calcineurin inhibitors

Q14.3: Name some Calcineurin inhibitors.

Answer:

- Cyclosporine
- Tacrolimus: AKA Fk506

Q14.4: What is the MOA of Calcineurin inhibitors?

Answer:

- Calcineurin is present in T cells
- Inhibition decreases the production of IL-2
  - IL-2 causes an increase in cell-mediated immunity
- Calcineurin inhibitors reduce cell-mediated immunity

Q14.5: What are the side effects of Calcineurin inhibitors?

Answer:

- Nephrotoxicity (Hyperkalemia)
  - Stop and start other immunosuppressants (all other immunosuppressants are non-nephrotoxic)

Q14.6: What is the advantage of Calcineurin inhibitors?

Answer: Does not produce Bone marrow suppression

Q14.7: What is the mechanism of action of mTOR Inhibitors?

Answer: Mechanistic target of rapamycin in T cells

Q14.8: Name a few mTOR inhibitor drugs

Answer:

- Sirolimus
- Everolimus

Q14.9: Which drugs block the CD25 receptor and act as IL-2 receptor production inhibitors?

Answer: Daclizumab, Basiliximab

Q14.10: What is the mechanism of action of Mycophenolate mofetil, and its main side effect?

Answer:

- Prodrug → active form IMPD (Inosine monophosphate dehydrogenase) enzyme
- Reversible inhibitors of the IMPD enzyme
- Enzyme required for purine production, lymphocytes are killed
  - Immunity falls
- Side effects: Bone marrow suppression

Q14.11: What is the mechanism of action of Muromonab (OKT-3)?

Answer:

- Blocks the CD3 receptor on T cells

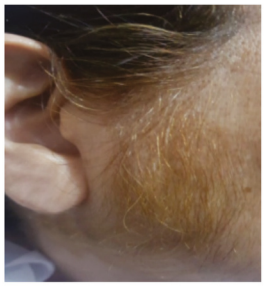
Q14.12: What are the common cosmetic side effects of Cyclosporine, and how are they managed?

Answer:

- Hyperplasia of gums, Mnemonic: **PCC**
  - **P**henytoin, **C**yclosporine, **C**CB- Amlodipine
  - Treatment
    - → Maintain good oral hygiene
    - → Antibiotic: Azithromycin



Hyperplasia of gums



Hirsutism

Q14.13: What is the mechanism of action (MOA) of Cyclosporine?

Answer: Cyclosporine enters T cells and binds to cyclophilin, which then inhibits calcineurin

Q14.14: Which drug can cause cholestatic jaundice by inhibiting bile excretion via P-Glycoprotein or MRP-2?

Answer: Cyclosporine (also inhibits excretion of bile)

Q14.15: What is the mechanism of action of Tacrolimus (FK506)?

Answer:

- It is a macrolide antibiotic
- It binds to FK binding protein and inhibits calcineurin

Q14.16: What are the uses of Thalidomide?

Answer:

- **T**-type 2 lepra reaction (ENL- erythema nodosum leprosum)
- **O**ral ulcer: In Behcet's disease
- **M**DS: Myelodysplastic syndrome
- **M**ultiple myeloma

Q14.17: What are the 2 enantiomers of Thalidomide?

Answer:

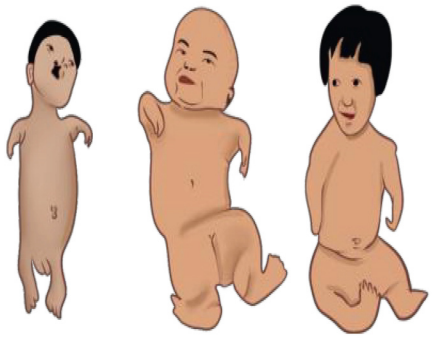
- R form can be converted to S form inside the body, and vice versa
  - o Enantiomeric conversation
  - o Avoided in Pregnancy
- Both enantiomers are contraindicated in pregnancy

R form	• Sedative action
S form	• Non sedative but teratogenic • S/E: phocomelia o Short limbs

Q14.18: What is the mechanism of action of Thalidomide, and what teratogenic effect is it known to cause?

Answer:

- Thalidomide causes phocomelia
  - o Thalidomide inhibits cereblon protein
    - → Inhibits angiogenesis
    - → Inhibits TNF alpha
    - → Inhibits IL-6



Phocomelia

Q14.19: What is a dangerous side effect of Thalidomide?

Answer: Neurotoxicity

Q14.20: Name two newer anticancer derivatives of thalidomide.

Answer: Lenalidomide and Pomalidomide.

Q14.21: What diseases are treated with Lenalidomide and Pomalidomide?

Answer: Myelodysplastic syndrome (MDS) and multiple myeloma

Big Question 15: What are immunostimulants, and how do they differ from immunosuppressants?

Broad Answer: Immunostimulants, also known as immunostimulators, are substances that activate or enhance the immune system's activity. In contrast to immunosuppressants, which dampen the immune response, immunostimulants are used to strengthen the body's natural defenses to fight diseases, particularly infections and cancer

Q15.1: What are immunostimulants?

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Answer: Drugs that increase or stimulate immunity

Q15.2: What is Aldesleukin, and what cancers is it used to treat?

Answer: It is a recombinant form of IL-2 used to treat renal cell carcinoma (RCC) and melanoma

Q15.3: What are the uses of Levamisole?

Answer: Levamisole is an antihelminthic drug used for ascariasis and acts as an immunostimulant by increasing interleukin production

- It is also used in refractory cases of nephrotic syndrome

Q15.4: What is Imiquimod used for, and what is its mechanism of action?

Answer:

- Imiquimod is a topical drug that stimulates Toll-like receptor 7 (TLR-7) on white blood cells
- It is used to treat basal cell carcinoma and condyloma warts (genital warts caused by HPV)
- It is contraindicated in pregnancy

Q15.5: How are condyloma warts treated during pregnancy?

Answer:

- Condyloma warts in pregnancy are treated with cryotherapy
- Imiquimod is not used