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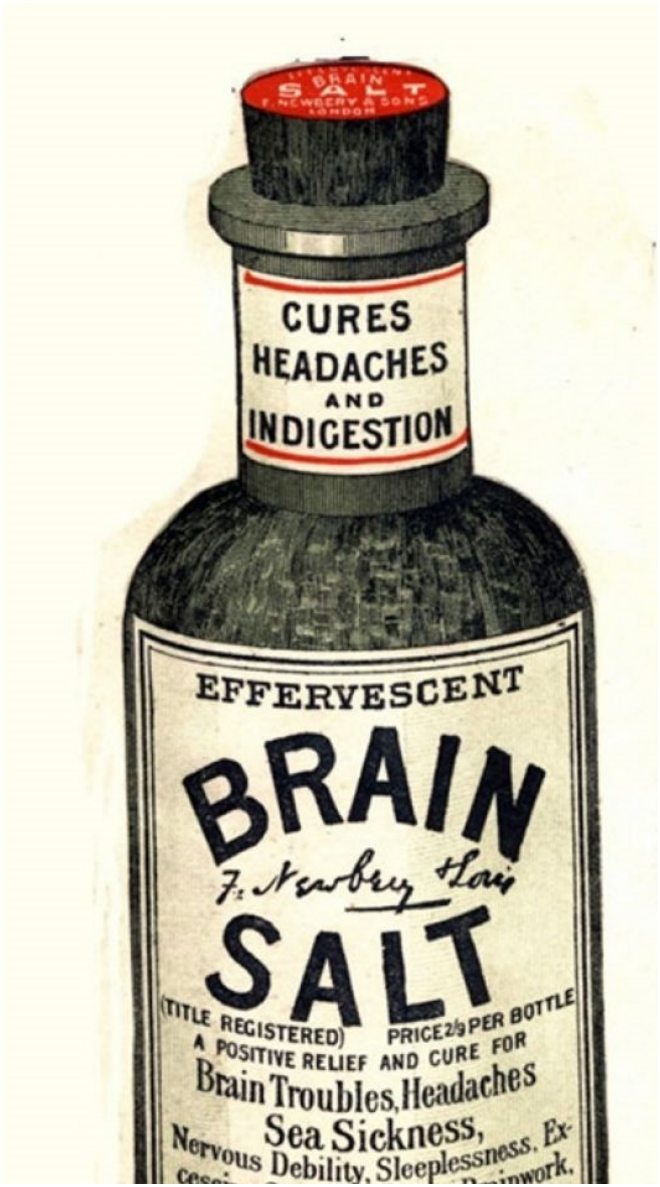

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Benzodiazepines 2017-2-D

Stem: A 50-year-old woman presents in an agitated state after self-harming. Diazepam is prescribed. We will start with Pharmacology.			
TOPIC	QUESTIONS	KNOWLEDGE	NOTES
Question 1 Benzodiazepines **Subject:** Pharmacology LOA: 1 *Katzung 13th, 374-7*	a) What is the mechanism of action of benzodiazepines? *Prompt: What receptor is involved?*	Binds to molecular components of **$GABA_A$ receptor** in neuronal membranes in **CNS** (ɣ subunit of the pentamer). **This receptor is a chloride ion channel.** The BDs do not substitute for GABA (major inhibitory neurotransmitter) but appear to enhance GABA's effects without directly activating $GABA_A$ receptors or opening the chloride channels. This causes an increase in the frequency of channel-opening events.	**Bold** plus concept
	b) What are the organ level effects of Diazepam?	**Sedation** – calming effect, **anxiolysis**; low dose effect- psychomotor & cognitive depression, amnesia **Hypnosis**; **Anaesthesia** – at higher doses; **Anticonvulsant** effect; **Muscle relaxation** **Respiratory depression & Cardiovascular depression** – at higher doses and when hypovolaemic/CCF/chronic heart dis.	3 of bold to pass
	c) What are the clinical uses of Diazepam in the ED?	Anticonvulsant, sedation of agitated patient, Etoh/benzo withdrawal, various toxidromes	2 to pass (can take into account part b answer)

Benzodiazepines 2011-2

Question 3 Benzodiazepines	a)What benzodiazepines are commonly used in the ED? b)What is the mechanism of action of benzodiazepines? (Prompt: describe how they interact with receptors) c) What are the clinical effects of benzodiazepines?	a)Diazepam, lorazepam, midazolam, clonazepam, temazepam, b) Agonist **at GABA $_A$ receptor** which is chloride ion channel binding between alpha1 & gamma2 subunit (BZ site) – more selective than barbs. Low affinity for $GABA_B$. GABA inhibition enhanced. c) **Sedation**, hypnosis, **anticonvulsant**, muscle relaxation, **resp depression** (esp if resp disease), CVS depression, decreased contractility, decr vasomotor tone (esp if CVS disease)	>= 2 Bolded Bolded

Benzodiazepines 2010-2

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.

Benzodiazepines 2005-2

TOPIC: Benzodiazepines NUMBER: 3

OPENING QUESTION	**How do benzodiazepines work at the receptor level?**	**COMMENTS**
POINTS REQUIRED	1 GABA receptor. Bind to varying subunits, mainly γ or α. Separate site to GABA	
	2GABA opens Cl channels and increases membrane polarisation	
	3Do not directly activate the receptor but facilitate the effect of GABA	
PROMPTS		
SECOND QUESTION (if needed)	**What are the clinical effects of benzodiazepines?**	
POINTS REQUIRED	**Sedation** Including disinhibition and amnesia	
	Hypnosis Decreased latency of onset Increased stage 2 NREM Decreased REM	
	Anaesthesia (adjunct)	
	Anticonvulsant Variable Particularly clonazepam, lorazepam, diazepam, nitrazepam	
	Muscle relaxation	
	Respiratory depression Respiratory centre depression usual cause of death	
	Cardiovascular depression if vulnerable or excessive dose	
THIRD QUESTION	**What is flumazenil?** **How does it work?** **Describe potential adverse effects from the use of it** **the management of benzodiazepine toxicity**	
POINTS REQUIRED	1. vomiting / seizures/ unmasking withdrawal	

Carbamazepine 2017-1-B

Stem: Moving onto Pharmacology. The patient is on carbamazepine.			
Question 2 Carbamazepine **Subject:** Pharm LOA 1	a) What receptors do carbamazepine affect?	a) **Sodium channel blocker,** adenosine receptors Anti-cholinergic (anti-muscarinic)	Bold to pass
	b) What are the most common dose-related adverse effects?	- nystagmus, diplopia, ataxia (cerebellar) - drowsiness - anti-cholinergic effects - dry mouth, tachycardia, blurred vision, delirium - CVS- hypotension	1 cerebellar sign plus one other
	c) What important drug interactions does carbamazepine have?	c) - **Induces CYP450/induces hepatic drug metabolizing enzymes** and P-glycoprotein, results in increased clearance of some drugs, reducing their therapeutic blood levels (e.g. warfarin, phenytoin, valproate, lamotrigine, diazepam, phenobarbitone) - Can result in breakthrough seizures - Increases metabolism of OCP reducing its effectiveness	Bold plus one example

Carbamazepine 2012-1

Question 3 LOA: 1 **CARBAMAZEPINE**	Outline the clinical uses of carbamazepine	**Anticonvulsant;** partial and generalised tonic-clonic seizures Treatment of bipolar mood disorder Trigeminal neuralgia	Anticonvulsant + 1 other use
	Describe the mechanism of its anticonvulsant activity	**Blocks sodium channels** Inhibits high-frequency repetitive firing of neurons Presynaptic blocker of synaptic transmission (similar to phenytoin)	
	Outline some of the side effects of carbamazepine *Prompt: What other organ systems can it effect?*	**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.	CNS + one other
	Optional: Can you name some drug interactions involving carbamazepine	**Enzyme induction** (all anticonvulsants including itself). Valproic acid + phenytoin may inhibit carbamazepine elimination	

Carbamazepine 2009-1

		Insulin: inhibits or stimulates insulin secretion	
Question 3: Carbamazepine	1. Describe the mechanism of action of carbamazepine.	Anticonvulsant: a) blocks Na channels b) Inhibits high-frequency repetitive firing of neurones c) Presynaptic blocker of synaptic transmission d) similar action to phenytoin	Pass: (a)
	2. How is carbamazepine metabolised?	a) Metabolised by microsomal enzymes b) enzyme induction occurs c) active metabolites (clinical significance uncertain)	Pass: (a)
	3. What is its effect of the metabolism of other drugs?	If (b) is not volunteered above – Enzyme induction increases the rate of metabolism of other drugs eg primidone, phenytoin, valproate, clonazepam. Some of these drugs also can inhibit carbamazepine metabolism	Pass: Enzyme induction

Clonazepam 2007-2

3.2 Clonazepam (BD)	What is the mechanism of action of clonazepam?	**Binds to GABA**-A , potentiates GABAergic **inhibition through hyperpolarisation** (does not act as direct GABA analogue), increases frequency of chloride channel opening, acts throughout brain but the distribution of the different GABA A receptor isoforms varies across the CNS
	What are the clinical uses of clonazepam?	Strong amnestic effect, **anticonvulsant**, anxiolytic, **sedative-hypnotic**
	What properties make clonazepam an effective anticonvulsant.	Lipid soluble/**blood brain barrier**, acts on alpha 1 GABA receptor isoform, potentiates inhibitory interneurones

Midazolam 2016-2-C

Stem: Moving onto Pharmacology. She has another seizure and is given Midazolam.			
Question 2 Midazolam including pharmacokinetics **Subject:** Pharmacology LOA: 1	1. What are the pharmacokinetics of Midazolam?	1. -**Water soluble** hence oral/IM/intranasal -**Poor oral bioavailability** -**Highly Protein Bound** -Crosses BB barrier easily at body pH. -**Short elimination half-life** 1.5-2.5 hours. -hepatic metabolism/renal excretion	**2/4 Bold**
	2. What is the mechanism of action of midazolam?	**2.** -Binds to GABA-A receptor (or complex) -**Potentiates GABAergic inhibition** through hyperpolarization (through Chloride) -Acts throughout brain	**Bold**
	3.What are the clinical effects of midazolam?	3. -Strong amnestic effect -Anticonvulsant -Anxiolytic -Sedative-hypnotic -Antiemetic -Reduced sensitivity to CO2	**2 other than anticonvulsant**

Midazolam 2013-1

Question 4 **MIDAZOLAM** LOA: 1	What are the clinical indications for the use of midazolam?	Anxiolysis, **sedation, anticonvulsant,** antiemetic	**Bold to pass**
	What are the advantages and disadvantages of the various routes of administration?	PO, IV, IM, PR, IN, Buccal	**Reasonable discussion of IV + 1 other**
	What are the adverse effects?	**Excess sedation, respiratory depression,** decreased motor skills, impaired judgment, hypotension + occasionally rashes	**Bold to pass**

Midazolam 2007-1

2.3 Midazolam	What is the mechanism of action of midazolam?	**Binds to GABA-A Chloride channels**, potentiates GABAergic inhibition through hyperpolarisation , acts throughout brain	
	What are the pharmacokinetics of Midazolam?	**Water soluble** hence oral/IM/intranasal but crosses BB barrier easily at body pH. **Short elimination half-life** 2-4 hours. (Note for examiners who may have forgotten- 56% renal excretion!)	
	What are the pharmacodynamics of Midazolam?	Strong amnestic effect, **anticonvulsant**, anxiolytic, **sedative-hypnotic**	/2

Midazolam 2004-2

Midazolam	What is the mechanism of action of midazolam ? What is the drug antagonist for midazolam OD ? What adverse events may be associated with the use of flumazenil for midazolam toxicity ?	GABA complex binding Cl channel opening , inhibitory effect on CNS Flumazenil Resedation Withdrawal/seizures	

Phenytoin 2016-2-C

Stem: Moving onto Pharmacology. He has a seizure and is loaded with phenytoin.			
Question 3 Phenytoin – pharmacokinetics **Subject:** Pharm LOA 1	Describe the pharmacokinetics of Phenytoin	High oral availability (90%), poor IMI Peak serum concentration 3-12hrs later **Highly plasma protein bound** (90%) Vd 45L/70kg (brain, liver, mm, fat) **Elimination is dose-dependent** (capacity limited / nonlinear / saturable elimination) At low blood concentrations first order kinetics; at higher blood concentrations – **hepatic enzymes saturated – elimination slows** t1/2 variable (12-36hrs) as a result **Metabolised** to inactive metabolites **by the liver** then urinary excretion (< 2% excreted unchanged)	Bold to pass incl. concept of dose-dependent elimination
	What is the rationale for using a loading dose of phenytoin?	Otherwise need 4 half lives to get to **steady state**, so reach **target** concentration more rapidly Dose = VolumeDist x TargetConc	Bold or Concept

Phenytoin 2015-1-D

Stem: She has a seizure and you decide to treat her with Phenytoin. We will now move onto Pharmacology.			
Question 4 Phenytoin Subject: Pharm LOA: 1	1. What is the mechanism of action of phenytoin?	Primarily **Na+ channel blockade/reduced neuronal Na+ conductance** and prolongation of inactivated state of Na+ channel. Reduces Ca++ influx into cells and decreases glutamate release and enhances GABA release. Inhibit the generation of rapidly repetitive action potentials	Bold
	2. What are the risks associated with intravenous phenytoin administration?	**Hypotension and bradycardia with rapid infusion** (due to diluent). Allergic reactions. Limit rate of infusion to maximum 50mg/min (30-60 minutes). Less likely with fosphenytoin.. Local necrosis if extravasation	Bold to pass.
	3. Describe the elimination kinetics of phenytoin and why it is important clinically?	**Dose-dependent elimination.** First order elimination at low serum concentrations, however elimination **becomes zero-order as concentration rises** with prolongation of elimination half-life. Implication- Small recurrent dose increase may => toxicity	Explains concepts
	4. What are the common features of acute overdose/intoxication with phenytoin?	Sedation, coma, nystagmus, ataxia, cerebellar toxicity. No cardiac toxicity with ingested overdoses of phenytoin.	2 to pass

Phenytoin 2010-2

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.

Phenytoin 2010-1

Question 2: Drugs in status epilepticus P374-92	1. Describe how phenytoin is administered in status epilepticus? *What's the mg/kg dose?* 2. Describe the adverse effects of phenytoin ? *What about short term vs long term effects?* *What about in iv administration?*	IV load 13-20mg/kg,, given diluted in saline (precipitates in glucose at max rate in adults of 50mg/min Continued 100mg Q6-8hrly Dose related nystagmus, ataxia, diplopia long term: gingival hypertrophy, hirsuitism mild facial coarsening & peripheral neuropathy abnormal Vit D levels (osteomalacia) low folate levels; megaloblastic anaemia; Foetal hydantoin syndrome. Idiosyncratic: skin rash; SJ syndrome; Lymphadenopathy; agranulocytosis. Rapid iv may cause hypotension/arrhythmia Drug interactions; reduced CL & binding in neonates	Dose mg/kg, iv route safe rate CNS + skin + CVS in iv admin

Phenytoin 2008-2

Question 3: Phenytoin	1. Describe the pharmacokinetics of phenytoin?	Weak acid pKa 8.3; oral abs almost complete 90%, with peak serum conc 3-12hrs later. Slow release formulation also. IMI: incomplete abs with drug precipitation in the muscle, fosP OK **Highly plasma protein bound,** metabolised to inactive metabolities with urinary excretion, < 2% exc unchanged in urine. **Dose dependant kinetics**; Vd 45L/70kg. t1/2 av 24 hours (conc dependant). Therapeutic level 10-20mg/L. Drug interactions via plasma protein binding or via enz induction (CYP2C19 & CYP2C9). Alters TFT results; reduced CL neonates; foetal hydantoin syndrome	Pass: highly protein bound and dose dependant kinetics
	2. Describe the pharmacodynamics of phenytoin? *Prompt: what is the effect on action potentials?*	**Block sodium channels** & inhibits the generation of repetitive APs blocks sustained high frequency repetitive firing of APs). Preferential binding to & prolongation of the inactivated state of the Na channel (use dependant effect on Na conductance). **Other electrolyte effects** -alters K conductance; alters Ca conductance ad decreases Ca permeability, inhibits Ca influx therefore affecting neurotransmitter & hormone release; -interacts with membrane lipids ? stabilising membranes; -paradoxical excitation in some neurones; -alters membrane potentials and the conc of amino acids; affects neurotransmitters NA, Ach & GABA. High conc inhibits serotonin and NA release, promotes uptake of DA & inhibits MAO activity.	Pass: Na channel, And one other effect

Valproate 20141-B

Stem: Moving to pharmacology: The child's mother has epilepsy and takes valproate.			
Question 3 Valproate **Subject:** Pharm LOA: 1	1.What are the possible pharmacodynamic mechanisms of Na Valproate? Prompt: what ion channels/ neurotransmitters are most likely involved?	**GABA** increased presynaptically by reduced GABA breakdown to succinate (ABAT/ GAT1), (> Cl- inh post synaptic GABR channel)/ possible increased production (GAD) Direct inh actions on post synaptic **Na Channel** particularly high freq gates and Ca+ (membrane stabilisation-reduces voltage gated outflow), Blocked NMDA receptor activation effects?	Bold
	2.What are the adverse effects?	Nausea/vomiting/ GI (v common); **Severe hepatotoxicity**- liver failure (> young/ other hep tox drugs/ liver damaged); Marked fetal abnormality rates (8-9%)/ reduced IQ + other possible developmental effects; Thrombocytopaenia/ bruising; Pancreatitis; alopecia, neuro (asthenia, tremor, nystagmus etc); Hypersensitivity reactions	Bold and 1 other

Valproate 2012-2

Question 5 Seizure medications LOA: 1	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 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	Highly protein bound and small Vd to pass
	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

Valproate 2011-2

Question 2: Valproate	a) What are the proposed mechanisms of action of valproate? b) Describe the toxic effects of valproate? *c) What interactions does valproate have with other anti-seizure drugs?*	a)**Blocks Na channels** thereby blocking sustained high frequency firing of neurones. Blockade of NMDA receptor mediated excitation. Increase GABA levels b) **Hepatotoxicity**, Mostly within 4 months of initiation of treatment, Treat with intravenous L-carnitine. GI, tremor, weight gain, appetite, sedation, allergy Malformations in pregnancy *c) Phenytoin inhibits metabolism and displaces from plasma proteins* *Phenobarbitore & carbamazapine inhib metab* *Lamotrigine decreases clearance*	Bolded Bold +1 to pass Supplementary

Valproate 2005-1

Valproate	Describe the mechanism of action of sodium valproate? What potential drug interactions can occur with sodium valproate?	**Three possible mechanisms:** • **Effect on sodium channels (blocker)** • **Effect on K+ channels (enhance efflux)** • **Increase in GABA via inhibition of GABA T, and decrease GABA breakdown via conversion to succinic semialdehyde (seen at high doses)** **(2 of 3 mechanisms)** • **Inhibition of its own metabolism at low doses.** • **Decreases metabolism of phenobarbitone, phenytoin and carbamzepine** • **Displaces phenytoin from plasma proteins** **(1 of 3)**	

Amitriptyline 2016-1-B

Stem: A 65 year old man presents with ischaemic pain in his leg. He is on amitriptyline. Starting with Pharmacology.			
TOPIC	QUESTIONS	KNOWLEDGE **(essential in bold)**	NOTES
Question 1 Amitriptyline– mechanism of action, side effects **Subject:** Pharm LOA: 1	Describe the pharmacodynamics of amitriptyline What are the toxic effects of amitriptyline and how are they mediated?	Blocks reuptake of **serotonin and noradrenaline**, and blocks muscarinic, sympathetic α_1, $GABA_A$, Na+ channel and histamine receptors. Monoamine vs neurotrophic vs neuroendocrine theories. • Blurred vision, dry mouth, tachycardia, retention, delirium (anticholinergic) • Sedation (antihistamine) • Hypotension (anti-alpha effects), • Wide QRS and bradycardia (Na channel blockade) • Seizures (direct central effect)	**Bold** and 2 other receptors Must name effects and cause for at least 3 groups

Antidepressants 2008-1

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

Carbamazepine 2005-2

TOPIC: Anti seizure Drugs_____NUMBER: 3

OPENING QUESTION	What is the mechanism of action of	COMMENTS
POINTS REQUIRED	Tricyclic compound Blocks sodium channels Inhibits high frequency repetitive firing neurons Decreases pre synaptic transmission Inhibits uptake and release of Nor-adrenaline from brain synapses Does not influence GABA uptake	
	Well absorbed Peak levels 6-8 hours 70% protein bound Does not displace other drugs Half life 36 hours initially Induces liver enzymes and dose has to increase markedly over first few weeks.	
SECOND QUESTION (if needed)	**What are the clinical indications for its use ?**	
POINTS REQUIRED	Partial Tonic-clonic With phenytoin if difficult to control tonic-clonic Trigeminal neuralgia & other pain syndromes	
THIRD QUESTION (if needed)	**What are its potential adverse effects ?**	
POINTS REQUIRED	Toxicity diplopia Ataxia GIT upset Blood dyscrasias – aplastic anaemia, agranulocytosis Skin rash	
	Alters clearance of other drugs Drug reactions due to induction of liver enzymes Primidone Phenytoin Ethosuximide Valproate Valproate and Propoxyphene may also decrease metabolism and increase steady state drug levels	

Lithium 2015-1-B

Stem: Moving onto Pharmacology. Her medications include Lithium			
Question 2 Lithium **Subject:** Pharm LOA: 1	Q1. What are the adverse and/or toxic effects of lithium?	Neuro - tremor, choreoathetosis, **ataxia,** dysarthria, hyperactivity, **confusion,** withdrawal. Thyroid - reversible **hypothyroidism**. Renal - **polyuria, polydipsia** (nephrogenic diabetes insipidus), chronic interstitial nephritis, nephrotic syndrome. Cardiovascular - oedema, worsening of sick sinus syndrome	**At least 3 bold**
	Q2. Describe the pharmacokinetics of lithium	**Oral absorption** (peak 0.5-2 h but complete 6-8 h). **Distributes in TBW. Excreted unchanged in urine.** Plasma half-life 20 h. Therapeutic concentration 0.6-1.4 mmol/L	**Bold, plus some appreciation of longer half-life.**
	Q3. How can you assess lithium toxicity and how do you treat it?	**Measure levels** (should be 10-12 h after last dose) >2 mmol/L should be considered toxic. Treatment is supportive and haemodialysis (Prompt that Li is an ion).	**Bold, plus some concept that levels should be measured well after last dose.**

Lithium 2012-1

Question 3 LOA: 1 **LITHIUM**	Describe the pharmacokinetics of Lithium	**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**	
	What are some of the drug interactions with lithium	**Thiazide diuretics**- 25% reduction in lithium clearance Newer NSAID's – similar reductions in clearance Neuroleptics (except clozapine) and antipsychotics- enhancement of extrapyramidal syndromes	
	What are the some side effects of lithium *Prompt: What other organ systems effects are there?*	**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

Lithium 2005-2

SUBJECT: PHARMACOLOGY
TOPIC: Lithium _____ **NUMBER: 5**

OPENING QUESTION	**Describe the pharmacokinetics of lithium**	COMMENTS
POINTS REQUIRED	1 Absorption virtually complete by 6-8 hours	Adequate knowledge
	2 Distributed to the TBW with initial Vd of 0.5 L/kg rising to 0.8 mg/kg.	
	3Very slowly redistributed from the extracellular compartments to the intracellular compartment.	
	4 No protein binding.	
	5 No metabolism.	
	6 Excreted unchanged in the urine with elimination half-life about 20 hrs.	
SECOND QUESTION	**What factors may influence lithium excretion?**	
POINTS REQUIRED	1 Renal function (Glomerular filtration rate)	
	2 Water and sodium status (increase lithium reabsorption in proximal tubule in sodium or water depleted states	
	3 Drugs: thiazide diuretics, NSAIDs reduce clearance	
	4 Lithium serum concentration	
THIRD QUESTION (if needed)	**Describe the adverse effects associated with lithium**	
POINTS REQUIRED	1 May be associated with therapy or toxicity	
	2 Neurologic: tremor, motor hyperactivity, movement disorders, ataxia, dysarthria, aphasia ...	
	3 Psychiatric: confusion, withdrawal	
	4 Thyroid: hypothyroidism	
	5 Renal: Nephrogenic diabetes insipidus (leads to polydipsia and polyuria)	
	6 Oedema	
	7 Other: Skin	

Lithium

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

Serotonin Syndrome 2012-2

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

SSRIs 2008-2

Question 3: SSRIs	1 What is the mechanism of action of the SSRI drugs *Prompt selective serotonin reuptake inhibitors* *Prompt for delayed onset of action- possible mechanisms*) 2 What receptor/channel effects lead to the SSRI side effect profile *Prompt why are SSRIs safer than TCAs?*	i) **Amine hypothesis** – modulation of **NET + SERT** pathways by reuptake inhibition ? > serotonin response ii) Prolonged synaptic exposure to Serotonin leads to iii) prob **time frame 3-6 weeks** due to presynaptic/ post synaptic receptor / storage regulation iv) SSRIs **v HT specific** v TCA 300-7000:1 Very **specific for HT**(partic 1) receptors –therefore **serotonin syndrome/ restlessness. Minimal autonomic** NE activation + mild muscarinic / Na channel, **H1** block effects (**safety/ tolerance**). Possibly some α block (sexual dysfunction)	**General understanding** knowledge of amine hypothesis and b) delayed response c) prob alteration in pre/post synaptic **specific HT + 1 other**, Serotonin syndrome Minimal autonomic = good tolerance/ safety modulation receptors and storage

Tricyclic Antidepressants 2014-2-D

Stem: A 50 year old woman is brought to the ED with an amitriptyline overdose. Commencing with Pharmacology.			
TOPIC	QUESTIONS	KNOWLEDGE **(essential in bold)**	NOTES
Question 1 Tricyclics including Volume of distribution (Chp 30) **Subject:** Pharm LOA: 1	Which factors determine the volume of distribution of a drug? Describe the volume of distribution of tricyclic antidepressants How does this influence their toxicity? What therapies for tricyclic toxicity might reduce their tissue distribution?	**Drug factors**; lipid solubility (high in TCA), pKa, pH, protein binding (high in TCA). **Patient factors**; age, gender, comorbid disease (eg. Oedema or ascites), body fat, blood flow to tissues. TCAs have a **large Vd** (5-30L/kg), tissue **concentrations are high** especially in well perfused organs such as **the brain and heart.** **Alkalinisation** (Bicarbonate or hyperventilation) increases **plasma protein binding of the free drug** removing it from the tissues reducing its tox	At least 2 from each group bold bold

Tricyclic Antidepressants 2011-2

Question 3 Tri-cyclic anti-depressants	a)What are the pharmacokinetics of tricyclic anti-depressants? b) What are the toxic effects of tricyclics in overdose? *c)What drugs could be used in the treatment of tricyclic toxicity in overdose?*	a) Oral, well-absorbed, bioavail 40-50%, **long half-time**, high first pass metabolism, high tissue protein binding, high lipid solubility, **large VOD,** metabolised in liver, active metabolites **b)Sedation**- plus drug interactions, sympathomimetic tremor, insomnia, **antimuscarinic**- blurred vision, constipation, urinary, confusion, tachycardia cardiovascular- alpha-blocker, Na channel blocker, orthostatic **hypotension**, **arrhythmias**, psychiatric- psychosis, agitation, withdrawal **seizures**, weight gain *c)* *Supportive- dopamine/NA for hypotension* *Quinindine like cardiac toxicity- sodium bicarb 50-100 mEq IV, Intralipid*	Bold Bolded *supplementary*

Tricyclic Antidepressants 2008-2

Question 3: Tricyclic antidepressants	1. What is the mechanism of action of the tricyclic antidepressants? Prompt: Name one amine? "Where does it happen? 2. Describe the toxic effects in overdose and how are they mediated?	Block amine (NAdr or Serotonin) reuptake pumps at presynaptic nerve endings prolongs duration of action of neurotransmitters at postsynaptic receptors. Most non selective Antimuscarinic. tachycardia, dry mouth, blurred vision, delirium, coma, Agitation; Urinary retention, reduced gastric motility, Respiratory depression; Neuromuscular irritability and seizures Sympathomimetic: tremor. Insomnia Sedation: additive effects alpha1-antiadrenergic – postural hypotension, Hypotension, dizziness fast sodium-channel blockade – reduced myocardial contractility, QT prolongation, cardiac arrhythmias;	Amine block, reuptake inhibitor some antimuscarinic cardiac (mix) Na channel block effects

Sumatriptan 2005-2

TOPIC: Anti migraine agents **NUMBER: 4**

OPENING QUESTION	**How does Sumatriptan work in the treatment of migraine headache?**	**Comments**
POINTS REQUIRED	• A selective agonist for $5HT_{1D}$ + $5HT_B$ • These receptors are found on cerebral & meningeal vessels • It causes vasoconstriction	Serotonin agonist to pass
SECOND QUESTION	**Please describe the pharmacokinetics of Sumatriptan**	
POINTS REQUIRED	• Bioavailability 15% (other agents in the group have availabilities of 40-70%) • T ½ = 2-3 hours • Given S/C, nasally, orally	Poor bio-availability given s/c
THIRD QUESTION	**What are the pros and cons in using Sumatriptan for migraine?**	
POINTS REQUIRED	<u>Pros</u> • Mild side effect eg tingling, dizziness, muscle weakness, neck pain, injection site reactions • Effective <u>Cons</u> • Contraindicated in patients with IHD due to coronary spasm • Short duration of action (several doses required for prolonged attack) • Very expensive	Coronary spasm
PROMPT		

Triptans 2011-1

Anti-migraine medication	What drugs can be used in the treatment of an acute attack of migraine?	**simple analgesia** (eg paracetamol, aspirin, codeine); **metoclopramide, prochlorperazine**; ergot alkaloids eg ergotamine (+/- caffeine added); **chlorpromazine**; **triptans** eg sumatriptan (opoids can be used but not choice)	**3 bold**
	How do triptans work?	structural analogue of 5-HT; **selective agonists at 5-HT1 receptors; cause vasoconstriction, particularly on cerebral arteries**	**2 bold**
	Chlorpromazine can be used to treat acute migraine. What are the major side effects of chlorpromazine?	**hypotension; sedation; anticholinergic** (dry mouth, dry eyes, urinary retention, constipation); **extrapyramidal (eg acute dystonia)**; pain with IM injections, risk of muscle necrosis	**2 bold**

Levodopa 2007-2

2.4 Levodopa	Why is levodopa used in combination with carbidopa? What are the adverse affects of levodopa?	Carbidopa is a peripheral dopa decarboxylase inhibitor. Because it doesn't penetrate the blood brain barrier, it reduces the peripheral metabolism of levodopa → ↑ levodopa levels, ↑ half-life resulting in more dopa being available for entry into brain to exert its effects. GIT: Anorexia, nausea and vomiting in up to 80% of patients. Due to stimulation of emetic centre in brainstem. Incidence ↓ to < 20% if a peripheral decarboxylase inhibitor is added. CVS: Arrhythmias-tachycardia, ventricular ectopics, AF. Due to ↑ catecholamine formation peripherally. Postural hypotension Dyskinesias: Up to 80% of those receiving levodopa for long periods. Behavioural effects: Depression, anxiety, agitation, insomnia, nightmares, euphoria and mood changes. More common if taking a levodopa with a decarboxylase inhibitor. Due to higher levels presenting to the brain. Fluctuations in clinical response occurs with increasing frequency as treatment continues. Miscellaneous: Mydriasis, acute glaucoma, Coombs positive haemolytic anaemia, gout, abnormalities of taste and smell, Brownish discolouration of saliva, urine or vaginal secretions, priapism, abn urea, LFTs. Drug Interactions: Pyridoxine enhances metabolism of levodopa. Hence effect ↓. **3 systems to pass**	

Antipsychotics 2012-1

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	

Antipsychotics 2011-1

Antipsychotic side effects and their treatment	What are the major side effects of phenothiazine antipsychotics?	**Anti-cholinergic:** dry mouth, dry eyes, urinary retention, constipation; Sedation; Weight gain; **Extra-pyramidal:** dystonia, Parkinson-like effects, akathisia, tardive dyskinesia; Hypotension; Neuroleptic malignant syndrome	Bold with 1 example of category
	What mechanisms of drug action are responsible for these side effects? Prompt: What receptors are involved?	Anti-muscarinic; Alpha blockade; D2 antagonism; Serotonin receptor antagonism; Anti-histamine (H1)	At least 3
	How could the extra-pyramidal side effects be managed? Prompt: What about acute EP side effects? Prompt if time for additional marks: What about chronic EP side effects	Lower dose; Switch to an atypical drug (lower incidence of extra-pyramidal effects); Administer **benztropine** or diazepam; No effective treatment for tardive dyskinesia: prevention vital; monitor for early signs and reduce or cease anti-psychotic asap	Bold

Antipsychotics 2010-2

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

Antipsychotics 2005-1

Antipsychotic agents – side effects	What adverse reactions can be associated with the use of antipsychotic agents?	• Anticholinergic • Disturbance of Ach/Dopamine balance leading to EPS (extrapyramidal Syndrome) Parkinsonism Akathisia Dystonia Long term effects – tardive dyskinesia • NMS, Neuroleptic malignant syndrome • Antialpha • Antihistaminic • Jaundice • Endocrine **(Bold x 3 + 1 of the other)**	bold

Chlorpromazine 2012-2

		accumulation occurs).	
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.	

Chlorpromazine 2009-1

Question 3: Chlorpromazine	1. What are the clinical uses of chlorpromazine?	**Antipsychotic** especially for schizophrenia Sedative for agitation Antiemetic	Antipsychotic and one other
	2. What are the phamacodynamic properties responsible for these effects?	Antipsychotic D_2 blockade in mesolimbic & mesofrontal systems Antiemetic dopamine receptor blockade in medullary chemoreceptor trigger zone & peripherally on receptors on stomach Sedation 5HT blockade	Dopamine blockade
	3. What are its adverse effects?	Autonomic loss of accommodation, dry mouth, **urinary retention**, constipation **orthostatic hypotension**, sexual dysfunction CNS **Parkinsonism**, akathisia, dystonia, **Neuroleptic Malignant Syndrome** Tardive Dyskinesia Confusion Seizures **Sedation** Endocrine **Hyperprolactinaemia** – Amenorrhoea, galactorrhoea, infertility, impotence Ocular Corneal deposits	Any 3 adverse effectss

Haloperidol 2014-2-C

Stem: We will now move onto pharmacology. He is agitated. You use Olanzapine to sedate him.			
Question 4 Olanzapine & atypical antipsychotics (Chp 29) **Subject:** Pharm LOA: 2	1. By what routes can Olanzapine be administered? 2. What dose, and route would you use in this situation? 3. What are the advantages of olanzapine over older "typical" antipsychotics? Prompt: e.g. chlorpromazine 4. What are some of its disadvantages? Prompt if needed – what about longer term effects	**1. Oral** (Tab or wafer); **Parenteral**- IMI, Depot IMI 2. Gives dose (10-20mg), same for each route 3. less hypotension; less tachycardia; **less extrapyramidal effect**; high clinical potency; less effect on prolactin; more effective vs neg&pos psychotic symptoms and cognition; multiple routes of admin 4. Anticholinergic effects; lowered seizure threshold; weight gain; DM; Hyperlipidaemia; expense	**Bold** **Reasonable answer** **Bold** **2 disadvantages**

Olanzapine 2014-2-C

Stem: We will now move on to Pharmacology. Haloperidol is suggested for her agitation.			
Question 2 Haloperidol (pp 503-513) **Subject:** Pharm LOA: 2	What are the pharmacodynamics of haloperidol?	Butyrophenone- **high potency D2 receptor effects (dopamine antagonist), high extra-pyramidal side effects, low sedative**, low hypotensive, minimal anticholinergic effects, minimal 5-HT and H1 blockade effects.	**2/3 Bold**
	How does olanzapine differ?	Thienobenzodiazepine- less D2 receptor effects, **high 5-HT receptor blockade effects, low extrapyramidal effects, medium sedative**, low hypotensive and anticholinergic effects, low H1 blockade effects	**2/3 Bold**

Olanzapine 2007-1

2.5 Olanzepine	What the pharmacological characteristics of olanzepine? How does it differ from haloperidol?	Olanzepine = Thienobenzodiazepine, most D4, alpha-1, 5-HT receptor effects, also H1 effect, high potency, very low extrapyramidal effects, medium sedative, low hypotensive effects, causes weight gain long term **(must get 2)** Haloperidol = Butyrophenone, most D2 receptor effects, high potency, very high extrapyramidal effects, low sedative, low hypotensive effects, cheap. **(must get 1)**	/2

Olanzapine 2006-1

Olanzapine	What are the advantages of olanzapine over the older antipsychotics? *Prompt with* How does Olanzapine compare with haloperidol in terms of sedation, hypotensive effect and extrapyramidal toxicity? **2 out of 3, prompts allowed**	Can be given as tablet, wafer or injection (wider **Less unwanted dopamine effects**, eg tardive dyskinesia, NMS **Drug** / **Usual daily oral dose range (mg)** / **Sedation** / **Postural hypotension** / **Anticholinergic** / **Extrapyramidal** / **Weight gain** haloperidol: 1-7.5 / + / + / + / +++ / ++ olanzapine: 5-20 / +++ / + / ++ / + / +++ Like clozapine, olanzapine has a wide range of receptor affinities. It is relatively well tolerated but drowsiness and dizziness can occur. Excessive weight gain may precipitate type 2 diabetes. Transient elevation of liver enzymes has been associated with olanzapine, but this does not appear to be of clinical significance.
	What are the clinical conditions Olanzapine is prescribed for?	Wide Spectrum of use: Autism spectrum disorders. Behavioural emergencies Delirium: mood and behavioural disturbances; palliative care; AIDS Dementia: General; Sleep disorder in patients with dementia (palliative care) Acute treatment of mania: Olanzapine Schizophrenia **2 of list**

Adrenaline 2017-2-B

Image not found

Adrenaline 2009-1

Question 2: Adrenaline	1. What are the effects of adrenaline on the blood vessels in different tissue? 2. What receptors mediate these effects?	Vascular resistance Cutaneous α Mucous membranes α Skeletal muscle β_2, α Renal α, D Splanchnic α, β Venous tone α, β	Pass: 3 tissues + receptors
	3. Describe the effects of adrenaline on other organs besides the heart.	**Respiratory** Bronchodilation **Eyes** Pupillary dilation, Intraocular pressure – decreases, also decrease production of aqueous humor) Relaxation of **gastric** smooth muscle **Genitourinary** Uterine smooth muscle relaxation, Bladder relaxation, Bladder sphincter contraction, Ejaculation **Apocrine** sweat glands – palm of hands **Salivary** glands leading to dry mouth **Lipolysis** – increased fatty acids and glycerol in circulation **Liver** – enhanced glycogenolysis **Metabolic acidosis** Decreased extracellular **potassium** **Leucocytosis** **Insulin** inhibits or stimulates insulin secretion	3 organs

Adrenaline 2005-2

TOPIC: SYMPATHOMIMETIC AGENTS _____ **NUMBER:** 2

OPENING QUESTION	**Describe the effects of an intravenous adrenaline infusion on the CARDIOVASCULAR system.**	**COMMENTS**
POINTS REQUIRED	1. Predictable physiological effects from a combination of alpha and beta stimulation, i.e.: – Increased cardiac output (chronotropy + inotropy) – (low dose: beta > alpha): vasodilation with widened pulse pressure – (higher doses: alpha > beta): vasoconstriction with narrowing of pulse pressure	Must know all to pass (except difference between high dose and low dose rates)
PROMPTS	1. "How does the effect of adrenaline on the cardiovascular system vary with the plasma adrenaline concentration?"	
SECOND QUESTION (if needed)	**What are the potential side-effects or complications of an adrenaline infusion**	
POINTS REQUIRED	1. GENERAL- Anxiety, tremor, nausea, vomiting, pallor	
	2. HEART & CIRCULATION- Palpitations and/or arrhythmias, myocardial ischaemia, hypertension	Must get 2 & 3to pass
	3. METABOLIC (beta effect) - hyperglycaemia, metabolic (lactic) acidosis, hypokalaemia	
PROMPTS		
THIRD QUESTION (if needed)	**How does the effect of adrenaline differ from noradrenaline?**	
POINTS REQUIRED	1. Noradrenaline peripheral alpha effect- vasoconstriction	
	2. Adrenaline mixed peripheral alpha and beta as above	
	3. Noradrenaline lesser cardiac effect	
	4. Slightly different side-effect profile (metabolic effects due predominantly to beta receptor activation)	
PROMPTS	"What are the differences in receptor effects of these two agents?"	

Adrenaline, Dobutamine 2003-2

Pharm Session 2 Topics	Questions	Essential knowledge	Comments	Pass / Fail (Score)
B receptor agonists	1. Regarding B agonists, by what cellular mechanism do they exert their effects?	Bind to specific **receptor.** **G-protein activation.** Stimulate adenyl cyclase. **Increased cyclic AMP.** **Increased free intracellular Ca.** Activate protein kinase.	**Bold items required to pass.**	
	2. Compare the cardiovascular of adrenaline and dobutamine.	**Adrenaline has B1, B2 and alpha effects.** Increased **inotrope and chronotrope.** Peripheral **vasoconstriction in most vascular beds.** Vasodilatation in skeletal muscle beds (B2). May reduce TSVR. **Dobutamine is a selective B1 agonist.** **Increases cardiac output** with less reflex tachycardia as it has fewer B2 effects. Comes as racemic mixture of +ve and –ve isomers. One isomer has B agonist and alpha antagonist effects; the other has alpha agonist effects.	**Bold items required to pass.**	

Amphetamines 2009-2

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

Atropine 2016-1-A

Stem: Moving onto Pharmacology, she is given Atropine			
Question 2 Atropine including Pharmacokinetics **Subject:** Pharm LOA: 1	What is the mechanism of action of atropine?	A competitive, reversible **muscarinic ACh receptor antagonist** Binds to muscarinic receptors, preventing the release of IP3 (inositol triphosphate), DAG (diacyglycerol) and the inhibition of adenylyl cyclase caused by muscarinic agonists. Anticholinergic agent (equipotent at M_1,M_2,M_3Rc)	Bold to pass
	Describe the organ effects of atropine	Eye – mydriasis & cycloplegia CNS – delirium, decrease tremor in Parkinson's disease CVS - tachycardia Resp – bronchodilation & decrease secretions GIT – decrease saliva secretion, decrease gastric acid secretion, decrease mucin production, decrease gastric emptying, decreased gut motility and intestinal transit time increases GUT – relaxes ureteric and bladder wall smooth muscle, urine retention Skin – decreased sweating	Need 3 organ systems with an example to pass
	What is atropine used for clinically?	**Rx symptomatic bradyarrhythmias / bradycardia** Ophthalmology – as a mydriatic & cyloplegic Occas. in paediatric RSI using suxamethonium (not routine any more) esp 2nd dose Drying of secretions eg in cholinergic nerve agent / OP poisoning or in palliative care Traveller's diarrhoea	Bold plus 1 to pass
	Extra question: Describe the pharmacokinetics of atropine?	Route of admin: IV, oral, nebulized, topical Absorption: well absorbed orally Distribution: **wide Vd** (including CNS) Half life = 2 hrs Metabolism & Excretion: 40% phase I and phase II metabolism and renally excreted 60% excreted renally unchanged	

Atropine 2012-2

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

Atropine 2010-1

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)	

Atropine 2008-1

3.2 Atropine	What is the mechanism of action of atropine?	Reversible block of **cholinergic muscarinic** receptors	
	Give examples of organ effects	CNS: decrease tremor and rigidity in Parkinson's disease Eye:– mydriasis and cycloplegia Cardiovascular: SA (and AV) node; blocks vagal slowing -> rel tachycardia and incr conduction (shorten PR)_, block coronary vasodilation Respiratory: blocks M receptors on smooth muscle and secretions Gastrointestinal: Blocks motility and secretions Genitourinary Relaxes smooth muscle in ureters and bladder wall (spasm) and slows voiding (retention) Skin: decreases sweating **(must get 3)**	
	What are the features of atropine poisoning	Agitation and delerium Raised temp Blurred vision / mydriasis Dry mouth / flushed skin Tachycardia **(must get 4)**	/4

Atropine 2007-1

3.2 Atropine	What is the mechanism of action of atropine?	Reversible block of **cholinergic muscarinic** receptors	
	Give examples of organ effects	CNS: decrease tremor and rigidity in Parkinson's disease Eye:– mydriasis and cycloplegia Cardiovascular: SA (and AV) node; blocks vagal slowing -> rel tachycardia and incr conduction (shorten PR)_, block coronary vasodilation Respiratory: blocks M receptors on smooth muscle and secretions Gastrointestinal: Blocks motility and secretions Genitourinary Relaxes smooth muscle in ureters and bladder wall (spasm) and slows voiding (retention) Skin: decreases sweating **(must get 3)**	
	What are the features of atropine poisoning	Agitation and delerium Raised temp Blurred vision / mydriasis Dry mouth / flushed skin Tachycardia **(must get 4)**	/4

Atropine 2003-2

Muscarinic blockers	1.Can you describe the basic machanism of action of atropine. Prompt: ask about specific receptor if just say anticholinergic	Anti-cholinergic Anti-muscarinic at all three types of muscarinic receptors No significant nicotinic effect	Must say anti -muscarinic	
	2. What are the therapeutic applications of drugs that block muscarinic receptors?	Heart Gut Eye Organophosphate poisoning Parkinsons Motion Sickness Respiratory (IB) Urinary disorders	Any 4	
	3.What are the toxic effects of antimuscarinic overdose?	Delirium Hyperpyrexia Mydriasis Tachycardia Dry mouth Urinary retention Dry as a bone Red as a beet	5 out of 8	

Benztropine 2015-1-C

Stem: A 40 year-old man develops a dystonic reaction following a metoclopramide injection. Starting with pharmacology			
TOPIC	QUESTIONS	KNOWLEDGE **(essential in bold)**	NOTES
Question 1 Benztropine Subject: Pharm	How does metoclopramide cause a dystonic reaction?	Metoclopramide is a **dopamine antagonist** and causes an imbalance in the anticholinergic/ dopamine transmission in the basal ganglia.	Bold
LOA: 1	You treat the dystonic reaction with benztropine. What is its mechanism of action?	**Blocks the** muscarinic **cholinergic receptors**; an antimuscarinic agent.	Bold
	What are the potential side effects of benztropine?	Tachycardia, sedation, mydriasis, urinary retention, dry mouth	**Knows 3**

Benztropine 2006-2

5. Benztropine	1. **What is benztropine?** 2. **What are the adverse effects of benztropine?** (1 FROM EACH CATEGORY)	**Centrally acting anti-muscarinic** **CNS – drowsy, confusion, hallucinations** **PNS –dry mouth, blurred vision, mydriasis, retention, N/V, constipation** **Cardiac – tachycardia, palpitations**	

Indirect Cholinomimetics 2003-2

Indirect acting Cholino-mimetics pp98-105	1.What is the mechanism of action of indirectly acting cholinomimetics?	**Inhibition of the enzyme acetylcholinesterase thereby increasing the concentration of endogenous acetylcholine in the vicinity of cholinoreceptors** Action on both nicotinic and muscarinic receptors. Action on the neuromuscular end plate and autonomic ganglion cells	To pass: must get bold item	
	2.What types of indirectly acting cholinomimetics are there? Please give examples.	Reversible: Group 1.Alcohols – edrophonium Group 2.Carbamates – neostigmine, physostigmine, pyridostigmine Irreversible: Group 3. Organophosphates – Ecothiophate, insecticides	To pass: Must either delineate reversible and irreversible groups or give two well explained examples	
	3.What are the cardiovascular effects of these groups of drugs?	Both sympathetic and parasympathetic ganglia can be activated **Parasympathetic effects generally predominate Bradycardia, decreased CO, decreases contractility, no change or modest decrease in BP.** OD may cause tachycardia and hypotension.	To pass: Must at least get bold items	

Metaraminol 2015-1-B

Stem: We will now move to Pharmacology. He develops neurogenic shock and is treated with metaraminol.			
Question 3 Metaraminol (chp 9) **Subject:** Pharm LOA: 1	What is the mechanism of action of Metaraminol?	Direct **alpha 1 receptor agonist** – some indirect effect through increased noradrenaline.	Bold
	What are its effects on the cardiovascular system?	**Vaso and arterio – constriction** in vascular beds. Arterioconstriction → ↑**BP** Direct cardiac effects less important HR slows due to vagal feedback CO unchanged or slight decrease as ↑VR and hence SV	Bold
	What role do sympathomimetics have in management of shock?	Temporising only While other treatment instituted – fluids, etc Efficacy not proven Useful in 'failure' sympathetic NS (eg/ spinal injury or anaesthesia)	Understanding of temporary only

Noradrenaline 2015-2-B

Stem: He is quadriplegic and hypotensive. Moving onto Pharmacology. A Noradrenaline infusion is commenced			
Question 3 Noradrenaline **Subject:** Pharm LOA: 1	(a) What receptors do NA act on	**Predominantly α 1 receptor** → vascular smooth muscle constriction Also α 2 receptor (presynaptic) – inhibits NA release (negative feedback) Some effect on β 1&2 receptors (more potent effect on β 1)	Need to mention predominant α 1 and one other receptor.
	(b) How does NA increase blood pressure Prompt : what is the effect of NA on blood vessels	α 1 activity → vasoconstriction → **↑ total peripheral resistance** → ↑DBP β 1 activity → **↑ myocardial contractility** → ↑ SBP Overall rise in both DBP & SBP	Bold
	(c) How does NA affect the heart rate?	β 1 activity ↑heart rate. However compensatory baroreflex causes reflex bradycardia → **therefore minimal change in HR**	Bold

Noradrenaline 2011-2

Question 4 Noradrenaline	a) What is the adrenoreceptor selectivity of noradrenaline? (prompt "what receptors does it act on") b) Describe the cardiovascular effects of infused noradrenaline	a) **alpha1 = alpha2; Beta1** >> Beta2 alpha 1: post-synaptic effector cells, especially smooth muscle alpha 2: presynaptic nerve terminals, platelets, lipocytes, smooth muscle beta 1: post synaptic effector cells, especially heart, lipocytes, brain b) 1. **Increases peripheral vascular resistance** 2. **Increases SBP and DBP** 3. Little chronotropy 4. **Positive inotropy**	all 3 bold to pass 2 of 3 bold to pass

Ethanol 2017-2-D

Stem: Moving on to Pharmacology. Ethanol abuse is the most likely cause of his symptoms.			
Question 5 Ethanol **Subject:** Pharmacology LOA: 1 Katzung 13th edition pp 384-386	a) Describe the pharmacokinetics of ethanol. *Prompt: How is it metabolised?* b) What does zero-order kinetics mean? c) What other drugs have zero order kinetic metabolism.	Absorption: rapid from GIT (peak level in 30mins) Distribution: rapid. Vol of Distribution: TBW (0.5-0.7 L/kg) Metabolism: **Predominantly liver**. Mainly by **alcohol dehydrogenase** and less by microsomal ethanol oxidising system (MEOS). **Zero-order**. Excretion: Lungs, urine (small amounts) Elimination occurs at a constant rate independent of drug concentration Phenytoin, theophylline, warfarin, salicylate, heparin, paracetamol	Bold to pass concept one

Ethanol 2017-1-D

Stem: Moving onto Pharmacology.			
Question 5 Ethanol **Subject:** Pharm LOA: 2	a) What are the pharmacodynamic effects of ethanol?	CNS: sedation, disinhibition, impaired judgement, impaired motor skills, ataxia, slurred speech -> coma, respiratory depression CVS: depressed contractility Smooth Muscle: vasodilator (-> hypothermia)	3 x CNS plus 1 other
	b) What are the pharmacokinetics of ethanol?	Absorption – rapid from GI tract peak levels within 30 min Distribution – rapid Vd ~TBW 0.5-0.7L/kg **Metabolism** - liver – **ZERO order** and mainly by alcohol dehydrogenase Excreted - lungs, urine	Bold plus 2
	c) What does zero –order kinetics mean?	That independent of the drug concentration the elimination of the drug occurs at a constant state	Understand concept

Ethanol 2016-1-A

Stem: Moving onto Pharmacology.			
Question 5 Ethanol **Subject:** Pharm LOA: 1	1) What are the clinical features of acute ethanol consumption?	**CNS-**sedation, disinhibited, impaired judgement, impaired motor skills, ataxia, slurred speech->coma, resp depression Heart-depressed myocardial contractility Smooth muscle-vasodilator ->hypothermia in OD, + uterine SM relaxation	Must mention CNS + one other
	2) Describe the pharmacokinetics of ethanol	Absorption-**rapid from GI tract** (water soluble), peak levels within 30 minutes Distribution –rapid Vol Distribution ~TBW (0.5-0.7 L/kg) **Predominantly liver metabolism -zero order kinetics** (over 90% oxidised liver-to acetaldehyde). Mainly via **Alcohol dehydrogenase (ADH),** less by microsomal ethanol oxidising system (MEOS) Excreted –lungs, urine	Bold to pass-must mention ADH
	3) Name other drugs that have zero order kinetic metabolism	Phenytoin, theophylline, warfarin, salicylates, heparin, paracetamol	One to pass

Dantrolene 2007-2

3.5 Dantrolene (SB)	Describe the actions of Dantrolene What are the uses? What is the dose for acute management of malignant hyperthermia?	ACTIONS • Interferes with release of Ca^{++} from SER, by binding to the SER Ca^{++} channel ("ryanodine receptor"), hence reducing excitation coupling. • Motor units that contract rapidly are more sensitive (hence only slight depression of cardiac and smooth muscle) USES: • Spasmolysis (cerebral palsy, MS, stroke) • Malignant hyperthermia (hereditary impairment of SER to sequester/reuptake calcium that has been released into the cell) DOSE for MH: 1 mg/kg IV, repeat as needed to 10 mg/kg	/4

Ketamine 2017-2-C

Stem: Moving on to Pharmacology. He was given Ketamine to reduce the injury.			
Question 2 Ketamine **Subject:** Pharm LOA: 1	Describe the pharmacodynamics of ketamine. What are the systemic effects of Ketamine?	**NMDA receptor antagonist**. Inhibits reuptake of catecholamine and serotonin. Potent short acting sedative, amnestic, analgesic and anaesthetic agent CNS: dissociative **anaesthesia**. (Cataleptic state) Profound **analgesia**. Cerebral vasodilator and increases cerebral blood flow and cerebral metabolic rate (Increases ICP – not clinically significant). May have anticonvulsant properties CVS: **haemodynamically stable**, increases HR, BP and cardiac output, cardiac workload and myocardial oxygen consumption. Respiratory: **Intact airway reflexes**. Min. respiratory depression. Causes lacrimation and salivation that may cause laryngospasm in children. Bronchodilator. Ocular: nystagmus	**Bold to pass** **Bold** + 1 other
	What are the adverse effects?	CNS - emergence phenomenon - dysphoria, hallucinations, seizures GI – vomiting Resp – Laryngospasm, increased salivation	One adverse effect

Ketamine 2017-1-D

Stem: Moving to Pharmacology. He requires intubation. Ketamine is used as the induction agent.			
Question 3 Ketamine **Subject:** Pharm LOA: 1	a) What is the mechanism of action of ketamine?	• Ketamine mechanism of action is complex, but the major effect is probably produced through the **inhibition of the NMDA (N-methyl- D aspartate) receptor complex** or • **blockade** of the membrane effects of the excitatory neurotransmitter glutamic acid at the **NMDA (N-methyl- D aspartate) receptor complex**	Bold
	b) Besides the anaesthetic effect what are the other indications of ketamine?	• Analgesia, Bronchodilator effect in asthma, Acute behavioural disturbance, Procedural sedation	2 to pass
	c) In what conditions might you avoid using ketamine?	• Allergy, RICP, RIOP, Recent or current URTI, Shock	at least one to pass (excluding allergy)
	BONUS: What are the organ system effects of ketamine?	• Organ system effects o CNS - Cerebral vasodilation and increase blood flow o CVS - Increase in BP,HR,COP (centrally mediated sympathetic stimulation) o Resp - Relaxation of bronchial smooth muscle o Other - Increase salivation (secretion), lacrimation, nystagmus, myoclonus	

Ketamine 2016-2-D

Stem: Ketamine is given for analgesia. Moving onto Pharmacology.			
Question 2 Ketamine pharmacokinetics and Pharmacodynamics **Subject:** Pharm: LOA: 1	a. Describe the pharmacokinetics of ketamine *Prompt: Why does it wear off quickly?*	1. **Highly lipid soluble, hence rapid onset. Effect terminated by redistribution** to inactive tissue sites. Low protein binding (12%). **Metabolised in liver** (N-demethylation by cyt. P450) -> norketamine (1/3 – 1/5 potency of ketamine) -> hydroxylated & conjugated into H2O sol. Inactive metabolites -> **excreted in urine**	Bold to pass
	b. What are the CNS effects of ketamine?	**Dissociative anaesthetic,** profound analgesic, stimulates symp. n.s., incr. cerebral bl. flow (cerebral v/d, raised ICP), nystagmus, partial amnesia, anticonvulsant	Bold + 1 to pass
	c. What are the cardiac and respiratory effects of ketamine?	**CVS** - Incr. BP, HR & CO, lesser direct myocardial depressant **Resp –** bronchodilation, minimal resp. depression, maintain airway reflexes, bronchorrhoea, laryngospasm (paeds), hypersalivation	1 CVS and 2 Resp effects to pass

Ketamine 2015-1-D

Stem: A 6 year old boy has sustained a laceration to the sole of his foot. It is to be repaired under ketamine sedation. We will start with Pharmacology.			
TOPIC	QUESTIONS	KNOWLEDGE **(essential in bold)**	NOTES
Question 1 Ketamine (pp 444-445) **Subject:** Pharm LOA: 1	1. What is the mechanism of action of ketamine?	**Antagonism of NMDA** (subtype of glutamate) **receptors.** Inhibits reuptake of catecholamines and serotonin	Bold
	2. What are its clinical effects?	**Dissociative anaesthetics.** Profound analgesia, stimulate sympathetic nervous system, bronchodilatation, minimal respiratory depression, stable CVS. increased Cerebral bd flow, partial amnesia, nystagmus	Bold +2
	3. What are its adverse effects? [Prompt- Are there any airway concerns?]	**Unpleasant emergence reaction** (eg vivid dreams or hallucination), **laryngospasm**, increased salivation, vomiting, myoclonus	Bold
	4. Give an appropriate route and dose for procedural sedation in this child? [What other routes are available?]	**1-2 mg/kg IV, 4-10 mg/kg IMI**	Can state either IV or IM dose

Ketamine 2013-1

Question 4 **KETAMINE** LOA: 1	What are the indications for ketamine	**Induction agent, procedural sedation, analgesia**	**2 of bolded**
	What are the routes of administration?	**IV, IM,** IN, epidural, PO, PR, SC	**IV, IM + 1 other**
	What is the IV dose used for induction of general anaesthesia?	**1-2 mg/kg**	**Bolded**
	Name some of the adverse effects.	**Hypersalivation, larygospasm(peds), vomiting(recovery phase), emergence reactions, Hypertension, tachycardia, raised ICP**	**Emergence reactions + 2 other**

Ketamine 2009-2

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

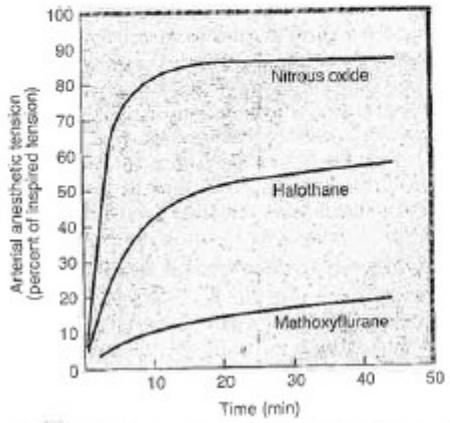
Ketamine 2006-2

3. Ketamine	**What type of anaesthesia does ketamine produce?** **Which receptor action produces the anaesthesia?** **What are the cardiorespiratory effects of ketamine?** (1 CVS, 1 RESP FOR PASS)	**Dissociative anaesthetic: analgesia, amnesia, catatonia +/- LOC** **Blockade of glutamic acid (excitatory neurotransmitter) at NMDA receptor** **CVS: HR, BP, CO increase central SNS excitation** **Resp: decreased rate, airway reflexes remain intact, bronchodilator**	

Ketamine, Propofol 2012-2

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**

Nitrous Oxide 2012-2

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 action (rapid onset-rapid recovery)**	**Bolded concept to pass**
LOA: 1	Draw the arterial anaesthetic tension vs time for nitrous oxide vs halothane or Methoxyflurane		A curve

Nitrous Oxide 2006-1

Nitrous oxide	What are the organ effects of nitrous oxide?	CNS: Analgesic, amnesic. Inc CBF Renal: Decreased GFR, inc filtration fraction & inc renal vasc resistance CVS: Dose dependant myocardial depression Resp: Reduced resp response to CO2 & hypoxia **1 CNS and 1 non CNS**	
	What is the mechanism of action of nitrous oxide? *How does NO affect GABA* *Any other mechanisms by which NO works?*	**Directly activate GABA A receptors**	-GABA A receptor Cl channel. Facilitate GABA mediated inhibition at GABA receptor sites -membrane hyperpolarisation -decreased duration of opening of nicotinic receptor activated channels. Decreased excitatory effect of ACh

Pancuronium 2010-2

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

Propofol 2016-2-A

Stem: Moving onto Pharmacology. He requires sedation to have his arm attended to and Propofol is used			
Question 4 Propofol (Pharmacokinetics and Pharmacodynamics **Subject:** Pharm LOA: 1	1) Please describe the pharmacokinetics of propofol?	IV admin only. Rapid onset/recovery due to **redistribution** from brain-> skeletal muscle-> fat, rather than metabolism. **Distribution t ½ 2-4 mins** Elimination t ½ 4-23 mins Duration of action 3-8 mins Metabolism- rapidly in liver, some extra-hepatic (lung) Excretion - Urinary as glucuronides & sulphates, < 1% unchanged	**Bold** with reasonable understanding of drug redistribution
	2) What are the adverse effects of propofol?	**Hypotension**- vaso/venodilatation and -ve inotropic effect **Apnoea**- dose-related central depression of respiratory drive. Pain on injection Soy/egg allergy	**Bold**
	3) How can you limit adverse effects when using propofol?	Caution with simultaneous co-administration of opiates/benzodiazepines. Titrate small doses (10-20mg aliquots) slowly to effect. Reduce doses in the elderly or with poor cardiovascular reserve. Caution with haemodynamically unstable patients	**Any 2**

Propofol 2015-1-B

Stem: Moving on to Pharmacology. There is a fracture dislocation of his left shoulder. His shoulder is reduced under Propofol sedation			
Question 3 Propofol **Subject:** Pharm LOA: 1	Q1. Please outline the pharmakokinetics of propofol	IV administration only, **Distribution half life 2 - 4 minutes**, **Elimination half life 4 -23 minutes,** Duration of action 3 - 8 minutes - **Rapid onset and recovery due to redistribution of drug** from brain to skeletal muscle and then fat (rather than metabolism), Rapidly metabolised in the liver but as total body plasma clearance > hepatic flow, likely some extrahepatic mechanism (mostly lung), Excretion in the urine as glucuronides and sulphates < 1% unchanged	**Bold, reasonable understanding of redistribution of drug**
	Q2. What dose of propofol is used for induction of general anaesthesia? How does this differ from a procedural sedation dose?	PROCEDURAL SEDATION DOSE: 0.5 - 1.0 mg/kg single bolus dose or titrate in 10 - 20 mg aliquots particularly in conjunction with morphine, INDUCTION DOSE: **1 - 2.5mg/kg (adults)** and 2.5-3.5mg/kg in kids	**Bold**
	Q3. What clinical effects should be anticipated when using propofol?	anaesthesia/sedation, respiratory depression, transient **apnoea**, **hypotension** through vaso and venodilation, no analgesic properties, potential allergic reaction (soy, eggs), pain at injection site, metabolic acidosis when given as an infusion, antiemetic properties	**Bold + 2 more**
	Q4. How can you limit adverse effects when administering propofol?	smaller total doses, titrated doses, no opiates or benzodiazepines given simultaneously, IV fluid bolus, caution in the elderly and in those with poor cardiovascular reserve	**2**

Propofol 2013-2-C

The patient develops airway obstruction and is going to be intubated. We are now moving to Pharmacology.			
Question 2 **PHARMACOLOGY** **PROPOFOL** LOA: 1 (Katzung 12th ed p 438-440)	1. Describe the pharmacokinetics of propofol.	**1. Distribution half life 2-4 minutes** **Elimination half life 4-23 minutes** **Rapid onset and recovery**. Termination of drug effect due to **redistribution** from brain to sk muscle and then fat (rather than metabolism). Duration of action 3-8min Rapidly metabolised in liver and extrahepatic sites (lungs). Water soluble metabolites excreted in urine.	**Bold**
	2. What is the usual induction dose of propofol?	**2. 1-2.5mg/kg adults,** 2.5-3.5mg/kg in kids	**Bold**
	3. What clinical effects are expected after this dose of propofol is administered.	**3. Anaesthesia / Sedation**. Respiratory depression. Transient **apnoea**. **Decreased blood pressure** through vaso and venodilation (most pronounced of induction drugs). Does NOT have analgesic properties Anti-emesis, Metabolic acidosis, Pain at injection site	**Bold**
	4. List some drug interactions of propofol important in the setting of sedation/anaesthesia	**4.** Opioids – enhance respiratory depression Benzodiazepines - enhanced sedation and respiratory depression	**1 of 2**

Propofol 2013-1

Question 4 PROPOFOL LOA: 1	What are the indications for the use of Propofol? What properties of Propofol make it suitable for procedural sedation? What are adverse effects of Propofol?	**Induction agent, maintenance of anaesthesia procedural sedation** **Rapid onset and offset** Localised pain with bolus administration. Dose related **depression of respiratory drive** (central effect) and apnoea. Muscle movements, hypotonus and rarely tremor. **Hypotension** (reduced arterial resistance venodilation and negative inotropism).	**2 bold to pass** **Bold to pass**

Propofol 2012-1

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)	

Propofol 2009-2

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
	(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

Propofol 2003-1

QUEST 3. Propofol

FIRST QUESTION	Describe the pharmacokinetics of propofol	
	Distribution after IV with t ½ 2-8 mins, **elimination** t ½ 30-60 mins Rapidly metabolized in liver (10x faster than thio) by conjugation to glucuronide and S04 Excreted in urine, <1% excreted unchanged Total body clearance greater than hepatic blood flow (extrahepatic mechanisms must also be at work)	
SECOND QUESTION	What are the adverse effects of propofol	
	Resp. – apnea **CV – marked decrease in BP during induction (decr. peripheral resistance)** - **greater neg.inotropic effects on heart** Pain at site of injection	

Rocuronium 2017-1-C

Stem: She requires urgent intubation. Moving on to Pharmacology.			
Question 2 Rocuronium **Subject:** Pharm LOA: 1	a) What type of drug is Rocuronium?	**Nondepolarizing** muscle relaxant. Steroid derivative	Bold
	b) What are the pharmacokinetics of Rocuronium?	Absorption: IV BA = 1 **Dose: 1.2 mg/kg (accepted range 0.9-1.2mg/Kg)** **Onset: 45-60sec** **Duration: 20 – 75 minutes** **Metabolism: liver** **Elimination: Liver 75-90%, and kidney**	3 Bold
	c) How does Suxamethonium differ from Rocuronium?	**Duration of action is much shorter,** Sux 5-10 min Different side effects and contraindications Sux is a depolarizing muscle relaxant with phase I and Phase II. Phase I is augmented by pseudocholinesterase inhibitors Sux is metabolized by plasma pseudocholinesterase Roc has an antidote **–** sugammadex	Bold plus 2

Rocuronium 2012-2

Question 3 Non Depolarising Muscle Relaxants LOA: 1	What's the mechanism of action of Rocuronium? (Prompt: receptor level)	**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.	Non-depolarising NM blocker. Initially acts as competitive inhibitor for Ach at nicotinic receptors
	Describe the pharmacokinetics of rocuronium. *Prompt: Describe rocuronium's distribution and elimination.*	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.	Rapid distribution. **Short T1/2.**
Question 4	Can you give me an example of a	**Calcium Carbonate** or Ca- acetate, citrate	Need to name 1

Suxamethonium 2016-1-D

Stem: A 30 year old woman is septic and requires intubation. You use suxamethonium in your rapid sequence intubation			
TOPIC	QUESTIONS	KNOWLEDGE **(essential in bold)**	NOTES
Question 1 Suxamethonium including pharmacokinetics **Subject:** Pharm LOA: 1	1. What is the mechanism of action of suxamethonium? Prompt. Where does it act?	**Depolarizing neuromuscular blocker** Phase I (depolarising)- Reacts with nicotinic receptor, opens channel, depolarizes NM endplate with spread to adjacent membranes, causing fasciculation prior to paralysis. Phase II (desensitising) – Continued or repeated exposure to sux – end plate depolarisation decreases – membrane repolarises but cannot be depolarised as is desensitised	Must get bold with understanding concept
	2. What are the pharmacokinetic properties of suxamethonium?	**Rapid onset (30-60 seconds)** **Short duration of action (2-8 minutes)** **Hydrolysed rapidly** by plasma cholinesterase	2 of 3
	3. What are the adverse effects of suxamethonium?	Muscle pain from fasciculation Bradycardia Potassium release – burns, CHI, trauma, stroke Raised Intraocular Pressure Raised Intragastric pressure Malignant hyperthermia Prolonged paralysis (reduced or abnormal cholinesterase)	4 of 7

Suxamethonium 2013-1-A

Due to her worsening respiratory failure, she requires intubation			
Pharmacology Suxamethonium MOA, adverse effects	What is suxamethonium	**depolarising muscle relaxant** producing rapid neuromuscular blockade at **motor endplate nicotinic receptors.** Structurally two acetylcholine molecules linked end to end	Pass = bold
	Describe the mechanism of action of suxamethonium	**Phase I (depolarizing)** binds to nicotinic receptor; **opens channel** and causes **depolarisation of motor end plate**; spreads to adjacent membranes causing contractions of muscle motor units (fasciculations); **depolarised membranes remain depolarised (& unresponsive to subsequent impulses)** causing flaccid paralysis Phase 2 (desensitising) With continued exposure, the initial end plate depolarisation decreases & membrane becomes repolarised; membrane cannot be depolarised again as it is *desensitised* (mechanism unclear however ? due to channel block becoming more important than agonist action at receptor)	Pass = bold
	What are the important adverse effects of suxamethonium?	**hyperkalaemia** (eg burns, trauma patient); cardiac arrhythmias (eg if given with halothane) / **bradycardia** (repeat doses); increased IOP; increased intragastric pressure; muscle pain (likely related to fasciculation); malignant hyperthermia, prolonged paralysis	Pass 2 bold + 2 others

Suxamethonium 2009-2

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
		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	

Suxamethonium 2006-1

Succinylcholine	Describe succinylcholine and its metabolism?	**Depolarizing neuromuscular blocking drug** **Hydrolyzed by plasma cholinesterase** to succinic acid & choline	Two linked acetylcholine molecules Action at motor end plate terminated by diffusion away into ECF
	What are the adverse effects of depolarising neuromuscular blockade?	**Hyperkalaemia** Renal Failure Burns > 24 hours Demyelination Spinal Cord Injury Muscular Dystrophies CVA **Increased IOP, intragastric & ICP (1 of)**	Paralysis & prolonged Apnoea CVS - negative inotrope & chronotrope Muscle Pain

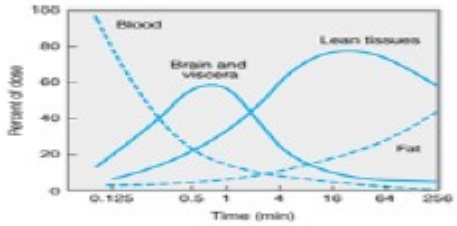
Suxamethonium 2003-1

FIRST QUESTION	What are the pharmacokinetics of suxamethonium?	
	Short half life Plasma cholinesterase hydrolysis	
SbECOND QUESTION	What are the adverse effects of suxamethonium	
	1.Cardiac arrythmias – low dose negative inotropic/chronotropic response, bradycardia when 2nd dose 5 mins after first 2.Hyperkalemia – burns, nerve damage, NM disease, CHI, peritoneal infections, RF 3.Incr. IOP 4.Incr.intragastric press – risk emesis 5.Muscle pain	Hyperkalemia Increased press (1)

Thiopentone 2011-1

Thiopentone	Describe the distribution of thiopentone following an IV bolus What are the potential adverse effects of thiopentone? Prompts: What are the CNS effects? What are the CVS effects	To highly vascular tissue and rapidly crosses BBB. **High lipid solubility**. Then **rapidly redistributed** to body fat. Advantages: Rapid, Controllable, Amnesic, **Reduction of ICP**, anticonvulsant Disadvantages: **Hypotension,** Venous irritant, Myocardial depression, minimal muscle relaxation and analgesia, hepatic metabolism (vs inhalational agents)	Bold Bold

Thiopentone 2008-1

Thiopentone	Describe the pharmacokinetics of thiopentone	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.  	
	What adverse effects does it cause when used as an anaesthetic induction agent ?	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	

Vecuronium 2015-2-B

Stem: He requires intubation and vecuronium is administered. Moving on to pharmacology.			
Question 2 Vecuronium **Subject:** Pharm LOA: 1	(a)What is the mechanism of action of vecuronium	**Non depolarising neuromuscular blockade** **Competitive antagonist** for acethylcholine at **nicotinic receptors** of **neuromuscular junction** Large doses will enter ion channel's pore directly → more intense blockade Also blocks prejunctional Na channels → interfere with Ach mobilization at nerve endings	Must mention blockade type, & either receptor type or ACh.
	(b) Describe the pharmacokinetics of vecuronium Prompt : what is its onset time, what is its duration of action, how is it eliminated	Highly polar/ionic Poorly absorbed from GIT Given IV **Onset within 1 min**; **Max effect at 3-5 mins** **Duration of action : 20-35 mins** **Short half life** **Rapidly distributed** to extracellular space Small volume of distribution (~blood vol), Plasma protein binding : 60-90%, **Eliminated by liver** (75-90%), rest by kidney	4 of 6 bold to pass

Bupivicaine 2016-1-B

Stem: Moving onto Pharmacology. You use bupivacaine as the local anaesthetic prior to intercostal catheter insertion.			
Question 4 Bupivacaine LOA: 1	*a. Describe the mechanism of action of bupivacaine.*	Amide local anaesthetic, **blocks voltage-gated Na channels.**	Bold
	b. Describe the pharmacokinetics of bupivacaine.	**Metabolised by the liver**, Distribution half-life 28 min, elimination half-life 3.5h, large V_D of 72 L, 95% protein bound, lipophilic. **Duration of action 4 to 8 hours** (longer than lignocaine or ropivicaine).	Bold
	c. Give examples of its clinical use.	Use as a nerve block in low conc 0.25% for local infiltration, digital ring block, femoral, intercostal, intrapleural, epidural (post-op), brachial plexus, sciatic nerve, intra-articular.	Name 2 (do not accept IVRA)
	d. List some of its toxic effects.	Sedation, visual and auditory disturbance, **cardiac arrhythmia**, hypotension & arrest, **seizure.**	Bold

Bupivicaine 2014-1-A

Stem: We are now moving to pharmacology. You decide to use Bupivicaine as the local anaesthetic to insert a chest tube			
Question 4 Bupivicaine **Subject:** Pharm LOA: 1	1. What is the mechanism of action of bupivacaine? 2. How long will a bupivacaine block last? 3. What are the potential adverse effects from bupivacaine? 4. How can the risk of these effects be minimised in the ED?	1. **Blocks** voltage-gated **sodium channels in nerve**. Threshold for excitation increases, conduction slows, AP rise declines, AP generation abolished. If Na current blocked over length of nerve, propagation is ceased. 2. **3-6 hours** 3. **CNS toxicity** (sedation/light headedness/visual&auditory/tongue&mouth numbness/metallic taste/nystagmus/restlessness/ muscle twitches/seizure/resp depression), **Cardiac toxicity** (arrhythmias/cardiovascular collapse/cardiac arrest), Local toxicity (trauma/neurotoxicity) Allergy 4. Ask re Hx of allergy, Use safe max dose (<2mg/kg), withdraw pre injection, avoid vessels-anatomical consideration (above rib below) & use USS. Ask pt to flag Sx e.g. taste/tongue numb. Avoid hypoxia/acidosis.	Bold Approximate or long duration Bold Extra

Lignocaine 2017-2-D

Stem: Moving on to Pharmacology. A central venous line is inserted using local anaesthetic.			
Question 5 Local Anaesthetics **Subject**: Pharm LOA: 1	(a) What is the maximum safe dose of lignocaine for local anaesthesia?	Plain – **3mg/kg** (to maximum 300mg) With Adrenaline - **5mg/kg** (to max 500mg)	(3-5mg/kg) (5-7mg/kg)
	(b) What factors affect absorption of lignocaine after local infiltration?	Dose, site of injection, drug-tissue binding, tissue blood flow, vasoconstrictors	3/5 factors
	(c) What are the toxic effects of lignocaine?	**CNS:** EARLY/MILD: circumoral /tongue numbness, metallic taste, paraesthesia, sedation MODERATE: nystagmus, muscle twitching, N&V, tinnitus SEVERE seizures, sedation **CVS:** cardiovascular collapse, hypotension, bradycardia, rarely, arrhythmia, worsen CCF or conduction blocks **GIT**: anorexia N&V (through CNS effects) **Haem:** methaemoglobinaemia **Allergy:** rare with amides	CNS + 2 examples CVS + 2 examples

Lignocaine 2016-2-B

Stem: Moving onto Pharmacology. Lignocaine is used as the local anaesthetic.			
Question 5 Lignocaine **Subject:** Pharm LOA: 1	Describe the mechanism of action of Lignocaine?	Na channel blocker, Class 1 B **Blocks** (activated and inactivated **Na Channels** = **blocks nerve conduction**. Less effect in infected tissue	Bold to pass
	What are the toxic effects of lignocaine?	CNS – Early : **tongue/oral numbness/metallic taste**. Nystagmus, muscle twitching, N+V, Tinnitus, visual disturbance. Severe: **Seizures**, sedation. CVS – **cardiovascular collapse**, hypotension, bradycardia, arrhythmia (rare), worsen CCF, conduction blocks GIT – anorexia, N+V (through CNS effects)	3 BOLD to pass Prompt "Any other systems affected?"
	What factors affect systemic absorption after local infiltration?	Dose, site of injection, drug tissue binding, tissue blood flow, vasoconstrictors (combined preparation)	3 of 5

Lignocaine 2015-1-A

Stem: Moving onto Pharmacology. You use lignocaine as the local anaesthetic			
Question 2 Local Anaesthetics **Subject:** Pharm LOA: 1	Describe the mechanism of action of lignocaine? What factor affect systemic absorption after local infiltration What are the toxic effects of Lignocaine	Na channel blocker, Class 1B. **Blocks** (activated & inactivated) **Na channels = Blocks nerve conduction**. Less effect in infected tissue Dose/ Site of injection/ Drug tissue binding/ Tissue blood flow/ Vaso constrictors (combine preparation) **CNS -** Early: **tongue/oral numbness/metallic taste**, parathesia, sedation. Moderate: nystagmus, muscle twitching, N&V, Tinnitus, visual disturbance Severe: **Seizures**, sedation **CVS- Cardiovascular collapse** Hypotension, bradycardia, rarely arrhythmia, worsen CCF or conduction blocks GIT Anorexia, N&V (thru CNS effects)	Bold 3 of 5 Bold

Local Anaesthetics 2011-2

Question 4 Local anaesthetics	a) What classes of local anaesthetics are used in the ED? *(Prompt for examples)* b) What factors affect the systemic absorption of lignocaine after local infiltration? c) What are the toxic effects of lignocaine?	**a)Amides**: lignocaine, prilocaine, bupivacaine, ropivicaine **Esters**: cocaine, benzocaine, procaine, tetracaine **b)** Absorption: **dose**, site of injection, drug-tissue binding, tissue blood-flow, vasoconstrictors, **c)** **CNS**: All can get: sleepiness, light-headed, visual, auditory disturbance, restlessness Early tox: circumoral/tongue numbness, metallic taste **Serious/higher**: Twitching, nystagmus, **seizures** Direct neurotoxicity – radicular irritation with spinals **CVS**: Na channel (depress abnormal pacemaker, excitability, conduction) v Ca channel effects at high doses – decrease myocardial contractility, arteriolar dilatation, hypotension, with bupivicaine can get idioventricular rhythm, broad QRS, EMD Haem: methaemoglobinemia Allergy: rare with amides as not metab'd to PABA	1 of each Bold + 1 CNS: seizures and 1 other CVS: arrhythmia

Local Anaesthetics 2009-2

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

Local Anaesthetics 2006-1

Topical anaesthetics	What is the mechanism of action of local anaesthetics?	**Sodium channel blocker** **Voltage gated**	Interfere with propagation of AP by blocking the increase in sodium permeability during depolarization. Provide pain relief by blocking nociceptive fibers. Other fibers are affected as well. Sensitivity depends on: fiber diameter, fiber type, degree of myelination. Sensory modalities are affected in the following order: pain, cold, warmth, touch, and pressure. Most local anesthetics are weak bases, pKa 7.5-9.0.
	How are local anaesthetics classified? Give an example of each group?	**Esters and Amides:** Esters are hydrolyzed by plasma and liver esterases. Amides are metabolized in the liver. Patients with severe hepatic damage or advanced congestive heart failure may be unusually sensitive to these drugs. Some amides are partially excreted unchanged in the urine Esters: cocaine, procaine, amethocaine and chloroprocaine, amides lignocaine, prilocaine, mepivacaine and bupivacaine. **1 example of each**	Allergic reactions are rare, especially with amide local anesthetics.
	Describe the ideal local anaesthetic for topical application? *What clinical situations would you use topical anaesthesia for?* *What are the contraindications to using topical Las?*	Ease of application (Not messy; No dressing; Well tolerated by kids; Not painful) Rapid Onset of action Low (nil) systemic toxicity eg MetHb with EMLA in neonates High analgesic efficacy Reasonable duration of action Not allergenic May be applied to the skin, the eye, the ear, the nose and the mouth as well as other mucous membranes. EMLA cream a eutectic mixture of LAs provides surface anaesthesia of the skin (partic paeds). A mixture of base forms of lignocaine & prilocaine in equal proportions in an emulsion. Cutaneous contact (usually under an occlusive dressing) should be maintained for at least 60 min prior to venipuncture Other LA agents may be abs in significant amounts particularly after topical application to the more vascular areas, fatalities have occurred after application of these agents to mucosal surfaces.	Absorption of LAs through intact skin is usually slow and unreliable and high concentrations (e.g. 20% benzocaine or 40% lignocaine) are required. In general, cocaine, amethocaine, lignocaine and prilocaine are the most useful and effective local anaesthetics for this purpose. When used to produce topical anaesthesia, they usually have a rapid onset of action (5-10mins) and a moderate duration of action (30-60 mins).

Local Anaesthetics 2004-2

Local anaesthetics	Explain the chemical classification of local anaesthetics Explain tachyphylaxis associated with LA use	Amides and esters Increased ionisation	

Prilocaine 2007-1

3.3 Prilocaine	What is the mechanism of action of prilocaine	Blockade of voltage-gated **Na channels**	
	Describe the adverse effects of prilocaine	CNS: sleepy, light-headed, circumoral numbness, seizures Cardiovascular: direct and indirect, depress pacemaker, excitability and conduction Haematology: Methemoglobinaemia (accumulation of 0 –toluidine) Neurotoxicity Allergy **(must get 2)** Prompt adverse effects of local anaesthetics in general	
	How is prilocaine metabolized?	Amide link hydrolysed by P 450 **in liver** and then renal excretion	/2