TOPIC	QUESTIONS	KNOWLEDGE **(essential in bold)**	NOTES
Question 1 LOA: 1 **HALF LIFE**	Define drug elimination half life Is there a formula you can use? *Prompt: What factors affect half-life?* *Prompt: Can you explain what that means?* How does knowledge of a drug's half life help us clinically?	**Time required to change the amount of drug in the body by ½ during elimination** T1/2 = 0.7 x Vd/clearance (0.7 approx log 2) **Indicates time to steady state after dose change.** 50% after 1, >90% after 4	Concept required Both bold to pass
Question 2 LOA: 2 **PENICILLINS**	Describe the mechanism of action of penicillins How does resistance to penicillins occur? In general, what is the anti-microbial spectrum of penicillin G? *Prompt: Could you be specific*	**Inhibition of cell wall synthesis**. Interfere with transpeptidation. Covalently binding to PBP. Important in the cross linkage. Bacteriocidal,. Only kills growing cells. a. Inactivation by beta lactamases b. Modification of target PBPs (Pneumo/entrococci) c. Impaired penetration of drug to PBP; impact on porin channels. Gram negatives d. Efflux pump (gram neg) Streptococci, meningococci, enterococci, some pneumococci, treponema pallidum, clostridia, non-betalactamase producing staphylococci	**At least 2 including beta-lactamases** **At least 3 bacteria**
Question 3 LOA: 1 **LITHIUM**	Describe the pharmacokinetics of Lithium What are some of the drug interactions with lithium What are the some side effects of lithium *Prompt: What other organ systems effects are there?*	**Absorption; rapid and near complete**. peak levels in 30-120min **Distribution; total body water** Vol.D 0.5 to 0.9L/kg Slow distribution Metabolism; none T ½; @20 hours. **Elimination; renal excretion** **Thiazide diuretics**- 25% reduction in lithium clearance Newer NSAID's – similar reductions in clearance Neuroleptics (except clozapine) and antipsychotics- enhancement of extrapyramidal syndromes **Neurological;** tremor, confusion, ataxia, dysarthria, new psychiatric symptoms Reduced thyroid function Nephrogenic diabetes insipidis – loss of responsiveness to ADH. Oedema Skin reactions; acneiform eruptions	2 neurologic symptoms

Question 4 LOA: 1 **ANTIEMETICS**	Name some antiemetics used in the Emergency Department. Compare the mechanisms of action of ondansetron and metoclopramide Describe the potential adverse effects of metoclopramide.	**Ondansetron (or Granisetron or Tropisetron)** **Metoclopramide** **Prochlorperazine** Diphenhydramine (or other antihistamines). Meclizine. Hyoscine. Benzodiazepines. Chlorpromazine. Droperidol Act at different receptors: Ondansetron: **Peripheral 5HT3 blockade** (vagal and spinal afferents, Reduces sensory visceral output) + Central 5HT3 blockade (vomiting centre and CTZ) Metoclopramide: **D2 blockade** (CTZ). Increases oesophageal motility. Increases LOS pressure. Increase gastric emptying CNS: Restlessness, drowsiness, insomnia, anxiety, agitation – common (20%), esp. elderly Extrapyramidal effects: **acute dystonia**, akathisia, parkinsonian effects, more likely with higher doses Tardive dyskinesia with chronic dosing	Bold to pass Bold to pass Must mention acute dystonia + one other CNS effect
QUESTION 5 LOA: 1 **DRUGS IN AGITATED PATIENTS**	List the drug classes which are used in management of acute agitation in the ED *Prompt: Can you give some specific examples?* What is the predominant mechanism of action of the atypical antipsychotics. Describe adverse effects of the atypical antipsychotics	**Benzodiazepenes** **Antipsychotics – Phenothiazines** eg chlorpromazine **Butyrophenones** eg haloperiodol **Atypicals** eg olanzapine , risperadone Barbiturates – phenobarbital **Serotonin** ($5HT_{2A}$**) receptor antagonism** Dopamine (D2) receptor antagonism (weaker effect) **Extrapyramidal reactions** - – less common than with older typical antipsychotics Tardive dyskinesia **Antimuscarinic effects** – dry mouth, urinary retention etc **Orthostatic hypotension** Weight gain Hyperglycemia Hyperprolactinemia Agranulocytosis (clozapine) Neuroleptic malignant syndrome	

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Question 1 LOA: 1 **PARTIAL AGONIST**	In the context of drug-receptor interactions, what is the difference between a full agonist and a partial agonist? Under what circumstances can a partial agonist act as a antagonist? *Prompt: Can you use opioids as an example?*	**High concentrations of full agonists can evoke a maximal response, but partial agonists cannot evoke maximal response at any concentration** In the presence of a full agonist Buprenorphine	
Question 2 LOA: 1 **TRIMETHOPRIM**	Describe the mechanism of action of trimethoprim Can you explain why trimethoprim and sulphonamides when used together are synergistic? How does resistance to trimethoprim occur?	**Inhibition of DNA synthesis**. Selective inhibition of bacterial dihydofolic acid reductase which is required from the step dihydrofolic acid to tetrahydrofolic acid. Much less efficient at inhibiting mammalian enzyme. **Inhibition of** sequential **steps in same pathway**. Sulphonamides inhibit dihydropteroate synthetase (PABA to DHFA), the step before that at which trimethoprim acts Reduced cell permeability Increased production of enzyme DHF reductase Alteration in the enzyme with reduced binding of drug	Any 1 of 3
Question 3 LOA: 1 **CARBAMAZEPINE**	Outline the clinical uses of carbamazepine Describe the mechanism of its anticonvulsant activity Outline some of the side effects of carbamazepine *Prompt: What other organ systems can it effect?* **Optional**: Can you name some drug interactions involving carbamazepine	**Anticonvulsant;** partial and generalised tonic-clonic seizures Treatment of bipolar mood disorder Trigeminal neuralgia **Blocks sodium channels** Inhibits high-frequency repetitive firing of neurons Presynaptic blocker of synaptic transmission (similar to phenytoin) **Ataxia** and diplopia, **drowsiness** (dose related CNS) **GI upsets** and hepatic dysfunction Erythematous **skin rash** Hyponatraemia and water intoxication Blood dyscrasias, including leukopenia common), and rarely aplastic anaemia and agranulocytosis. **Enzyme induction** (all anticonvulsants including itself). Valproic acid + phenytoin may inhibit carbamazepine elimination	Anticonvulsant + 1 other use CNS + one other

Question 4 LOA: 1 **INSULIN**	Describe the different types of insulin used in the routine management of Type I Diabetes. *Prompt: Please describe in terms of duration of action*	**Rapid and short acting** Clear soln, neutral pH, contain Zn rapid onset, short duration e.g. insulin neutral, insulin lispro, insulin glulusine - **Intermediate acting** Turbid soln, neutral pH, protamine in phosphate buffer (NPH) to prolong action e.g. insulin isophane, insulin aspart protamine **Long acting** Clear solution, soluble Slow onset, prolonged action Daily admin mimics basal insulin secretion e.g. insulin glargine, insuline detemir	Pass criteria: Identify existence of rapid, intermediate and long-acting insulin Aware that combination of therapies required to cover both basal requirements and post-prandial periods
	How are these properties used to achieve optimum glycaemic control?	Tight glycaemic control is achieved by a combination of insulins with different durations of action with an aim of replacing the basal insulin requirements (50%) and meal requirements (50%). This is done with **combinations of insulins with different duration of actions**	
	What type of insulin is used for intravenous infusion and why?	Short-acting regular soluble insulin as it immediately dissociates on dilution and so is able to more precisely delivered.	
	Optional: Describe the principles of operation of a subcutaneous insulin infusion device. PROMPT: Insulin pump.	External open-loop pump for insulin delivery. Delivers individualised basal and bolus insulin replacement doses based on blood glucose monitoring. Programmed by user. Consists of insulin reservoir, program chip, keypad and display screen attached to subcutaneously inserted infusion set.	

Question 5 LOA: 1 **DRUGS IN PROCEDURAL SEDATION**	List the classes of drugs used in emergency department procedural sedation *Prompt: for classes*	**Benzodiazepenes** **Dissociative anaesthetics (** ketamine**)** **Intravenous anaesthetics (** propofol**)** **Inhaled anaesthetics** (N2O ; volatile**)** **Opiates (** morphine**,** fentanyl)	**4 out of 5**
	Describe the elimination pharmacokinetics of propofol *Prompt: Why do patients wake up quickly?*	**Hepatic metabolism** producing inactive watersoluble compounds , excreted renally High plasma clearance exceeding hepatic clearance – thus extrahepatic clearance exists – probably via lungs. Termination of effect by **redistribution** from brain to skeletal muscle (waking after single induction dose at 8-10 mins) "Three compartment model" Short "half – life" making it suitable for infusions – rapid offset.	
	Describe the organ effects of propofol	**CNS: sedative/hypnotic – general depression of CNS activity**, reduced cerebral blood flow and reduction in ICP. Anti convulsant properties.Nil analgesic effect **Cardiovascular effects: hypotension secondary to arterial and venous vasodilatation** (reduced preload and afterload) – incr. effect with age and reduced intravascular volume. Some inhibition of baroreceptor reflex leading to small increase in heart rate response only **Respiratory effects: respiratory depression incl apnoea.** Reduction in tidal volume and rate Reduced response to hypercapnoea and hypoxia Reduction in upper airway reflexes. Other: Antiemetic	**One from CNS, CVS + Respiratory**
	Describe adverse effects of propofol	Effects related to organ system effects • Hypotension • Apnoea, respiratory depression • Loss of airway reflexes – obstruction and aspiration • Pain with injection Allergy – cross reactivity with egg allergy (emulsion) Propofol infusion syndrome (metabolic acidosis & tachycardia)	

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Question 1: LOA: 1 **DIFFERENCES IN DRUG METABOLISM**	What factors determine the difference in drug metabolism between individuals?	**Genetic** – enzyme level differences Diet – induce / inhibit enzymes Environmental – exposure to enzyme inducers **Age** – extremes have decreased enzyme activity or decreased levels of cofactors Sex – increased metabolic rate in males **Drug-drug interactions** – enzyme induction or inhibition, substrate competition **Disease states** - hepatic, pulmonary, cardiac, thyroid, inflammatory Liver size & function Circadian rhythm Body temperature	3 of 4 **bold** to pass
	What is meant by "enzyme induction"? *Prompt: What effect does it have on metabolism?* *Prompt: What effect does this have on the pharmacological action of the drug?*	Drug causes an increased rate of synthesis or decreased rate of degradation of enzyme causing: **accelerated substrate metabolism** **decreased pharmacological action** of the inducer or a co-administered drug.	**Bold** to pass
Question 2 LOA: 1 **PARACETAMOL**	Describe the metabolism of paracetamol? *Prompt: Does this change in toxic doses?*	Rapidly absorbed, peak conc at 30-60 minutes Slightly PP bound Partially metabolised by hepatic MEs to paracetamol glucuronide and sulphate (inactive) <5% excreted unchanged Half-life is 2-3 hrs	3 of 5
	What is the toxic dose and how does this cause toxicity?	150-200mg/Kg or >7g in adult. Conjugation AAs (gluthathione in particular) used up, metabolised to toxic metabs NAPQI. Toxic to liver / kidneys.	Reasonable approximation. Must have reasonable understanding of how toxicity is caused
	What are the clinical manifestations of toxicity?	GIT effects: **Hepatic** impairment. N/V, diarrhoea, abdo pain, dizzy, disorientation Renal failure	Hepatic + one other

Question 3 LOA: 1 **SELECTIVE B2 AGONISTS**	What B-receptor types are there?	B1, B2 + B3	Need B1 + B2
	What cellular processes do B-agonist - B-receptor coupling initiate?	Activation of all 3 receptor types results in stimulation of **adenylyl cyclase** and increased conversion of ATP to cAMP. Mediated by stimulatory coupling protein (Gs) via GDP and GTP	Need adenylyl cyclase
	What are the clinical uses of B2 selective agonists?	**Respiratory**, uterine and vascular smooth muscle relaxation Skeletal muscle K+ uptake	Need respiratory bronchodilation + one other
Question 4 LOA: 1 **WARFARIN**	What is the mechanism of action of warfarin?	Warfarin **inhibits reduction of inactive Vit K** epoxide (KO) to active hydroquinone (KH_2) form. Blocks γ-carboxylation of glutamate residues in **prothrombin (Factor II) and factors VII, IX and X** ,as well as endogenous anticoagulant protein C and S.	Need to know role of vitamin k
	Why is there a delay in the onset of action of warfarin?	8-12 hr delay due to partially inhibited synthesis and unaltered degradation of 4 vit k dependent clotting factors and depends on **degradation ½ life** in circulation eg factor VII- 6 hrs, IX 24-hrs, X - 40 hrs and II- 60 hrs)	Need to have some idea of delay in onset
	What pharmacological agents are used in the reversal of warfarin?	Vitamin K. FFP. Prothrombin Complex. Recombinant FVIIa	
	Optional: Describe the mechanisms of drug interactions with warfarin	Pharmacokinetic: Enzyme induction + inhibition. Altered protein binding Pharmacodymanic: Synergism. Competitive antagonism (Vitamin K)	3 required

Question 5 LOA: 1 **DRUGS IN AF** **SOTALOL**	List the classes of drugs used for the management of AF in the emergency department	B-blockers Ca-channel blockers Cardiac glycosides Class 1c antiarrhythmics Class 3 antiarrythmics	3 of 5
	Describe the pharmacodynamics of sotalol:	**Non-selective beta blocker, Class II** **Prolongs plateau phase Class III**	Need class II + III
	List the main side effects	Pro-arrthymic- Esp **prolongation of QT** and Torsades CCF Asthma, AV blockade	Prolonged QT + 1 other
	What drug interactions with Sotalol prolong the QT? *Prompt: What other interactions can occur with sotalol?*	**Drugs which prolong QT**- phenothiazines, Macrolides, eg erythromycin, quinolones antidepressants,- Increased risk of Torsades Drugs which cause hypokalaemia hypomagnesaemia increase risk of Torsades Myocardial depressant drugs- increased LVF Calcium channel blockers, class 1a antiarrythmics, may increase refractory time and contraction	2 examples