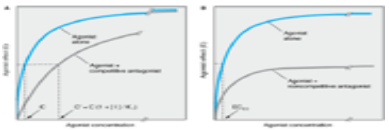
TOPIC	QUESTION	ESSENTIAL KNOWLEDGE	NOTES
Second Messengers	In reference to drug action what is a second messenger? What steps are involved in the action of a drug via a second messenger ? (Prompt - Illustrate this with an example)	A chemical eg Ca++ or cAMP that converts receptor binding to end effect through the production of an active intracellular element. Extracellular ligand specifically detected by a cell-surface receptor. Receptor triggers the activation of a G protein located on the cytoplasmic face of the plasma membrane. Activated G protein changes the activity of an effector element (usually enzyme or ion channel) This element changes the concentration of the intracellular second messenger. Example cAMP - Gs stimulates adenylyl cyclase which converts intracellular ATP to cAMP which stimulates cAMP-dependent protein kinases. Ca, Phosphoinositides cGMP (Pass –understanding of the concept that there may be a secondary process producing drug effect and able to name at least 1 second messenger)	

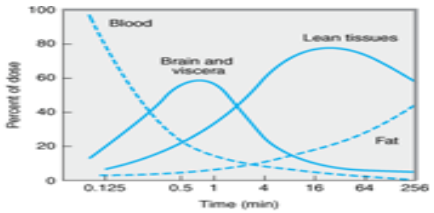
Angiotensin 2 Blockers	Describe the pharmacodynamics of therapeutic drugs that modulate the effect of angiotensin (Prompt to ACE & receptor blockers) What are the advantages of Angiotensin 2 receptor antagonists over ACE inhibitors ? (Specifically with respect to side effects)	ACE inhibitors – bind ACE reversibly preventing conversion of AI to AII. Inhibitory action on the renin-angiotensin system Stimulating action on the kallikrein-kinin system Angiotensin II inhibitors – competitive antagonists at A II receptor. As AII inhibitors do not result in production of bradykinins, there is a decreased incidence of cough and angioedema. Potentially greater effect as enzymes other than ACE can generate AII (Pass – able to describe actions and basic effects of ACE inhibitors and understanding that AII receptor antagonists and ACE inhibitors have different mechanisms.)	
LMWH	What are the pharmacodynamic differences between low molecular weight and unfractionated heparin? What are the advantages of low molecular weight heparin over unfractionated heparin?	Enoxaparin predominantly binds and inhibits factor Xa function, UFH binds to AT that inhibits factors II, IX, X Single daily or divided subcutaneous doses – facilitates patient mobility and OPD management. Routine monitoring not required (not mentioned in book) Reduced bleeding risk. Lower incidence of HITP. Improved efficacy over unfractionated heparin in ACS. Increased bioavailability (Pass – dosage differences and bleeding risk as well as factors II and IX less inhibited by LMWH (or at least that APTT is not accurate measurement of anticoagulation)	

Atropine	What is the mechanism of action of atropine ? What are the toxic effects of atropine? (Prompt - due to excessive use or abuse) What are the therapeutic uses for atropine ?	Antimuscarinic at cholinergic receptors Tachycardia, flushing, dry skin mucous, mydriasis membranes, ileus, urinary retention, acute angle glaucoma, central anticholinergic syndrome (delirium with visual hallucinations) Symptomatic bradycardias, especially when vagally mediated. OGP poisoning/ Inocybe Mushroom poisoning, drying of secretions. Adjunct to reversal of non depolarising muscle relaxants and suxamethonium administration in young infants. Antispasmodic, mydriatic. (Pass – antimuscarinic, at least 2 indications and 3 adverse effects involving 3 different body systems)	
Octreotide	Explain the rationale for the use of octreotide in upper gastrointestinal bleeding What are the pharmacokinetic differences between octreotide and somatostatin? (Supp Question – What other agents may be useful in the prevention and treatment of upper GI bleeding)	Octreotide reduces splanchnic blood flow, (? By glucagon release inhibition) therefore reduces portal venous pressure. This reduces blood loss from bleeding oesophageal varices and in some cases of severe duodenal ulcer related bleeding. Octreotide is a somatostatin analogue that has a longer half life than somatostatin (1.5hrs vs 3 min) so can be given as an IV infusion or subcutaneously. (Pass – reduces splanchnic blood flow)	

ACEM PRIMARY 1/2008 Pharmacology VIVA Afternoon Day 1 ***Candidate Number*****…… AGREED MARK……**

TOPIC	QUESTION	ESSENTIAL KNOWLEDGE	NOTES
Competitive vs Irreversible Antagonists	What is an antagonist ? Explain the difference between a competitive and irreversible antagonist (Illustrate this with an example)	Receptor antagonists bind to receptors but do not activate them. The primary action of antagonists is to prevent agonists from activating receptors In the presence of a fixed concentration of agonist, increasing concentrations of a reversible **competitive antagonist** progressively inhibit the agonist response; high antagonist concentrations prevent response completely. eg Propranolol and Noradrenaline **Irreversible** antagonists bind to the receptor either by forming a covalent bond with the receptor or by binding so tightly that the receptor is unavailable for binding of the agonist eg Phenoxybenzamine vs adrenaline  Changes in agonist concentration-effect curves produced by a competitive antagonist (Panel **A**) or by an irreversible antagonist (Panel **B**). In the presence of a competitive antagonist, higher concentrations of agonist are required to produce a given effect; thus the agonist concentration (C') required for a given effect in the presence of concentration [I] of an antagonist is shifted to the right, as shown. High agonist concentrations can overcome inhibition by a competitive antagonist. This is not the case with an irreversible (or noncompetitive) antagonist, which reduces the maximal effect the agonist can achieve, although it may not change its EC_{50}. Pass Be able to distinguish between competitive and irreversible antagonist	
Loop Diuretics	How does frusemide exert its action ? What are the adverse effects of frusemide? (Are any other organ systems effected ?)	Selective inhibition of NaCl reabsorption in the thick ascending loop of Henle Hypokalemic Metabolic Alkalosis Ototoxicity Hyperuricemia Hypomagnesemia . Allergy Skin rash Eosinophilia Interstitial nephritis Hyponatremia Pass – Na & loop of Henle, 4 adverse effects incl hypokalaemia & one non electrolyte	
Methylxanthine	What are the organ system effects of theophylline ? (Prompt both therapeutic and toxic)	CNS: Mild cortical arousal with increased alertness and deferral of fatigue. Bronchodilation. Nervousness and tremor. Overdose causes medullary stimulation, convulsions and death. CVS: Positive chronotropic and inotropic effects by inhibiting presynaptic adenosine receptors in sympathetic nerves and increasing catecholamine release at nerve endings. Produces tachycardia, increased cardiac output and BP. May cause arrhythmias. GIT: Stimulates gastric acid and digestive enzymes secretion. Kidney: Weak diuretic from increased glomerular filtration and reduced tubular sodium	

	How do these effects of theophylline correlate to its serum concentrations ?	reabsorption. Lung: Bronchodilation by relaxing airway smooth muscle and inhibits antigen-induced release of histamine from lung tissue. Theophylline has a narrow therapeutic window, and its therapeutic and toxic effects are related to its blood level: 5–20 mg/L: Improvement in pulmonary function. Anorexia, nausea, 15-20 mg/L: vomiting, abdominal discomfort, headache, and anxiety occur at concentrations of in some patients: >40 mg/L: Cause seizures or arrhythmias Pass –, CVS & Resp effects, narrow therapeutic window	

Thiopentone	Describe the pharmacokinetics of thiopentone What adverse effects does it cause when used as an anaesthetic induction agent ?	After IV bolus, rapidly crosses the blood-brain barrier. Plasma:brain equilibrium occurs < 1 min because of high lipid solubility. Rapidly diffuses out of the brain and highly vascular tissues, and redistributed to muscle and fat. Metabolized at rate of 12–16% per hour. <1% of the administered dose excreted unchanged by kidney.  Drops BP, SV, CO due to myocardial depressant effect and increased venous capacitance. Apnoea. Rarely precipitates porphyric crisis by inducing ALA synthase in liver Pass – 2 phase concept, hypotension	
Fluoroquinolones	What is the mechanism of action of fluoroquinolones ? What are the mechanisms of resistance to fluoroquinolones ? What are the clinical uses ciprofloxacin ?	DNA gyrase inhibitor/blocks protein production Resistance is due to one or more point mutations in the quinolone binding region of the target enzyme or to a change in the permeability of the organism. UTI Bacterial diarrhoea caused by Shigella, Salmonella, toxigenic *E coli*, Campylobacter Soft tissue, bone, joint, intra-abdominal and respiratory tract infections Treatment against multidrug-resistant organisms (pseudomonas and enterobacter) Prophylaxis and treatment against anthrax Gonococcal infection Chlamydial urethritis or cervicitis TB and atypical mycobacterial infections Eradication of meningococcal carrier state Prophylaxis in neutropenic patients Pass – DNA gyrase inhibition, 3 organ system uses	

ACEM PRIMARY 1/2008 Pharmacology VIVA Morning Day 2 ***Candidate Number*****……. AGREED MARK……**

TOPIC	QUESTION	ESSENTIAL KNOWLEDGE	NOTES
Bioavailability	Define the term bioavailability	Fraction of unchanged drug reaching the systemic circulation following administration by any route.	Need close approximation of defn
	What factors limit drug bioavailability following oral administration ?	(1) Extent of absorption (2) First-pass elimination (liver, gut)	Identify both factors (prompt if necessary)
	What methods of drug delivery are used to overcome bioavailability problems ?	Alternative route – sublingual, rectal, transdermal parenteral Administration pro-drug, increased dose	Give one example of an alternative route
Nitrates	What is the cellular mechanism of action of GTN ?	Denitration by glutathione S-transferase. Free nitrite ions released and form NO. NO activates guanylyl cyclise leading to increased cGMP and dephosphorylation of myosin and smooth muscle relaxation (precise mechanism unknown)	Production of NO leading to smooth muscle relaxation to pass
	How does GTN relieve angina pain ?	Venodilation leads to reduced venous return, reduce ventricular volume and reduced heart wall tension. This reduces myocardial O2 requirement.	Need to know that venodilation and reduced venous is major factor reducing myocardial o2 requirement.
	Outline the pharmacokinetics of sublingual GTN	Oral bioavailability is low due to extensive first pass hepatic metabolism by high capacity organic nitrate reductase. Rapid and efficient absorption by sublingual or intranasal routes but rapid elimination (t1/2 2-8 mins) and duration of action (15-30 mins) due to high capacity hepatic metabolism. Denitrited metabolites conjugated to to glucuronide and excreted in urine.	Poor oral bioavailability due extensive first pass metabolism and effective alternative routes of administration to pass
Beta Lactams	How does Penicillin exert its action ?	Inteferes in bacterial cell wall synthesis by binding to penicillin-binding-protein and preventing removal of terminal d-alanyl-d-alanine from peptides preventing crosslinking and formation of peptidoglycan.	Inhibits bacterial cell wall synthesis to pass.

	What are the mechanisms of resistance to B Lactam antibiotics ?	(1) Inactivation by B-lactamase (2) Modification of target PBPs (3) Impaired penetration of durg to target PBPs (4) Presence of efflux pumps	Inactivation of B-lactamase and one other to pass
Antiemetics	What clarrrrsses of drug can be used as antiemetics ?	(1) Serotonin 5-HT3 antagonists: the "trons" (2) Phenothiazines: prochlorperazine, promethazine (3) Butyrophenones: haloperidol (4) Substituted benzamides: metoclopramide (5) H1 antihistamines: diphenhydramine (6) Anticholinergics: hyoscine (Benzos, Cannabinoids, Corticosteroids)	Name three groups to pass – if name agents, prompt for group or mechanism of action.
	List and explain the adverse effects of prochlorperazine ?	Acute dystonia (dopamine blockade) Sedation (antihistamine effects) Anticholinergic effects (antimuscarine effects) Allergy	Acute dystonia + one other to pass
Drugs Binding To Biogenic Amine Transporters	How do anti-depressants exert their action ?	Thought to enhance amine-dependent synaptic transmission (serotonin and noradrenalin) by: (1) Inhibition of metabolism within nerve terminal (MAOIs) (2) Inhibition of reuptake from synapse (TCAs, SSRIs) (3) Increased release due to antagonism of specific serotonin and alpha2 noradrenalin receptors (Mirtazapine)	2/3 mechanisms to pass
	What are the relative advantages of different classes of antidepressants ? (Direct to adverse effects if no response)	Adverse effect profile Cost Efficacy Risk of overdose Dosing schedule Drug interactions	Able to discuss pros and cons of at least two