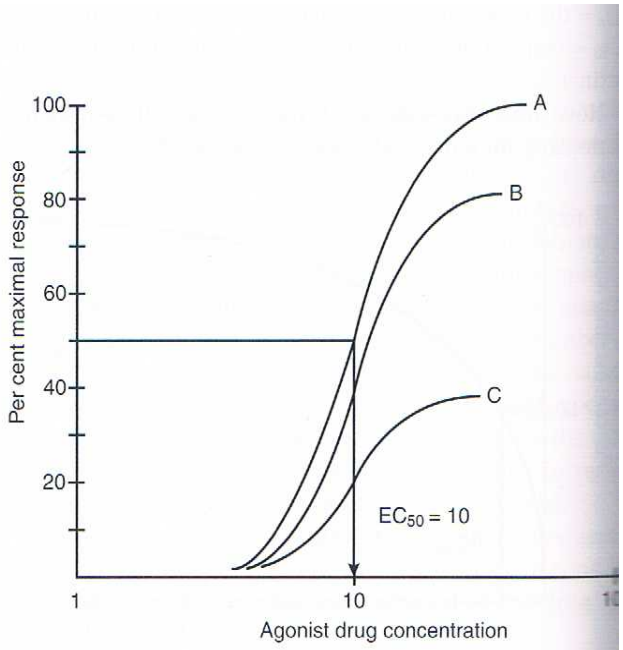
QUESTION	KNOWLEDGE	PASS CRITERIA
1. a. With regard to drugs, what is "potency".	Potency refers to the affinity or attraction between an agonist and its receptor. A good measure of drug potency is the EC_{50} – the concentration that produces 50% of the maximal response.	Demonstrate understanding of efficacy and potency.
b. How is this different to Efficacy?	Efficacy is the maximal response that a drug (agonist) can produce (E_{max}) when all receptors are occupied, irrespective of the concentration required to produce that response.	
c. Draw a concentration-response curve showing 2 drugs with the same potency but different efficacy.		

2. a. Describe the mechanism of action of glyceryl trinitrate. b. What are the clinical effects of nitrates	• Taken up by **vascular smooth muscle** • Interacts with tissue sulfhydryl groups • Releases free radical **nitric oxide** • Activates cGMP • Dephosphorylates myosin light chains • R**educes intracellular Ca levels** • Smooth muscle relaxation & **vasodilation** • Low doses – venodilation ⇒ ↓ preload & stroke volume • Higher doses – arterial dilation ⇒ **↓ blood pressure** ⇒ ↓ cardiac output & **↓ myocardial oxygen demand** + dilation of coronary arteries/redistribution of perfusion ⇒ **i**mproved oxygen delivery to myocardium & resolution of ischaemic pain **[Prompt if needed "What other clinical effects may be seen?"]** • Adverse effects: postural hypotension, tachycardia, dizziness, headache, flushing, blurred vision, dry mouth, rash	Must state • **vascular smooth muscle** • **nitric oxide** • **vasodilation** Must state • **↓ BP** • **↓ myocardial oxygen demand** • 2 listed other effects
3. a. What is pancuronium?	**Non-depolarising NM blocker** Quaternary ammonium compound Potent competitive antagonist of ACh at nicotinic receptors skeletal muscle motor end-plate Interruption of transmission requires > 70% occupancy; blockade requires > 95% occupancy	Nondepolarising NM blocker

b. Describe the pharmacokinetics of pancuronium?	Poorly absorbed after oral admin Rapidly and widely distributed after iv Rapid elimination ($T1_{/2}$ 30min) by urinary excretion unchanged drug (highly water soluble), and hepatic metabolism with biliary excretion **[Prompt: Describe its distribution and elimination]**	Rapid distribution Rapid elimination
c. What are the adverse effects of pancuronium?	Uncommon Minor tachycardia, hypertension, sl ↑ CO can occur Life-threatening anaphylaxis < 1:10,000	A cardiac and allergy effect
4. a. Describe the pharmacokinetics of lithium	Rapidly absorbed (except SR preparations) with peak plasma concs in 1-3hrs. High bioavailability. Not metabolised Renally excreted unchanged with partial reabsorption from PT. Long T ½ of 24hrs in adults Steady state plasma concs not reached for 5-7 days **(PROMPT – How long does it take to reach steady state plasma conc?)**	Long T ½ so steady state plasma concs not reached for days. Renally excreted unchanged.
b. What are the adverse effects of Lithium at therapeutic levels?	Tremor, nausea, polydypsia /polyuria, diarrhoea, weight gain. Long-term: Acne / psoriasis, hypothyroidism, nephrogenic diabetes insipidus (inhibits the effect of ADH on the DT cells -> polyuria).	Polyuria & Polydipsia OR NDI.
c. What are the signs/symptoms of lithium toxicity?	GIT: Vomiting. Neuro: Tremors, confusion, slurred speech, ataxia, drowsiness, blurred vision, seizures.	CNS effects with at least 3 symptoms

5. a. List the advantages of eye ointments over eye drops.	More stable Less absorption into lacrimal ducts Longer retention time on conjunctival surface Safer with potent drugs Ointment bases provide protection and comfort at night	2 to pass
b. List by action the types of drugs used topically in the eye	Mydriatics Miotics Cycloplegics Decongestants Antibiotics Antivirals Antiseptics Corticosteroids Local anaesthetics Stains eg. Fluoroscein	4 to pass
c. List the ideal properties of an ocular local anaesthetic	Quick onset of action (10-20 secs.) Useful duration of action (10-20 mins) No obvious effects on function or healing No interactions with drugs used concurrently	Quick onset and useful duration of action

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1. a. What routes of drug administration are there?	Enteral: Sublingual, buccal, oral, rectal Parenteral: SC, IM, IV, intrathecal, epidural Inhalational Topical	**Enteral/oral** + 3 non-enteral
b. What factors affect the rate of drug absorption from the small intestine?	Ionisation status of drug: alkaline Intestinal pH (7-8) favours absorption of un-ionised basic drugs Intestinal motility; increased motility lead to reduced transit time and drug absorption Gut surface area, blood flow, solubility of drug, formulation of drug **PROMPT: What is a specific drug factor**	Must mention drug factors and gut factors
c. What are potential disadvantages of rectal drug administration?	Erratic absorption because of rectal contents Local drug irritation Uncertainty of drug retention	1/3

2.
a. Describe the mechanism of action of ACE inhibitors
	• competitive **block conversion of angiotensin I to II** ⇒
	  ○ **decreased vascular tone** from prevention of vasoconstrictor effects of Ang II (main effect)
	  ○ **inhibition of aldosterone secretion** caused by Ang II leading to reduced Na & H_2O resorption ⇒ decreased BP
		3 in **bold** to pass

b. What are the adverse effects of ACE inhibitors	• **dizziness**, **hypotension** • headaches, weakness • loss of taste, nausea, diarrhoea • rash, fever, joint pain • **cough** • mild hyperkalaemia due to decrease in aldosterone secretion • acute renal failure	• hypotension or dizziness • cough • plus 2 others

c. What are some drug interactions that occur with ACE inhibitors	• Diuretics ⇒ hypotension • General anaesthetics ⇒ hypotension • Lithium ⇒ lithium toxicity • NSAIDS ⇒ hyperkalaemia & reduced effects of ACE inhibitor • Potassium sparing diuretics / potassium supplements ⇒ hyperkalaemia	2 to pass
3. a. What is the mechanism of action of erythromycin?	**Inhibits** RNA-dependent **protein synthesis** by binding to the 50S ribosomal subunit. **Bacteriostatic** (at high conc with selected organisms can be bactericidal)	Protein synthesis inhibitor Bacteriostatic
b. What is the mechanism for the drug interactions associated with erythromycin & give some examples?	**Inhibits hepatic CYP3A4.** Usually inhibits metabolism of other drugs metabolism causing increased activity. Examples: benzodiazepines, carbamazepine, cisapride (cardiotoxicity), digoxin, warfarin, theophylline, cyclosporine, tacrolimus	Inhibit hepatic metabolism One example
c. What are the adverse effects of erythromycin?	Common: **GIT**: abdo cramp, diarrhoea, N&V, candida (oral,vag) Rare: hypersensitivity, hearing loss, pancreatitis, hepatotoxicity Rapid iv may cause ventric arrhythmias.	GIT plus another
4. a. Describe the pharmacokinetics of phenytoin.	Oral absorption slow and variable: Time to peak levels 1.5-3hrs. Saturable hepatic metabolism leading to non-linear PK and variable T ½ of 7-42hrs. Metabolites excreted in the bile & urine.	Saturable metabolism/non-linear pharmacokinetics

b. What are the adverse effects of phenytoin?	Idiosyncratic: hirsuitism. gingival hyperplasia & overgrowth with bleeding, acne & facial coarsening. Dose related neurotoxic effects: drowsiness , dizziness, blurred vision, hallucinations, slurred speech, clumsiness, dizziness and confusion. Rapid IV administration associated with CV collapse. **PROMPT: Are there any specific problems with IV administration.**	Dose-related CNS effects Cardiac with IV administration & 1 other.
5. a. What are the indications for benzodiazepine use?	Anxiety Disorders Preoperative Medication Insomnia Sleep Disturbances Seizure Disorders Panic Disorder Alcohol Withdrawal Muscle Spasm Induce amnesia during cardioversion/endoscopic procedures	Seizures and 2 others
b. Explain the rationale for use of benzodiazepines in alcohol withdrawal	Down-regulation of neuro-inhibitory GABA receptors in alcohol dependent individual leads to symptoms of GABA deficiency in withdrawal. BZD act at a modulatory site on the the $GABA_A$ receptor to facilitate GABA binding to the $GABA_A$ receptors, enhance chloride channel opening, and overcome neuroexcitatory symptoms of GABA deficiency.	Facilitate GABA binding to the $GABA_A$ receptors Control neuroexcitatory symptoms of alcohol withdrawal.

QUESTION	KNOWLEDGE	PASS CRITERIA
1. a. What is meant by Total Body Clearance" of a drug	Describes the **ability of the body to eliminate a drug**. It refers to the theoretical volume of plasma emptied of drug per unit time (usually L/h). Total body clearance reflects the sum of all clearance process including **renal**, **hepatic** and **other**.	Definition
b. Name 2 drugs that have a high hepatic clearance and explain why this is important.	Lignocaine, Morphine, Propranolol, Pethidine. Drugs with high hepatic elimination may only be suitable for parenteral administration or have significant dosing variations depending on the route of administration. **PROMPT: How might it impact on route of administration**	2 drugs Demonstrate understanding
c. What factors determine drug half-life	Volume of Distribution and Clearance ($t_{1/2}$ = 0.693 x Vd/ Cl) Vd and clearance change with disease states - cardiac, hepatic and renal failure	Vd and clearance
2. a. What are the pharmacokinetic properties of frusemide?	• Rapid absorption after oral admin • Oral bioavailability 50% (range 10 –100%) • Highly protein-bound (>95%) • 50% conjugated in kidney & 50% excreted in urine unchanged (tubular secretion) • Elimination $t^1/_2$ 1.5 – 2 hours • Peak effect 30 minutes IV / 1 hour oral	Must list 3 properties
b. What are the site and mechanism of action of frusemide ?	• Actively secreted into lumen of nephron from proximal tubule cells via organic-base pump • Inhibits Na^+-K^+-$2Cl^-$ transporter in **thick ascending limb of loop of Henle** thus **preventing resorption of Na^+ & Cl^-** • Abolishes counter-current concentrating mechanism leading to a dilute urine	Must mention thick ascending limb of loop of Henle and reduced resorption of Na and Cl.

C. What are the adverse effects of the frusemide?	• Electrolyte disturbances – **hypokalemia**, **hyponatraemia**, hypomagnesaemia, hyperuricaemia • Postural **hypotension** & dizziness • Increased LDL & triglycerides, decreased HDL • Ototoxicity (high dose IV) • Drug interactions	Must list • Hypokalemia • Hyponatremia • Hypotension or dizziness • 1 other
3. a. What is the mechanism of action of cephalosporins	I**nhibit bacterial cell wall synthesis**, cell division and growth (similar to penicillins) **Bactericidal** Most effective in rapidly dividing cells.	Bolded material
How does the spectrum of microbiological activity for the 4th generation cephalosporins compare to that of earlier generations?	**Gram negative** as for 3rd generation e.g. E Coli, H Influenza, Klebsiella S**ome gm positive** (S Pneumonia) but less than 1st generation M**ore resistant to B Lactamases** than earlier generations	Bolded material
What is the relationship between penicillin allergy and cephalosporin allergy.	5-15% possibility of cross-reaction with penicillin allergy.	Aware of cross-reactivity
4. a. Describe the general pharmacokinetic characteristics of antipsychotic drugs	Most are readily but incompletely absorbed. Many undergo significant first pass metabolism Most are lipid soluble (lipophilic) Most have high PPB (92-99%) Most are completely metabolised by hepatic enzymes (oxidation; demethylation) These are catalysed by liver enzymes. **PROMPT: Use chlorpromazine as an example**	Lipid soluble. Hepatic metabolism + 1 other

Define the term “atypical” antipsychotic and provide an example.	Newer antipsychotic agents with less propensity to cause extra-pyramidal side-effects. Better at treating negative features of schizophrenia. They share a greater ability to alter $5HT_{2A}$ receptor activity than to interfere with D_2-receptor action. Examples: olanzapine; clozapine; quetiapine; risperidone; loxapine	Less EPS One example
c. Describe the adverse drug reactions to olanzapine.	Weight gain Sedation (but less than typical antipsychotics) Minor orthostatic hypotension Minor anticholinergic effects (dry mouth, urine retention etc) (Extrapyramidal effects less prominent)	2 effects
5. a. What is the mechanism of action of flumazenil?	Antagonist at the BZD binding site on the $GABA_A$ receptor (ligand-gated chloride channel). Decreases the binding of GABA. Blocks GABA-induced increase in Cl^- permeability and influx of Cl^- into the cell causing hyperpolarisation and decreased excitability of the neuron.	Specific BZD receptor antagonist at GABA receptor
b. What are the indications for flumazenil use	Avoid intubation or ICU admission in BZD overdose. Reverse BZD sedation after procedures Diagnostic role	Reverse the sedative effects of BZD
c. What potential problems should be anticipated when using flumazenil?	Precipitate seizures in mixed overdoses with BZD and proconvulsants Precipitate seizures in pts taking BZD to control epilepsy Precipitate withdrawal symptoms and seizures in BDZ-dependent Duration of action is only 1-3hrs thus repeated administration may be necessary Reversal of BZD-induced respiratory depression has not been demonstrated, so resp and cardiovasc support may be required Adverse Effects: headache, visual disturbance, increased anxiety, nausea, light-headedness	Precipitate fits Need for repeated doses