ACEM PRIMARY 2009.2 PHARMACOLOGY VIVA Thursday 17 Sept Session (am) *Candidate Number*..... AGREED MARK.....

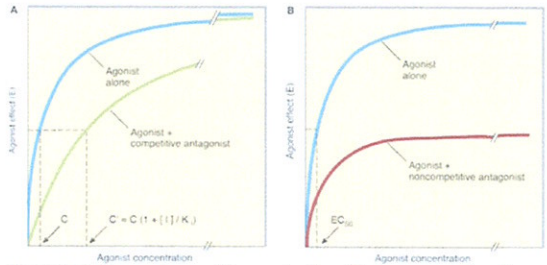
TOPIC	QUESTION	ESSENTIAL KNOWLEDGE	NOTES
Question 1: **Drug Biotransformation**	(a) What are the sites of drug biotransformation? (Prompt – Which is the major?)	**Liver** - GIT - lung - skin - kidneys	Must get Liver and two others
	(b) What is a **Phase 1 biotransformation** reaction?	Conversion of a parent drug to a **more polar / water soluble** form by the adding or unmasking of a **functional group**, most commonly by **oxidation** but also by reduction or hydrolysis. The hepatic CYP (P450) enzymes are responsible for the majority of these reactions.	Must mention **more polar** or **water soluble** & **oxidation**
	(c) What is meant by **enzyme induction,** in liver biotransformation?	**Repeated administration** of a substrate brings about either **enhanced enzyme synthesis** or **reduced enzyme degradation** causing **increased metabolism** of the substrate	Must mention **enzyme more active**, therefore **increased metabolism and reduced drug action** (2 of 3 bolds to pass)
Question 2: **Classification of drugs in acute asthma**	(a) Outline the groups of drugs that might be used in asthma and give an example of each?	• **sympathomimetics** • **corticosteroids** • **muscarinic** antagonists • other bronchodilators -magnesium • antihistamines (allergic basis) • methylxanthines • cromolyns • leukotriene inhibitors [antagonists] – montelukast, zafirlukast,zileuton • heliox –changing airflow dynamics • ?other smooth muscle dilators – ketamine; calcium channel blockers • Experimental -; IgE monocloncal antibodies - omalizumab	Must get 3 bolded groups and one other with one correct drug example per group to pass.
	(b) Outline the mechanism of action of corticosteroids in asthma	Corticosteroids do the following: • Reduce bronchial reactivity • **Inhibition of** (lymphocytic and eosinophilic) **airway mucosal inflammation** • Increase airway calibre	Must get bolded point to pass
Question 3: **Propofol**	(a) Describe the pharmacokinetics of propofol?	Intravenous administration **Distribution $t_{1/2}$ 2-8 min**, redistribution $t_{1/2}$ 30-60 min **Metabolism- rapidly in liver**; total body clearance is greater than hepatic blood flow, suggesting extrahepatic mechanisms **Excretion- urine** as glucuronides and sulphates- <1% unchanged	Required for Pass: a) bold

TOPIC	QUESTION	ESSENTIAL KNOWLEDGE	NOTES
	(b) What are the side effects of propofol?	Respiratory- dose-related **depression of central ventilatory drive**, apnoea, Cardiac- **Marked decrease in blood pressure** through decreased peripheral arterial resistance and venodilatation, and direct negative inotropic effect. Soy/egg allergy, Pain on injection	b) Knowledge of respiratory and cardiac effects of propofol
Question 4: **Warfarin**	(a) What is the mechanism of action of warfarin?	• Blocks synthesis of Clotting Factors II, VII, IX, X and Anticoagulant proteins C and S • Coupled to Deactivation of Vitamin K	Blocks factors II, VII, IX, X

	(b) What drug interactions with warfarin prolong the INR (prompt for mechanism)?	• Pharmacokinetic: (↑ INR)
		  • Inhibit transformation of Warfarin: S-Metronidazole, Fluconazole, Bactrim; R & S-Amiodarone, Disulfiram, Cimetidine
		  • Displace albumin bound warfarin: phenylbutazone, sulphinpyrazone
		• Pharmacodynamic: (↑ INR)
		  • Aspirin – affects platelet function
		  • 3rd generation Cephalosporins – reduce gut flora producing Vit K
		  • Heparin – directly prolongs INR
			2 examples

	(c) How is the action of Warfarin reversed?	• Vitamin K: FFP:Prothrombin complex – Prothrombin X: Recombinant Factor VIIa	2 of 4
Question 5: **Activated Charcoal**	(a) In a poisoned patient what modalities are available for decontamination?	Skin – remove clothes, wash contaminated skin GIT – emesis, gastric lavage, activated charcoal & cathartics / whole-bowel irrigation	3 of 5 to pass
	(b) How does activated charcoal work?	Adsorption due to its large surface area	
	(c) Name some drugs or agents that activated charcoal is NOT effective in adsorbing?	Ions: Fe, Li, K Alcohols, cyanide Corrosives (acids and alkalis)	2 examples
	(d) Name a drug where repeated doses of activated charcoal may assist in elimination of the drug	Carbamazepine, dapsone, theophylline	One drug

ACEM PRIMARY 2009.2 PHARMACOLOGY VIVA Thursday Session (pm) *Candidate Number*..... AGREED MARK.....

TOPIC	QUESTION	ESSENTIAL KNOWLEDGE	NOTES
Question 1: **Dose Response**	(a) Draw and explain a Dose-Response curve for an agonist		Must demonstrate relationship of concentration to effect
	(b) Show how this curve is altered in the presence of an irreversible (non-competitive) antagonist	 **Figure 2-3.** Changes in agonist concentration-effect curves produced by a competitive antagonist (**A**) or by an irreversible antagonist (**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 - Non-competitive antagonist has lower maximal effect
	(c) How does this differ from a competitive antagonist?		Pass – Higher conc. of agonist to produce similar effect
Question 2: **Classification of drugs used in diabetes mellitus**	(a) Outline the groups of drugs that are used to treat hyperglycaemia in diabetes mellitus.	• **Insulin** • **Sulfonylureas -** • **Biguanides** • Meglitinides • D- phenylalanine derivatives • Thiazolidinediones • Alpha-glucosidase inhibitors	Must get 3 bolded groups to pass.
	(b) Contrast the mechanism of action of sulfonylureas and biguanides.	Sulfonylurea: • **Increase insulin release from pancreas** • Reduction of serum glucagon levels • Closure of potassium channels in extrapancreatic tissues Biguanide: • **Action does not depend on functioning pancreatic B cells** • May directly stimulate glycolysis in tissues with increased glucose removal from blood; • May reduce hepatic gluconeogenesis; • May slow of absorption of glucose from the GI tract; • May reduce glucagon levels	Bold to pass

TOPIC	QUESTION	ESSENTIAL KNOWLEDGE	NOTES
Question 3: **Ketamine**	(a) How does ketamine affect the cardiovascular system?	HR, BP and cardiac output increase Stimulate central SNS, and inhibits re-uptake of noradrenaline at sympathetic nerve terminals	(a) Demonstrated understanding of CV effects of ketamine
	(b) What are the side effects of ketamine?	Sialorrhoea **Decreased RR** Postoperative disorientation Sensory and perceptual illusions **Emergence phenomenon** Vomiting **Raised ICP**- increases cerebral blood flow, oxygen consumption and ICP Rash	2 bold + 1 other
Question 4: **TPA**	(a) How does TPA work?	• Fibrinolytic. Binds to fibrin in a thrombus and converts entrapped inactive plasminogen to active plasmin to initiate local fibrinolysis	Definition
	(b) What are the indications for TPA use?	• STEMI • PE with haemodynamic instability • Acute Ischaemic Stroke: • Severe DVT	AMI, stroke and 1 other
Question 5: Amphetamines	(a) What is the mechanism of action of amphetamines?	**- Indirectly cause increased release of catecholamines at synapses** - Competitively inhibits dopamine transport in pre-synaptic neurone (DAT), inhibits VMAT causing non-vesicular release of dopamine into synapse (& similarly for other catecholamines)	First point to pass
	(b) Describe the effects of amphetamines?	1. Catecholamines; (increased arousal & decreased sleep) elevated HR (dysrhythmias) and BP (CVA) 2. Dopamine release; euphoria, potentially abnormal movements & psychosis 3. Serotonin; Appetite suppression, hallucinogenic & hyperthermia	CNS stimulation and cardiovascular effects to pass

ACEM PRIMARY 2009.2 PHARMACOLOGY VIVA Friday Session (am) *Candidate Number*..... AGREED MARK.....

TOPIC	QUESTION	ESSENTIAL KNOWLEDGE	NOTES
Question 1: **Drug Clearance**	(a) What formula describes **Drug Clearance**?	Ratio of rate of elimination of a drug to its concentration in blood / plasma or $CL = \frac{\text{Rate of elimination}}{\text{Conc}}$	Must get formula to pass
	(b) What is **Flow Dependent Elimination**? (prompt if needed – High extraction)	For drugs that are readily cleared by their organ of elimination (high extraction ratio), **the rate of elimination is dependent on rate of drug delivery to the organ – determined by blood flow** and plasma protein binding. (Systemic $CL = CL_{renal} + CL_{liver} + CL_{other}$)	Must mention **drug delivery / blood flow** to pass.
	(c) Can you name any drugs that have Flow dependent elimination	Hepatic –lignocaine; propanolol; verapamil' morphine; pethidine	One example to pass
Question 2: **Side effects of NSAIDs**	(a) What are the side effects of the non-steroidal anti-inflammatory agents?	**Allergy;** rash; pruritis Nausea, abdominal pain, diarrhoea **GI irritation / ulcers** **Bleeding secondary to inhibition of platelet aggregation** **Nephrotoxicity** Peripheral oedema; fluid retention Headache	3 bold to pass
	(b) What specific side effects occur with aspirin?	Salicylism – vomiting, tinnitus, hearing loss and vertigo Exacerbation of asthma Histamine induced flushing Irreversible platelet inhibition Raised LFTs	Any 2 to pass
Question 3: **Suxamethonium**	(a) Describe the mechanism of action of suxamethonium	Phase I (**depolarising**)- reacts with Nicotinic receptor, opens the channel, causing depolarisation of the motor end plate, not metabolised at the synapse, and so membranes remain unresponsive to subsequent impulses- lack of "repriming" leads to **flaccid paralysis.** Phase II (desensitising) Unclear, but channel block may be more important than agonist action. Action is terminated by diffusion away from the end plate into the extracellular fluid, where it is metabolised by plasma cholinesterase.	Demonstrated understanding of mechanism of action
	(b) What are the side effects of suxamethonium?	b) **Bradycardia**- negative inotropic and chronotropic effects (inc. second dose bradycardia)	3 bold to pass

TOPIC	QUESTION	ESSENTIAL KNOWLEDGE	NOTES
		Hyperkalaemia (esp burns, nerve damage, NM disease, closed head injury) **Increased intra-ocular pressure** **Increased intragastric pressure** (inc. aspiration) **Muscle pain** (in up to 20%) **Malignant hyperthermia** (when combined with volatiles) ***Sux apnoea*** in susceptible patients	

Question 4:
 	
Calcium Channel Blockers
	• What is the mechanism of action of CCBs?	• CCBs bind to receptors on alpha1,2, gamma and delta subunits of L-type Ca channel→↓ frequency of opening of Ca channels in response to depolarisation→↓ transmembrane Ca current→ ↓ Ca influx→
		  ◦ vascular smooth muscle relaxation
		  ◦ ↓ contractility in cardiac muscle
		  ◦ ↓ SA node pacemaker rate
		  ◦ ↓ AV node conduction velocity
			Need anti-arrhythmic and smooth muscle effects

	• What are the toxic effects of CCB's	• Cardiovascular: cardiac arrest; bradycardia; AV block; heart failure, hypotension • Minor: flushing, dizziness, nausea, constipation, peripheral oedema	2 cardiovascular
Question 5: Topical Anaesthetics	(a) What is the mechanism of action of local anaesthetics?	**- blockade of voltage-gated Na channels in neurones** - increasing doses lead to higher excitation threshold, slower impulse conduction, lower AP **- blocks conduction if 2-3 nodes of Ranvier in a myelinated nerve affected**	Blockage of Na channels and blocked conduction to pass.
	(b) Which local anaesthetics are used topically?	Lignocaine – oral spray for procedures, viscous for pharynx, with prilocaine in EMLA, other mixtures for wound and ENT care, eye drops EMLA (Eutectic Mixture of Local Anaesthetics – mixture of lignocaine and prilocaine) – skin anaesthesia for cannula insertion, etc. Cocaine – ENT procedures (combines vasoconstriction) Proxymetacaine, amethocaine, oxybuprocaine – eye drops Benzalkonium – oral gels	2 agents