ACEM PRIMARY 2012/2PharmacologyVIVA **Morning Session 1** ***Candidate Number.....*** **AGREED MARK.....**

TOPIC	QUESTIONS	KNOWLEDGE	NOTES
Question 1 Clearance-renal and hepatic	What is drug clearance?	Clearance predicts the rate of elimination in relation to drug concentration. **CL=rate of elimination/concentration**	**Bold**
LOA 1	Which organs are involved in drug clearance?	2 main organs are **kidney and liver**, others are blood, muscle, lung. CL systemic= CL liver + CL kidney + CL other	**Bold**
	What factors affect renal clearance?	**Renal function, renal blood flow**, plasma protein binding, ionization	Bold
	Please name drugs that are predominantly cleared by the kidneys?	ampicillin, **gentamicin**, vancomicin, digoxin, enalapril, metformin, lithium	At least bold plus 2 others-prompt: Any drugs that need dose changes in patients with poor renal function?
Question 2 Oral hypoglycaemics	Describe the pharmacokinetics of metformin?	Well absorbed, not protein bound, not metabolised, elimination t1/2: 1.5-3 hours, **excreted by kidney** as unchanged compound	Bold
LOA: 1	What are the side effects of metformin?	Gastrointestinal most common 20%, decreased absorption Vit B12, **lactic acidosis** esp with renal disease, ETOH, chronic cardiopulmonary disease	Bold
	With regard to sulphonylureas, what is	**Increase insulin release from the pancreas** bind	Patients more prone to hypo

	the mechanism of action of glipizide? (prompt: it's a sulphonylurea)	to receptor associated with ATP sensitive K channel, inhibits efflux of K ions, results in depolarization and opens ca channel, influx of Ca causes release of preformed insulin Reduction of serum glucagon levels Closure of potassium channels in extrapancreatic tissues	than with biguanides eg metformin
Question 3 Non Depolarising Muscle Relaxants LOA: 1	What's the mechanism of action of Rocuronium? (Prompt: receptor level) Describe the pharmacokinetics of rocuronium. *Prompt: Describe rocuronium's distribution and elimination.*	**Non-depolarising NM blocker**. In low doses it predominantly acts as a **competitive inhibitor of Acetylcholine** at nicotinic receptors. In larger doses it can enter the pore of the ion channel -> greater NM blockade. It can also block prejunctional sodium channels-> interference with the mobilisation of AChl at nerve endings. Undergoes **rapid distribution.** Highly ionized - so small Vd (80-140ml/kg). Undergoes hepatic metabolism (75-90%) and renal excretion. Duration of action is 20-35mins.	Non-depolarising NM blocker. Initially acts as competitive inhibitor for Ach at nicotinic receptors Rapid distribution. **Short T1/2.**
Question 4 Calcium	Can you give me an example of a preparation of calcium that is taken orally?	**Calcium Carbonate** or Ca -acetate, citrate, glubionate, gluconate, lactate or phosphate	Need to name 1

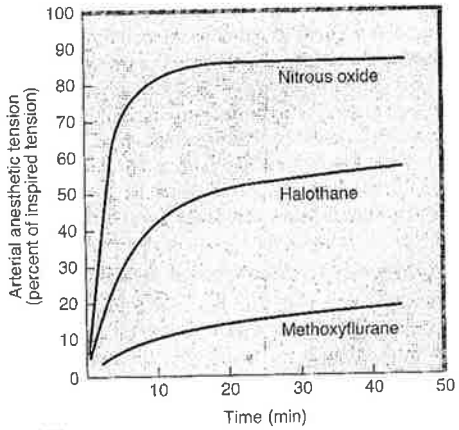
LOA: 1	What are the possible uses of oral calcium preparations?	i) Treatment of **hypocalcaemia** (eg. in patients with hypoparathyroidism, vit D deficiency, chronic renal disease or malabsorption). ii) As an antacid	hypocalcaemia.
	What are the potential adverse effects of giving calcium intravenously?	Irritation of the veins. Cardiac arrhythmias with rapid administration. Hypercalcaemia.	phlebitis
Question 5 Anti-influenza agents LOA: 2	List some anti-influenza agents	Zanamivir, Oseltamivir, Amantadine, Rimantadine	1 to pass
	What is the mechanism of action of zanamivir (relenza) and oseltamivir (tamiflu)?	Neuraminidase (a glycoprotein) inhibitors: disrupt viral replication and release Active against both influenza A and B;	Some concept
	What are the indications for their use?	Approved for treatment of uncomplicated influenza; 5 day course of therapy within 36 – 48 hrs of symptom onset shortens severity and duration of illness; may decrease incidence of respiratory complications	1 to pass
	What is the relevance of these agents to emergency medicine practice? PROMPT: what about during the recent	May be of use to **higher risk groups** eg indigenous, pregnant women, older people and immunocompromised, however primary prevention by **vaccination is preferred**. Used	One of bold

	flu pandemic?	preferably at **early phase of pandemic** to limit spread and numbers infected, and limit severity of disease in those infected.	

ACEM PRIMARY 2012/2Pharmacology VIVA Afternoon Session 2 ***Candidate Number.....*** **AGREED MARK.....**

TOPIC	QUESTIONS	KNOWLEDGE **(essential in bold)**	NOTES
Question 1 Volume of distribution LOA: 1	Define the "volume of distribution" of a drug.	Defined as the volume in which the amount of drug in the body would need to be uniformly distributed to produce the observed concentration in blood, plasma or water. Vd = Amt drug in body/C	Pass: either definition or formula
	How is it possible for a drug to have a VD of 2500L in an adult?	**Higher concentrations in extra vascular tissues than in blood – e.g. lipid soluble** (not homogeneously distributed)	Pass: either not homogeneously distributed or extra vascular tissue higher conc
	Give an example of a drug with a: - high VD - low VD	High: Morphine, chloroquine, digoxin, clonidine, fluoexitine, tricyclics, β blockers, diazepam, Low/approximating ECF/TBW: aspirin, frusemide, antibiotics (gentamicin, amoxicillin, cephalexin), tolbutamide, phenytoin, valproic acid, lithium, warfarin, theophylline, indomethacin, sulphamethoxazole.	**One of each** **One of each**
	What is the importance of Vd in the overdose situation PROMPT – for example (drug name)?	**Drugs with large Vd (TCAs) cannot be dialyzed** whereas **drugs with a low Vd (ASA, lithium)** can.	**Bold**– use these to prompt; should be able to designate "high" or "low" VD to pass.
Question 2	Describe the central nervous effects of	1) central	**Bold to pass**

Morphine LOA: 1	Morphine Describe peripheral effects?	• **analgesia** • euphoria • **sedation** • **respiratory depression** • cough suppression • miosis • truncal rigidity • nausea / vomiting • temperature 2) peripheral: • **cardiovascular** • GI- **constipation** • Biliary • Renal • Uterus • Neuroendocrine • Pruritis • immune	candidate should be able To describe in detail of each one in bold
Question 3 Nitrous oxide	Explain the solubility characteristics of nitrous oxide	Nitrous oxide possesses **low solubility** in the blood, reaches **high arterial tension rapidly, Rapid equilibrium in the brain** and **fast onset of**	**Bolded concept to pass**

LOA: 1	Draw the arterial anaesthetic tension vs time for nitrous oxide vs halothane or Methoxyflurane	**action (rapid onset-rapid recovery)**  	A curve
Question 4 Warfarin Interactions LOA: 1	Describe the mechanisms by which drugs interact with Warfarin. *Prompts* *Please describe pharmacokinetic interactions* *Please describe pharmacodynamic interactions* Give some examples of drugs that increase the INR.	**PK - Enz inhibition** (majority), **Enz induction**, altered, plasma protein binding, altered abs **PD** – Synergism (**impaired haemostasis)** Competitive antagonism (**clotting factor synthesis/concentration**) **↑ INR**: aspirin, heparin, corticosteroids metronidazole, fluconazole, trimethoprim-	Must get one example of PK and PD Must give at least 1 example of each

	Give some examples of drugs that decrease the INR.	sulfamethoxazole, third generation cephalosporins, macrolides, amiodarone, SSRIs, tramadol ↓ **INR:** Vit K, diuretics, barbiturates, phenytoin, carbamazepine, rifampicin, diclox, azathioprim	
Question 5 Serotonin Syndrome LOA: 2	Describe the mechanism by which Serotonin Syndrome occurs. *Prompt: What receptors are involved in SS?* How do drugs cause excessive stimulation of serotonin receptors? *Prompt: Can you give an example*	**Excessive stimulation of serotonin receptors in the CNS** due to overdose of single drug or concurrent use of several drugs. Predictable, not idiosyncratic. Inhibition of serotonin metabolism: meclobemide, amphetamines Prevention of serotonin reuptake in nerve terminals: fluoxetine, paroxetine, sertraline, venlafaxine, tramadol, TCA Serotonin release or increased intake of serotonin precursors: tryptophan, lithium,	Must get bold items Must identify at least 1 mechanisms with corresponding example

ACEM PRIMARY 2012/2Pharmacology VIVA **Morning Session 3** ***Candidate Number.....*** **AGREED MARK.....**

TOPIC	QUESTIONS	KNOWLEDGE **(essential in bold)**	NOTES
Question 1 Signalling mechanisms LOA: 1	List the various molecular mechanisms of transmembrane signalling.	1. Lipid soluble ligand crosses membrane and binds to intracellular receptor. 2. Transmembrane receptor protein with ligand binding to extracellular domain regulating intracellular enzymatic activity 3. Transmembrane receptor protein that binds and stimulates protein tyrosine kinase 4. Ligand-gated transmembrane ion channels 5. Transmembrane receptor protein, G protein, intracellular second messenger	Describe 3 mechanisms to pass
	Describe the function of the system involving G proteins	Transmembrane signally system with 3 separate components. Extracellular ligand binds to specific **cell surface receptor**. This receptor then activates **G protein** located on cytoplasmic surface of membrane. Activated G protein changes activity of **effector element** (enzyme or ion channel) leading to a change in concentration of **second messenger**.	Bold concepts to pass

	Give an example of a drug that acts via this system.	B agonist: B adrenoreceptor, G_S protein, adenylcyclase, increased concentration cAMP. (other examples include glucagon, thyrotropin, histamine, serotonin, acetylcholine, opioids)	Correct example to pass. Extra points for describing components
Question 2 adenosine LOA: 1	What are the indications for use of Adenosine? How does it work? How do the specific pharmacokinetic properties of adenosine influence the method of administration?	**Conversion of paroxysmal SVT to sinus rhythm.** Activation of inward rectifier K+ currents and inhibition of calcium currents. Leads to marked hyperpolarisation and suppression of calcium-dependent APs. Effect is direct inhibition of AV nodal conduction and increase in AV node RP. This **interrupts re-entry pathway thru AV node**. **Very rapid metabolism** by adenosine deaminase in red cells and vessels walls = very short elimination t1/2 (<10s) and duration of action (~30s). Must be given by **rapid intravenous bolusing.** If initial dose ineffective then subsequent dose should be increased (no accumulation occurs).	Bold to pass AV node conduction interruption Bold to pass
Question 3 Phenothiazines LOA 2	What are the side effects of chlorpromazine? (If required: What are the mechanisms of these side effects?)	**Hypotension – alpha blockade** Parkinson's, akthesia, **dystonic reactions – D2** Lactation – D2 Sedation – antihistamine Neuroleptic malignant syndrome – dopamine Confusion, tachycardia – anti muscarinic	Two bolded side effect any dyskinesia sufficient) and one correct mechanism.

	How do the newer atypical anti psychotic agents differ from chlorpromazine?	Newer agents have less side effects.	
Question 4 Tisssue Plasminogen Activator LOA 1	Describe the mechanism of action of tissue plasminogen activator (tPA)?	Activates **plasminogen to form plasmin**, resulting in fibrin digestion. Preferentially activates plasminogen bound to fibrin by several hundred fold therefore is considered **clot specific.** Short half life therefore heparin is essential adjunct. Naturally occurring.	Bold
	What are the clinical uses of tPA? *Prompt: Are there are any other time-critical indications?*	**AMI, unstable PE, acute ischaemic stroke**, severe DVT, intra arterial peripheral limbs	First 3 to pass
	What are the complications of tPA?	**Haemorrhage.** Physiological hemostatic thrombi at site of vascular injury eg GIH, or systemic lytic state resulting from formation of plasmin, producing fibrinogenolysis and destruction of other coagulation factors esp V and VIII.	Must give more than one site.
Question 5 Seizure medications	Describe the pharmacokinetics of sodium valproate	Well absorbed PO, bioavailability >80% Food may delay abs for several hours. Peak plasma levels 2 hrs if empty stomach 90% **protein bound** (fraction bound reduces as	Highly protein bound and small Vd to pass

LOA: 1		total dose increases). Highly ionized and highly protein bound, therefore **Small VD**, essentially confined to extracellular water, approx. 0.15L/kg 95% hepatic metabolism, (some to active metabolites), 5% unchanged in urine Clearance is low and dose dependent, T1/2 is approx. 15/24 (9-18) and reduced if taking other antiepileptic drugs	
	Describe the toxic effects of sodium valproate.	Mild : Transient GI inc anorexia, nausea and vomiting. Rash, alopecia and increased appetite. Weight gain. Major Overdose: **CNS:** coma, cerebral oedema (potentially fatal) Bone marrow depression Metabolic effects: hyperNa, hypoCa, hyperammonaemia CVS, renal effects Severe and idiosyncratic **1.** Hepatotoxicity – rarely fatal, usually in under 2 yo, or multiple meds. Elevation of LFTs in 40%. May be reversible **2.** Thrombocytopaenia	CNS to pass

TOPIC	QUESTIONS	KNOWLEDGE **(essential in bold)**	NOTES
Question 1: Factors affecting drug metabolism LOA: 1	What factors are responsible for differences in drug metabolism between individuals? Can you give an example of a drug-drug interaction?	Genetic factors Diet and Environmental Age and Gender Drug-Drug Interactions Disease states Induces inhibitors Protein binding Renal clearance Pharmacodynamic interactions	Need 3 to pass Must give an example with correct mechanism
Question 2 Atropine LOA: 1	What is the mechanism of action of atropine? Describe the organ effects of atropine.	A reversible **muscarinic antagonist** Binds to the muscarinic receptor, preventing the release of inositol trisphosphate (IP_3) and the inhibition of adenyl cyclase which are caused by the muscarinic agonists. CNS: ⇓ tremor in Parkinson's Disease, delirium EYE: Mydriasis and cycloplegia CVS: Tachycardia LUNG: Bronchodilation and ⇓ secretions GIT: ⇓salivary secretion, ⇓ gastric secretion acid, pepsin and mucin, ⇓ gastric emptying, ⇑ Gut transit time GUT: relaxes ureteric and bladder wall smooth muscle and slows voiding; ⇓ sweating.	Bold to pass **3/6 organ effects** to pass

Question 3 Macrolides LOA: 2	Name some macrolide antibiotics? Describe the mechanism of action of macrolides? What organisms are macrolides effective against?	Erythromycin, roxithromycin, azithromycin, clarithromycin. **Inhibits bacterial protein synthesis** by binding to 50S ribosomal RNA, which blocks the aminoacyl translocation reaction and formation of initiation complexes (transpeptidation). May be inhibitory or bactericidal, particularly at higher concentrations. Gram + orgs: pneumococci, streptococci, staphylococci, corynebacteria Mycoplasma, Legionella, Chlamydia sp, listeria, some mycobacteria Gram – orgs: Neisseria sp, Bordatella pertussis, Treponema pallidum, Campylobacter sp, bartonella (Haemophillus less susceptible)	**Pass = 2** **Pass = bold** **Pass = 3**
Question 4 Induction agents LOA: 1	Give some examples of drugs used as anaesthetic induction agents? Describe the onset and recovery of propofol and ketamine? Describe the cardiovascular effects of propofol and ketamine?	Thiopentone, propofol, ketamine, fentanyl, midazolam, etomidate **Both have rapid, Ketamine has a slower recovery** and is often associated with emergence phenomena. Propofol–**marked decrease in BP during induction** via decreased peripheral arterial resistance and venodilation. Also greater direct negative inotropic effects cf other induction agents Ketamine – **produces does-related CV stimulation, increased HR, BP** and CO (by stimulating central symp nervous system +/- inhibiting NA reuptake at symp nerve terminals	**Pass = 2** **Bold to pass**

Question 5 Heparin LOA: 1	Describe the mechanism of action of heparin?	Binds to endothelial cell surfaces and plasma proteins and its activity depends on antithrombin Heparin binds to antithrombin, causes a conformational change in the inhibitor, exposing its active site for more rapid interaction with proteases. Heparin acts as a co factor for the antithrombin-proteases reaction Antithrombin inhibits proteases espec thrombin 2a, 9a, 10a by forming stable complexes with them and the presence of heparin accelerates this reaction 1000x The binding of AT III and unfractionated heparin ↑ degradation of both factor Xa and thrombin	**Binds to AT III**
	How is heparin reversed? *Prompt: is there a specific antidote?*	Stop the drug Administer antagonist **protamine** (100 units heparin-1mg protamine) which binds heparin to form a complex devoid of anticoag activity Excess protamine anticoag effect	**Bold**
	What are the potential adverse effects of heparin? Prompt: Are you aware of any less common but serious idiosyncratic effects?	**Bleeding** (elderly women, renal failure more prone) **TCP** (1-4%), rare pregnancy, lower rates in paediatrics. Mortality relates to thrombosis Allergy ↑ hair loss Reversible alopecia Accelerates the clearing of post prandial lipaemia by causing release of lipoprotein lipase from tissues Long term: osteoporosis, spontaneous fracture, mineralocorticoid deficiency	**Bold**