ACEM Primary Examination Vivas > Pharmacology > Cardiovascular system Organised by edvivas.com		
Antianginal Agents	GTN 2015-1-C	1
Antianginal Agents	GTN 2013-2-C	2
Antianginal Agents	GTN 2013-1	3
Antianginal Agents	GTN 2010-2	4
Antianginal Agents	GTN 2008-1	5
Antianginal Agents	GTN 2007-1	6
Antianginal Agents	GTN 2004-2	7
Antianginal Agents	Nitric Oxide 2005-1	8
Antiarrhythmics	Adenosine 2016-2-B	9
Antiarrhythmics	Adenosine 2012-2	10
Antiarrhythmics	Adenosine 2011-1	11
Antiarrhythmics	Adenosine 2005-2	12
Antiarrhythmics	Adenosine 2003-1	13
Antiarrhythmics	Amiodarone 2015-1-A	14
Antiarrhythmics	Amiodarone 2013-2-A	15
Antiarrhythmics	Amiodarone 2011-1	16
Antiarrhythmics	Amiodarone 2010-1	17
Antiarrhythmics	Amiodarone 2006-1	18
Antiarrhythmics	Digoxin 2015-2-C	19
Antiarrhythmics	Digoxin 2011-1	20
Antiarrhythmics	Digoxin 2009-1	21
Antiarrhythmics	Digoxin 2006-1	22
Antiarrhythmics	Digoxin 2004-2	23
Antiarrhythmics	Flecainide 2008-2	24
Antiarrhythmics	Lignocaine 2011-1	25
Antiarrhythmics	Lignocaine 2005-1	26
Antiarrhythmics	Lignocaine 2004-2	27
Antiarrhythmics	Propranolol 2016-1-C	28
Antiarrhythmics	Sodium Channel Blockers 2006-2	29
Antiarrhythmics	Sotalol 2012-1	30
Antiarrhythmics	Verapamil 2015-2-C	31

Antihypertensives	ACE inhibitors 2010-2	32
Antihypertensives	Angiotensin II Receptor Blockers 2016-2-B	33
Antihypertensives	Angiotensin II Receptor Blockers 2008-1	34
Antihypertensives	Antihypertensives 2009-1	35
Antihypertensives	Captopril 2014-1-A	36
Antihypertensives	Captopril 2005-2	37
Antihypertensives	Captopril 2003-1	38
Antihypertensives	Hypertensive emergencies 2011-1	39
Antihypertensives	Prazosin 2017-2-A	40
Antihypertensives	Ramipril 2017-2-B	41
Betablockers	Betablockers 2007-1	42
Betablockers	Betablockers 2005-1	43
Betablockers	Metoprolol 2016-2-B	44
Betablockers	Metoprolol 2014-2-A	45
Betablockers	Metoprolol 2010-1	46
Betablockers	Propranolol 2013-1	47
Betablockers	Propranolol 2004-2	48
Calcium Channel Blockers	Calcium Channel Blockers 2011-2	49
Calcium Channel Blockers	Calcium Channel Blockers 2009-2	50
Calcium Channel Blockers	Calcium Channel Blockers 2006-2	51
Calcium Channel Blockers	Verapamil 2017-2-C	52
Calcium Channel Blockers	Verapamil 2013-1	53
Diuretics	Acetazolamide 2007-2	54
Diuretics	Frusemide 2017-1-B	55
Diuretics	Frusemide 2014-2-B	56
Diuretics	Frusemide 2011-2	57
Diuretics	Frusemide 2010-2	58
Diuretics	Frusemide 2008-1	59
Diuretics	Frusemide 2004-2	60
Diuretics	Mannitol 2015-2-D	61
Diuretics	Osmotic Diuretics 2007-1	62
Diuretics	Thiazide Diuretics 2015-2-D	63
Diuretics	Thiazide Diuretics 2006-2	64
Drugs affecting thrombosis	Antiplatelet agents 2003-2	65

Drugs affecting thrombosis	Clopidogrel 2017-1-A	66
Drugs affecting thrombosis	Clopidogrel 2006-2	67
Drugs affecting thrombosis	Clopidogrel 2005-1	68
Drugs affecting thrombosis	Heparin 2014-2-B	69
Drugs affecting thrombosis	Heparin 2012-1	70
Drugs affecting thrombosis	Heparin 2008-1	71
Drugs affecting thrombosis	Heparin 2006-1	72
Drugs affecting thrombosis	Heparin 2003-1	73
Drugs affecting thrombosis	Rivaroxaban 2016-1-A	74
Drugs affecting thrombosis	Thrombolytics 2017-2-A	75
Drugs affecting thrombosis	Tissue Plasminogen Activator 2012-2	76
Drugs affecting thrombosis	Tissue Plasminogen Activator 2009-2	77
Drugs affecting thrombosis	Tissue Plasminogen Activator 2007-1	78
Drugs affecting thrombosis	Warfarin 2012-2	79
Drugs affecting thrombosis	Warfarin 2012-1	80
Drugs affecting thrombosis	Warfarin 2011-1	81
Drugs affecting thrombosis	Warfarin 2009-2	82
Drugs affecting thrombosis	Warfarin 2006-1	83

GTN 2015-1-C

Stem: We will now move to Pharmacology. She is now hypertensive. You commence a glyceryl trinitrate (GTN) infusion			
Question 4 Glyceryl Trinitrate **Subject:** Pharm LOA: 1	What is the mechanism of action of GTN	Nitrite -> **NO** -> ^ cGMP -> **Smooth m relaxation.** Prostaglandins may be involved	**Bold**
	What are its clinical effects?	1. Beneficial effects-**venodilation**, reduced venous return, decr ventricular pre-load, reduced LVEDV, reduced LV wall tension, **reduced myocardial oxygen consumption.** Vasodilation of epicardial coronary arteries, increased coronary collateral flow. **Decrease systemic BP** 2. Adverse effects - hypotension, tachycardia, headache	**2 of 3 Bold** **2 adverse effects**
	What are the indications for GTN use in the ED?	**Angina,** acute coronary syndrome, hypertensive urgencies/emergencies, APO, aortic dissection (with beta-blockade)	**Bold plus two others**

GTN 2013-2-C

Question 2 **PHARMACOLOGY** **GTN** LOA: 1 Katzung 12th ed Chapter 12) MoA, principles of tachyphylaxis	1. By what routes can GTN be administered?	1. **Sublingual, transdermal, IV, oral,** buccal, inhaled	Bold 3/4
	2. Why are parenteral routes favoured?	2. To avoid the **hepatic first pass** effect which significantly decreases bio-availability	bold
	3. What is meant by the term tachyphylaxis as it relates to Glyceryl Trinitrate (**GTN**)	3. Continuous exposure to nitrates – smooth muscle may develop tolerance. Particularly seen with continuous IV infusion or long acting preparations. (oral, transdermal)	Understand concept
	What is the implication of this for the dosing and administration of GTN	Concept of "drug-free" interval – at least 8h between doses	concept
	What is the theoretical basis for this phenomenon? (bonus)	(a) Diminished release of nitric oxide resulting from reduced bioactivation secondary to depletion of tissue thiol compounds, decreased tissue sulphydryl groups, increased generation of O2 free radicals , decreased availability of CGRP. (b) Systemic compensation – after > 1 day of therapy salt and water retention reverse favourable hemodynamic change	for better candidates
	4. When should GTN be used with caution?	4. **hypotension**, those on sildenafil, inferior&posterior MI/RV infarct, Fixed cardiac output (AS, tamponade etc), raised ICP, significant tachy/brady cardia, allergy	Bold +2

GTN 2013-1

Question 2 **GLYCERYL TRINITRATE (GTN)** LOA: 1	How does Glyceryl Trinitrate (GTN) exert its effect on smooth muscle? Describe the Pharmacokinetics of GTN **Prompt**: How is GTN given?	Nitrate→**Nitric Oxide→↑cGMP→** relaxation→**vasodilation** Also involves Prostaglandin E or prostacyclin **Low Bioavail** (<10-20%) Sublingual, transdermal or IV S/L: onset 1-3min, lasting 10-30min Liver metabolism and excreted by kidney Tachyphylaxis with continuous use	**Nitric Oxide , cGMP/second messenger, vasodilation** **Low Bioavailabilty** **Short halflife**

GTN 2010-2

2. a. Describe the mechanism of action of glyceryl trinitrate.	• Taken up by **vascular smooth muscle** • Interacts with tissue sulfhydryl groups • Releases free radical **nitric oxide** • Activates cGMP • Dephosphorylates myosin light chains • **Reduces intracellular Ca levels** • Smooth muscle relaxation & **vasodilation**	Must state • **vascular smooth muscle** • **nitric oxide** • **vasodilation**
b. What are the clinical effects of nitrates	• Low doses – venodilation ⇒ ↓ preload & stroke volume • Higher doses – arterial dilation ⇒ **↓ blood pressure** ⇒ ↓ cardiac output & **↓ myocardial oxygen demand** + dilation of coronary arteries/redistribution of perfusion ⇒ improved oxygen delivery to myocardium & resolution of ischaemic pain **[Prompt if needed "What other clinical effects may be seen?"]** • Adverse effects: postural hypotension, tachycardia, dizziness, headache, flushing, blurred vision, dry mouth, rash	Must state • **↓ BP** • **↓ myocardial oxygen demand** • 2 listed other effects

GTN 2008-1

Nitrates	What is the cellular mechanism of action of GTN ?	Denitration by glutathione S-transferase. Free nitrite ions released and form NO. NO activates guanylyl cyclise leading to increased cGMP and dephosphorylation of myosin and smooth muscle relaxation (precise mechanism unknown)	Production of NO leading to smooth muscle relaxation to pass
	How does GTN relieve angina pain ?	Venodilation leads to reduced venous return, reduce ventricular volume and reduced heart wall tension. This reduces myocardial O2 requirement.	Need to know that venodilation and reduced venous is major factor reducing myocardial o2 requirement.
	Outline the pharmacokinetics of sublingual GTN	Oral bioavailability is low due to extensive first pass hepatic metabolism by high capacity organic nitrate reductase. Rapid and efficient absorption by sublingual or intranasal routes but rapid elimination (t1/2 2-8 mins) and duration of action (15-30 mins) due to high capacity hepatic metabolism. Denitrited metabolites conjugated to to glucuronide and excreted in urine.	Poor oral bioavailability due extensive first pass metabolism and effective alternative routes of administration to pass

GTN 2007-1

1.2 GTN-Pharmacodynamics of	How does GTN exert its effect on smooth muscle? What are the clinical effects of GTN ?	Nitrite → **NO** →↑**cGMP** → **relaxation**. Prostaglandins also involved **Venodilation → reduced venous return → reduced LVEDV → reduced LV wall tension → reduced myocardial oxygen consumption (→ reduced cardiac output in normal people, possibly increased in pathological conditions where pretreatment preload is abnormally high)** **Prompts if needed:** - *"How does GTN relieve angina?"* - *"How does the effect of GTN on cardiac output differ between normal and disease states?"* Other: Arterial dilation → throbbing headache (relatively ineffective on resistance vessels) Other smooth muscle relaxation (eg amyl nitrite + enhanced erection) less important Decreased platelet aggregation, but no apparent beneficial therapeutic effect in this regard Methaemoglobinaemia from nitrite but not from GTN	/2

GTN 2004-2

Nitrates	What is the mechanism of action of glyceryl trinitrate in smooth muscle ? How do nitrates relieve angina ?	NO release, cGMP increases Preload reduction decreases myocardial work	

Nitric Oxide 2005-1

Nitric oxide	What are the effects of nitric oxide? What are potential therapeutic applications of nitric oxide.	**Smooth muscle relaxant** **Platelet inhibitor** **Immune regulator** **Neurotransmitter** **(1of 4)** **.Vascular effects** - on vascular smooth muscle tone and B.P. - may play a role in normal regulation of vascular tone -vasodilator action -inhibits neutrophil adhesion to vascular endothelium 2.**Hypertension associated with pregnancy** - resemble deficiency of NO and PG - possible role of enhancing NO levels via nutritional supp.w/L-arginine 3.**Respiratory disorders** - used via inhalation to newborns w/pulmonary hypertension and ARDS - decreases pulmonary arterial pressure and improves blood oxygenation - also used in open trials in adults with ARDS - may act also act as bronchodilator by relaxing airway smooth muscle 4.**Septic shock** -Urinary excretion of N03, oxidative product of nitric oxide in G- bacterial infection 5.**Atherosclerosis** - may act as antioxidant, blocking oxidation of LDL, preventing foam cell formation in the vascular wall **6.Platelets** -nitric oxide = potent inhibitor of platelet adhesion and aggregation — as in vascular sm.muscle, cGMP mediates protective effect of NO in platelets -may have additional effect on blood coagulation by enhancing fibrinolysis via effect on plasminogen **7.Organ transplantation** -. N0 reduces free radical toxicity, inhibits platelet and neutrophil aggregation and adhesion to vascular wall - too high concentration of NO may be detrimental – so need to inhibit synthesis to prolong graft survival **8.CNS** -modifies neurotransmitter release in different areas of the brain --also may have role in epileptic seizures - also has negative effects - causes destruction of photoreceptor cells in retina – prolonged increase in cGMP formation 9. **Peripheral nervous system** - NO promotes relaxation of sm.muscle in corpora cavernosa – impotence trials with NTG ointment and NTG patch **(any 1))**	

Adenosine 2016-2-B

QUEST. 2 Adenosine

FIRST QUESTION	What is the mechanism of action of adenosine?	
	It acts at adenosine receptors Enhances K conductance and inhibition of cAMP induced Ca influx – get marked hyperpoplarization and suppression of C-dependent A.P. Bolus dose, inhibits AV nodal conduction, increases AV nodal refractory period, lesser effects on SA nodal function PROMPT: Where in the heart does it act?	
SECOND QUESTION	How is it administered	
	Fast IV bolus via large vein	
THIRD QUESTION	What are the indications for the use of adenosine	
	Supraventricular tachycardia Unmasks Aflutter/Afib	
FOURTH QUESTION	What are the adverse effects?	
	Flushing in 20% patients SOB, chest burning in 10% High grade AV block short lived/ Afib H/ache, hypotension, nausea, paresthesias	Dyspnea High grade AV block

Adenosine 2012-2

Question 2 adenosine	What are the indications for use of Adenosine?	**Conversion of paroxysmal SVT to sinus rhythm.**	Bold to pass
LOA: 1	How does it work?	Activation of inward rectifier K+ currents and inhibition of calcium currents. Leads to marked hyperpolarisation and suppression of calcium-dependent APs. Effect is direct inhibition of AV nodal conduction and increase in AV node RP. This **interrupts re-entry pathway thru AV node**.	AV node conduction interruption
	How do the specific pharmacokinetic properties of adenosine influence the method of administration?	**Very rapid metabolism** by adenosine deaminase in red cells and vessels walls = very short elimination t1/2 (<10s) and duration of action (~30s). Must be given by **rapid intravenous bolusing.** If initial dose ineffective then subsequent dose should be increased (no accumulation occurs).	Bold to pass

Adenosine 2011-1

Adenosine	What are the principal effects of adenosine on cardiac conduction?	**Inhibits AV nodal conduction**	Bold
	Describe the pharmacokinetics of adenosine.	**Rapidly metabolised**. By red cells and endothelial cells **Very short elimination half-life** (seconds)	Bold
	What are the clinical implications of this pharmacokinetic profile?	Therefore must be given by **rapid IV bolus**. Side effects are short lived. No prolonged action to keep patient out of the arrhythmia. (Proximal IV site as preference).	Bold
	Name some indications and contraindications to its use.	Indication: **supraventricular tachycardia;** diagnostic Contraindications: AV block, sick sinus, acute asthma, lack of consent	SVT and 1 CI.

Adenosine 2005-2

TOPIC: Adenosine **NUMBER: 2**

FIRST QUESTION	**What are the principle effects of adenosine on cardiac conduction?**	
POINTS REQUIRED	1 Inhibits AV nodal conduction (increased PR interval)	1 &2 to pass
	2 Increases AV nodal refractory period	
	3 These effects are a result of enhanced K conduction and inhibition of cAMP-induced calcium influx resulting in hyperpolarisation and suppression of calcium-dependent action potentials	
PROMPTS		
SECOND QUESTION (if needed)	**How do the unusual pharmacokinetics of adenosine influence its use in therapeutics?**	Must know 1,2,3 to pass
POINTS REQUIRED	1 Rapidly metabolised in the blood with a elimination half-life of less than 10 seconds	
	2 Only suitable for IV use	
	3 Must be given by rapid bolusing to achieve therapeutic effects.	
	4 Repeat doses must be escalated	
	5 Will not be effective for supraventricular tachyarrhymthias caused by adenosine-blockers such as theophylline	
PROMPTS		

Adenosine 2003-1

QUEST. 2 Adenosine

FIRST QUESTION	What is the mechanism of action of adenosine?	
	It acts at adenosine receptors Enhances K conductance and inhibition of cAMP induced Ca influx – get marked hyperpoplarization and suppression of C-dependent A.P. Bolus dose, inhibits AV nodal conduction, increases AV nodal refractory period, lesser effects on SA nodal function PROMPT: Where in the heart does it act?	
SECOND QUESTION	How is it administered	
	Fast IV bolus via large vein	
THIRD QUESTION	What are the indications for the use of adenosine	
	Supraventricular tachycardia Unmasks Aflutter/Afib	
FOURTH QUESTION	What are the adverse effects?	
	Flushing in 20% patients SOB, chest burning in 10% High grade AV block short lived/ Afib H/ache, hypotension, nausea, paresthesias	Dyspnea High grade AV block

Amiodarone 2015-1-A

Stem: Moving onto Pharmacology. It is decided to treat him with Amiodarone			
Question 3 Amiodarone Subject: Pharm LOA: 1	What anti-arrhythmic class does amiodarone belong to?	**Class 3**: also class I,II,IV effects	Bold to pass
	What are the effects of amiodarone on the heart?	**Increases Action potential duration (APD) due to blockade** of rapid component of delayed **K^+ current**(I_{kr}). Chronic use also blocks slow K^+ rectifier. **Prolongs QT** (due to above effect) Blocks inactivated Na^+ channels. Weak adrenergic and Ca^{++} channel blocker	Bold to pass
	What other arrhythmias is amiodarone used for?	Atrial Fibrillation/ Ventricular tachycardia/Ventricular fibrillation/ Supraventricular (re-entrant/ accessory)	2 to pass
	What arrhythmias may amiodarone cause?	Torsades de pointes (rare < 1%), Bradycardia, Heart block	1 to pass

Amiodarone 2013-2-A

While in ICU, he goes into rapid AF and is treated with Amiodarone			
Pharmacology: Amiodarone Indications, mechanism of action, adverse effects	What are the indications for amiodarone?	**Treatment of atrial and of ventricular tachyarrhythmias.** Used both to revert VT & prevent recurrence. Used in VF/VT cardiac arrest (after 3 shocks & adrenaline).	Bold to pass.
	Describe the mechanism of action of amiodarone.	Has Class I, II, III & IV effects. **Prolongs the AP duration (hence QT interval) by K channel blockade.**	Bold to pass.
	Can you describe the possible adverse effects of amiodarone associated with both its short and long term use?	**Acute: Bradycardia** & heartblock ; **Hypotension;** Chronic: **Pulmonary fibrosis;** Abnormal LFTs & hepatitis; Skin deposits -> photodermatitis & grey-blue discolouration in sun-exposed areas; Asymptomatic corneal microdeposits; Optic neuritis (rare); Hypo/hyperthyroidism.	All bold and 1 other. Especially in those with pre-existing S/AVN disease. Due to peripheral vasodilation.

Amiodarone 2011-1

Anti-arrhythmics in AF	What anti arrhythmic drugs can be used in the management of atrial fibrillation	Beta-antagonists (class 2); calcium-antagonists (class 4); flecainide (class 1c); amiodarone (class 3); digoxin (unclassified); magnesium	Pass 3/5
	What are the mechanisms of action of amiodarone?	**Blocks Na, K, Ca channels; blocks beta adrenoreceptors;** prolongs AV conduction; decreases automaticity; decreases automaticity of purkinje fibres	Bold
	Prompt: what are the cellular mechanisms	Has actions on both rate and rhythm!	
	What are some important drug interactions with amiodarone?	warfarin (increased anticoagulant effect by inhibiting metabolism); digoxin (increases plasma concentration leading to toxicity); increased cardiac effects of other antiarrhythmic agents; phenytoin (increased plasma concentration)	At least 2

Amiodarone 2010-1

Question 4: Amiodarone P228-9	1. What are the cardiac effects of amiodarone at a cellular level?	Prolongs AP duration (by blocking K+ channels) Blocks inactivated Na channels. The AP prolonging action reinforces this effect. Blocks depolarized cells > normal cells. Mild antisympathetic. noncompetitive inhibitor of beta receptors; Weak adrenergic blocker - slows HR and A-V node conduction. Weak Ca channel blocker. Inhibits abnormal automaticity; slows sinus rate; increases PR interval	K block and 1 other
	2. What are the mechanisms of pharmacokinetic drug interaction with Amiodarone and give two examples.	Inhibits liver cytochrome metabolising enzymes Digoxin, Warfarin levels increase. Cimetidine increases amiod toxicity by decreasing hepatic clearance. Interacts with statins (artorvastatin and simvastatin; instead use pravastatin as not P450). Concentration and effects of Phenytoin, anaesthetics, cyclosporins, theophylline, procainamide, flecainide, quinidine are increased by amiodarone	Enzyme induction/inhibition + 1example of either

Amiodarone 2006-1

amiodarone	Describe the mechanism of action of amiodarone?	**Potassium Channel Blocker** (Class III) Prolongs RP, APD **Na channel blockade** Weak Ca & adrenergic blocking	Prolongs the effective refractory period by prolonging the action potential duration Blocks inactivated sodium channels (Class I) Weak adrenergic (Class II) and calcium channel (Class IV) blocking actions Vasodilator
	What are the clinical uses of amiodarone?	**Atrial & ventricular arrhythmias**	Maintaining normal sinus rhythm in AF Prevention of Recurrent VT
	Describe the potential adverse effects of amiodarone?	Cardiac: Bradycardia, Heart block, hypotension, negative inotropy Pulmonary fibrosis, Abnormal LFTs & hepatitis, Skin deposits Corneal microdeposits Hypo/hyperthyroidism. **2 cardiac, 2 extracardiac**	photodermatitis and a gray-blue skin discoloration -blocks the peripheral conversion of thyroxine (T_4) to triiodothyronine (T_3)

Digoxin 2015-2-C

Stem: Moving on to pharmacology. Her medications include digoxin.			
Question 4 Digoxin **Subject:** Pharm LOA: 1	What is digoxin's mechanism of action in heart failure	**Ca accumulation in cells** (due **Na- K+ ATP block**, Na in cells drive Na/Ca exchange) leads to a) **increased contraction strength,** b) > stroke vol/ CO per beat- with smaller EDSV, small heart, reduced RHt pressures/ volume c) slower HR- >er stroke volume (partic if AF), via effects on parasympathetic fibres/AV node	2/3 bold + one other
	Why are patients in heart failure prone to digoxin toxicity?	a) **poor renal function from low C/O,** b) **potential dehydration and/or other drug interactions** (e.g. ACE/ diuretics/ spironalactone/ ca channel blockers) c) potential effects on effective vol of distribution d)low K+ from other ht failure meds esp diuretics (makes pts higher risk from dig/toxicity) e) poor cardiac reserve/ output, altered digoxin handling during acute HF/ fluid distribution changes/other major illnesses	To pass 2 including 1 bold
	What are the features of digoxin toxicity Prompt: Any features from other organ systems	a) **high K (assocd strongly with mortality)** b) yellow/ green (or other) colour vision c) GI- D and V, nausea/ malaise-anorexia/ d) arrhythmias from > automaticity and also Av node block (partic brady but R on T as well) e) severe heart blocks- partic if previous blocks , worsening failure, low BP f) CNS, tiredness -lethargy- headaches, paraesthesias, Candidate may differentiate acute vs chronic	To pass hyperkalaemia + at least 2 others from 2 different groups.

Digoxin 2011-1

Digoxin side effects and toxicity	What are the features of digoxin toxicity?	G-I: anorexia, nausea, vomiting diarrhoea CNS: visual disturbances, confusion, nightmares, agitation, drowsiness Cardiac: features of bradycardia (progressing AV block, slow AF) and increased automaticity (VEBS and bigeminy, SVT with AV block, VT/VF)	Needs to recognise GI/CNS/Cardiac, as well as examples of bradycardia and inc. automaticity to pass
	What factors might predispose patients towards digoxin toxicity? Prompt: are there any interactions?	**Electrolyte imbalance** Hypokalaemia, hypercalcaemia, hypomagnesaemia **Organ disease** Renal impairment, hypothyroidism, **Other drugs** Amiodarone, calcium channel blockers, potassium depleting drugs	Bold (with at least one example of each) to pass

Digoxin 2009-1

Question 2: Digoxin	1. What are the actions of digoxin on the heart at therapeutic levels?	Mechanical (Na-K ATPase) Electrical: Direct – alters action potential Indirect (autonomic) - parasympathetic effects predominate Sensitisation of baroreceptors Central vagal stimulation Facilitation of muscarinic transmission	Pass: Mechanical and one other.
	2. Are the parasympathetic effects uniform through-out the heart?	No Affect atrial and A – V nodal function more than Purkinje or ventricular function	

Digoxin 2006-1

Digoxin	Describe the molecular action of digoxin?	**Na+/K+ ATPase ("sodium pump") inhibition**	Binds to α subunit which has different isoforms ∴ differing affinities for digoxin in various tissues Low concentrations occasionally stimulate the enzyme
	What are the cardiac effects?	Mechanical: ↑**contractility** due to ↑intensity of interaction of actin and myosin filaments due to ↑**free calcium** during systole	(i)↑intracellular Na+ and ∴ (ii) relative ↓expulsion of Ca+ by NaCa exchanger (Fig 13-1) Duration of contractile response neither shortened (as in case of βblockers) nor lengthened (as in case of methylxanthines)
	PROMPT for autonomic effects: What are the autonomic effects of digoxin?	Electrical: (i) Direct: **Shortening of action potential** and ∴ shortened atrial and ventricular refractoriness At toxic levels, resting membrane potential reduced, then as toxicity progresses depolarizing afterpotentials (ii) Autonomic- at lower doses **parasymp effects** predominate At toxic levels sympathetic outflow increased	Follows early brief prolongation of AP Probably due to ↑K+conductance Overloaded intracell Ca+ stores Atropine –blockable effects: sensitization of baroreceptors, central vagal stim, facilitation of muscarinic transmission (mainly atria and AV node where rich cholinergic innerv'n) Sensitizes myocardium and exaggerates all toxic effects
	What are the non cardiac manifestations of digoxin toxicity?	-all excitable tissue including smooth muscle and CNS **GIT** nausea, vomiting, diarrhoea, anorexia **CNS** disorientation, hallucinations, visual disturbances, agitation and comvulsions Gynaecomastia **1 GIT and 1 CNS example** (*prompt allowed)* Hyperkalaemia	Relative low sensitivity of non-cardiac tissue ?due to differing enzyme isoforms Nausea and vomiting a combination of direct and central effects
	?enough time for this question. Describe the pharmacokinetics of digoxin?	Well absorbed orally Moderate Volume of Distribution (6.3 L/kg) Not extensively metabolized, 2/3 excreted unchanged by kidneys	10% population with enteric bacteria that reduce oral bioavailability 20-40%plasma protein bound

Digoxin 2004-2

Digoxin toxicity	What are the clinical manifestations of digoxin toxicity ? What is the specific antidote for digoxin toxicity ? What are the indications for the use of digibind ?	At least one example of each of CNS, GIT and cardiac Digi whats it Cardiac arrhythmias, hyperkalaemia	

Flecainide 2008-2

Question 5: Flecainide	1. What is flecainide's mechanism of action?	**Na channel blockade** (class effect). Predominant action is to inhibit the fast, or sodium, channel which is largely responsible for the rapid upstroke of the myocardial action potential in cardiac conducting tissue **Class 1C action** - – minimal effect on the Action Potential Duration and dissociates from the Na channel with slow kinetics. (no effect on QT interval) Decrease the rate of rise (V_{max}, phase 0) of the action potential with little effect on duration.	Na channel block, class 1C
	2. Describe flecainide's pharmacokinetics. **Prompt** Usual oral dose Tambocar trade name	Well absorbed orally, half life ~ 20 hours, Peak plasma drug levels at ~ 3 hours (range 1-6 hrs), Vd ranges from 5 to 13.4 L/kg (mean 8.7 L/kg), 30% of a single oral dose (range 10 to 50%) is excreted in urine as unchanged drug – remainder by hepatic metabolism. Usual dose 100- 200 mg daily	2 things
	3. In which patients is it contraindicated?	Hypotension, LV dysfunction	Any answer

Lignocaine 2011-1

Lignocaine	Describe the mechanism of action of lignocaine on the heart.	Blocks activated & inactivated Na channels; greater effect on ischaemic tissue; no vagal effects. Class 1 B antiarraythmic action.	Na channel block and Class 1B
	Describe the adverse effects of lignocaine	CNS: dizzy, anorexia, N&V, tinnitus, tremor, visual disturbance, paraesthesia, slurred speech seizure, resp depression CVS: bradycardia, CVS collapse, uncommon proarrhythmia; can get SA arrest, impaired conduction may worsen/ precipitate pre existing CCF; ↓BP from myocardial depression Allergy GI as above	CNS & Cardiac with at least x 3 example total

Lignocaine 2005-1

Lignocaine	What are the pharmacodynamic effects of lignocaine on the heart?	• **Selectively blocks the fast Na channels of the depolarised cells, increasing their refractory period.** • Decreases pacemaker activity. • May cause hypotension by depressing myocardial contractility in those with heart failure. **(bold + 1)**	Type 1B antiarrhythmic. Affects cells with the longest APs, such as purkinje and ventricular cells as opposed to the atrial cells.
	What features distinguish lignocaine from other Class 1 Antiarrythmics?	• **Does not prolong the duration of the AP.** • Dissociates from the channel with rapid kinetics • Has no effect on normal cells. **(1 of 3)**	
	What are the clinical uses of lignocaine?	• **Type 1B Antiarrhythmic** • **Local Anaesthetic** • Post herpetic neuralgia **(2 of 3)**	

Lignocaine 2004-2

Lignocaine	Describe the mechanism of action of lignocaine on the heart Describe the adverse effects of lignocaine	Na channel blockade Stepwise CNS effects Cardiovascular Na blockade	

Propranolol 2016-1-C

Stem: Moving onto Pharmacology. She is treated with propranolol.			
Question 3 Propranolol (Beta Blockers) **Subject:** Pharm LOA: 1	1. Describe the pharmacodynamics of propranolol that make it useful in thyrotoxicosis. (Prompt: What are the cardiovascular effects?)	**B-Blocker: Competitive non selective B Blocker, blocking both B1 and B2 receptors** CVS: ↓BP, ↓HR (esp rate control of AF), both negatively inotropic and chronotropic. ↓catecholamine effects which are prominent in hyperthyroid. Inhibition of peripheral conversion of thyroxine (T4) to triiodothyronine (T3) (esp in propranolol cw other B-blockers) Has Na-channel blocking action ("membrane stabilisation")	Bold and 2 CVS effect
	2. What are the adverse effects of propranolol?	**CVS**: Bradycardia, Hypotension, worsening CCF, worsening ischaemia in PVD, QRS widening & arrhythmias in toxicity **CNS**: sedation, depression, dreams, In toxicity-coma/seizure/delerium **Resp**: worsening asthma/COPD, Other: decreased exercise tolerance, fatigue, impotence, ↓libido, mask symptoms of hypoglycaemia	1 example from each bold system

Sodium Channel Blockers 2006-2

2. Class 1 Anti-arrhythmics: mechanism of action	**How do you classify Class I anti-arrhythmic drugs** **Give an example of each** (1 EACH CLASS FOR PASS) **What are their different effects on the action potential**	**a, b, c** **1a: prolong, 1b: nil, 1c: minimal**	

Sotalol 2012-1

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

Verapamil 2015-2-C

Stem: A patient presents with a Verapamil overdose.			
TOPIC	QUESTIONS	KNOWLEDGE **(essential in bold)**	NOTES
Question 1 Verapamil **Subject:** Pharm LOA: 1	1. Describe the mechanism of action of verapamil	**Block** voltage-gated L-type **Ca channels** (α1 subunit), reduced frequency of opening when depolarised, resulting in **decreased** transmembrane Ca current, and **Ca influx**: Vascular smooth muscle relaxation (< Dihydropyridines) **Cardiac – decrease AVN conduction, contractility**, CO	Bold to pass
	2. What are the toxic effects of verapamil?	CVS: bradycardia, AV block, cardiac arrest, heart failure, hypotension Minor: flushing, dizziness, nausea, constipation, peripheral oedema	3 to pass 1 to pass
	3. What antidotes can be used to treat verapamil toxicity?	Calcium iv, high-dose insulin (euglycaemia) therapy	1/2 to pass

ACE inhibitors 2010-2

2.
a. Describe the mechanism of action of ACE inhibitors
	• competitive **block conversion of angiotensin I to II** ⇒
	  ○ **decreased vascular tone** from prevention of vasoconstrictor effects of Ang II (main effect)
	  ○ **inhibition of aldosterone secretion** caused by Ang II leading to reduced Na & H_2O resorption ⇒ decreased BP
		3 in **bold** to pass

b. What are the adverse effects of ACE inhibitors	• **dizziness, hypotension** • headaches, weakness • loss of taste, nausea, diarrhoea • rash, fever, joint pain • **cough** • mild hyperkalaemia due to decrease in aldosterone secretion • acute renal failure	• hypotension or dizziness • cough • plus 2 others
c. What are some drug interactions that occur with ACE inhibitors	• Diuretics ⇒ hypotension • General anaesthetics ⇒ hypotension • Lithium ⇒ lithium toxicity • NSAIDS ⇒ hyperkalaemia & reduced effects of ACE inhibitor • Potassium sparing diuretics / potassium supplements ⇒ hyperkalaemia	2 to pass

Angiotensin II Receptor Blockers 2016-2-B

Image not found

Angiotensin II Receptor Blockers 2008-1

Angiotensin 2 Blockers	Describe the pharmacodynamics of therapeutic drugs that modulate the effect of angiotensin (Prompt to ACE & receptor blockers) What are the advantages of Angiotensin 2 receptor antagonists over ACE inhibitors ? (Specifically with respect to side effects)	ACE inhibitors – bind ACE reversibly preventing conversion of AI to AII. Inhibitory action on the renin-angiotensin system Stimulating action on the kallikrein-kinin system Angiotensin II inhibitors – competitive antagonists at A II receptor. As AII inhibitors do not result in production of bradykinins, there is a decreased incidence of cough and angioedema. Potentially greater effect as enzymes other than ACE can generate AII (Pass – able to describe actions and basic effects of ACE inhibitors and understanding that AII receptor antagonists and ACE inhibitors have different mechanisms.)	

Antihypertensives 2009-1

Question 2 Antihypertensives	1. What are the sites of action of antihypertensive drugs (with examples)?	Vasomotor centre – clonidine, methyldopa Sympathetic ganglia - trimethaphan Sympathetic nerve terminals – guanethidine, reserpine **β receptors of heart** – β blockers **Angiotensin receptors of bv** – AT II receptor blockers α receptors of bv - prazosin **Vascular smooth muscle** – hydrallazine, SNP, Ca blockers, GTN **Kidney tubules** - diuretics β cells juxtaglomerular cells – β-blockers **ACE**	Pass 4 of bold.

Captopril 2014-1-A

Stem: We are now moving to Pharmacology. Her medications include captopril			
Question 4 ACE inhibitors **Subject:** Pharm	What is the mechanism of action of captopril?	**Angiotensin converting enzyme** (kininase II) **inhibitor**: inhibits hydrolysis of A1 to A2. Hence, **inhibits A2** effects (potent vasoconstrictor and increases Aldosterone secretion – salt and H2O retention) and decreases PVR, BP. Also, **inhibits bradykinin inactivation** to cause vasodilatation and decreased PVR, BP.	Bold to pass
LOA: 2	What are the adverse effects of captopril?	**Hypotension**, 1st dose esp. if hypovolaemic, diuretics, NaCl restriction, GI loss **ARF** esp. with bilateral RAS **HyperK+** esp. if renal insuff, DM **Cough, angioedema** (bradykinin, substance P), wheeze Fetal abnormalities (hypotension, anuria, renal failure – 2nd/3rd trim, increased teratogenesis – 1st trim) Altered taste, allergic skin rash, drug fever (10%)	3 of Bold to pass
	What drugs interact with captopril?	**K+ supplements, K+ sparing diuretics** – increase hyperK+ NSAIDs – impair BP reduction (block bradykinin) Other antihypertensives; haemaccel	Bold to pass

Captopril 2005-2

TOPIC: Angiotensin II Antagonists _____NUMBER: 2

OPENING QUESTION	**What is the mechanism of action of captopril**	**COMMENTS**
POINTS REQUIRED	Angiotensin converting enzyme inhibitor Stops conversion of Angiotensin I to Angiotensin II	
	Angiotensin II is potent vasoconstrictor Angiotensin II also increases aldosterone secretion Increased salt and water rentention	
	ACE (kininase II) also metabolises Bradykinin into its inactive form Increase in bradykinin causes vasodilation, decreased PVR and therefore decreased BP	
PROMPTS		
SECOND QUESTION (if needed)	**What are the potential adverse effects of captopril?**	
POINTS REQUIRED	1 Profound hypotension	
	2 ARF esp with renal artery stenosis	
	3 Hyper K+	Must get 4
	4 Cough Wheeze	
	5 Angiooedema	
	6 Fetal abnormalities Hypotension Anuria Renal failure Increased malformations Increased fetal death	
PROMPTS		

Captopril 2003-1

QUEST 2. ACE inhibitors

FIRST QUESTION	What is the mechanism of action of captopril	
	Inhibit converting enzyme peptidyl dipeptidase which a. **hydrolyzes AI to AII – get decreases peripheral vasc. resistance, CO and HR same** b. inactivates bradykinin – therefore get vasodilation, decr. Peripheral vascular resistance, decr. BP	
SECOND QUESTION	What are the clinical uses of captopril	
	a. CHF, after MI (better preservation of LVF – reduce post MI remodeling) b. Diabetic nephropathy – diminish proteinuria, stabilize renal function – improved intrarenal hemodynamics c. Hypertension	Know Know
THIRD QUESTION	What are the adverse effects of captopril	
	Hypotension after 1st dose if hypovolemic, diuretics, NaCl restriction, GI loss ARF (bilateral renal a. stenosis) Hyperkalemia – if renal insufficiency, DM Dry cough, angioedema (bradykinin, substance P) Fetal problems if 2nd, 3rd trimester Neutropenia, proteinuria from high dose captopril Minor – change taste, skin rash, drug fever	Know

Hypertensive emergencies 2011-1

Drugs used in hypertensive emergencies	List some drugs used in hypertensive emergencies. Tell us about the pharmacokinetics of Na nitroprusside . What are the potential toxicities of Na nitroprusside?	GTN , nifedipine , diazoxide , hydrallazine , nitroprusside , esmolol , labetalol IV administration, **onset minutes**, peak effect minutes, **1/2 life 2 minutes** (thiocyanate 3 days), duration of action 1-10 minutes, **elimination-RBC's to cyanide, liver to thiocyanate**, renally excreted **Cyanide toxicity** - hypotension , metabolic acidosis , pink skin , tachypnoea decreased reflexes , dilated pupils , coma **Thiocyanate toxicity** - ataxia , blurred vision , headache , nausea , vomiting , tinnitus, SOB, delirium, unconsciousness	At least 3 drugs 2/4 Bold Both bolded categories and 1 example of each.

Prazosin 2017-2-A

Stem: Moving on to Pharmacology. He is on Prazosin.			
Question 3 prazosin/alpha blockers **Subject:** Pharm LOA: 1 Katzung and Trevor 13th ed, chap 11.	a) What is the mechanism of action of prazosin? Prompt: Which receptors does prazosin bind to? Prompt: How does prazosin reduce blood pressure? b) List 3 other effects of prazosin. Prompt: What are the side effects of prazosin?	a) Prazosin selectively **blocks alpha-1 receptors** in arterioles and venules**.** Reduces arterial pressure by dilating both resistance and capacitance vessels. Alpha$_1$-receptor selectivity allows noradrenaline to exert unopposed negative feedback (mediated by presynaptic α_2 receptors) on its own release. b) Postural hypotension /dizziness / syncope - Reflex tachycardia / palpitations - Headache - Lassitude - Reduced prostate smooth muscle tone, thus alleviating prostatic urinary obstruction - Positive serum antinuclear factor - ↓LDL & TGs and ↑HD	Bold 3 to pass

Ramipril 2017-2-B

Stem: Moving onto Pharmacology. His medications include Ramipril.			
Question 3 ACE inhibitors **Subject:** Pharmacology LOA: 2 *Katzung 13th, 184-5.*	a) Discuss the pharmacodynamics of Ramipril. *Prompt: how does this class of drug work?* *Prompt: do they have other non-antihypertensive benefit (eg. in DM)?*	a) Inhibit the peptidyl dipeptidase (angiotensin converting) enzyme that hydrolyzes **angiotensin I to angiotensin II** **Stops inactivation of bradykinin**, a potent vasodilator, which works at least in part by stimulating release of nitric oxide and prostacyclin. Inhibits the renin-angiotensin system and and stimulates the kallikrein-kinin system. Diminishes proteinuria and stabilizes renal function (even in the absence of lowering of blood pressure) - particularly valuable in diabetes - now recommended in diabetes even in the absence of hypertension.	Bold to pass
	b) How is Ramipril eliminated? Why is this important?	b) **It is eliminated primarily by the kidneys.** Doses of these drugs should be reduced in patients with renal insufficiency.	Bold to pass
	c) What are some adverse and toxic effect of ACE Inhibitors?	c) Severe hypotension can occur after initial doses (esp. fluid deplete pts). **ARF** – esp. with bilateral renal artery stenosis or solitary kidney. Dry cough and wheeze. **Hyperkalemia** – esp. with K^+ sparing diuretics, DM and CRF. **Angioedema** Contraindicated in pregnancy. In high doses with CRF - neutropenia and proteinuria Altered taste Allergic skin reactions Drug fever (in up to 10% of pts) Effect may be reduced with concomitant NSAIDs	2 bold/total 4 to pass

Betablockers 2007-1

2.2 Beta Blockers	What are the pharmacokinetic features of Beta Blockers?	Well absorbed, low bioavailability, large volume of distribution. Most are metabolized in liver **(must get 2)**	
	What are the effects of beta blockers?	Decrease in hypertension, negative chronotrope and negative ionotrope, atrioventricular block, increased survival after AMI, Bronchospasm, decreased IO pressure **(must get 2)**	
	What are the effects of beta blocker in overdose?	Hypotension, bradycardia, cardiogenic shock, bronchospasm, seizures (cerebrotoxic), NB Propanolol causes arrhythmias through Type 1 antiarrhythmic effects (Na channel block) **(must get 3)**	/2

Betablockers 2005-1

Beta blockers (carvedilol)	Describe the pharmacodynamics of propranolol. How does carvedilol differ from propranolol?	• **Non-selective action on Beta receptors,** • **Membrane stabilizing action,** • **Antagonizes renin release from symp ns.** • **Competitive, pure antagonist.** **(2 out of 4 + 1 of the rest in notes).** Carvedilol has no local anaesthetic action. **Causes Alpha 1 adrenoceptor block, but effect on Beta receptor > Alpha receptor.** Stereoselective metabolism of its 2 isomers occurs(with polymorphism influenced Cytochrome P450 2D6 affecting R isomer metabolism). **(1 out of 3)**	Inhibits sympathetic ns stimulation of lipolysis, Inhibits liver glycogenlysis, Reduces aqueous humour production, Increases VLDL, Decreases HDL. Blocks B2 receptor in bronchial smooth muscle increasing airway resistance.

Metoprolol 2016-2-B

Stem: Moving onto Pharmacology. As part of the patient's ongoing management, you prescribe Metoprolol.			
Question 4 Metoprolol **Subject:** Pharm LOA 1	Describe the pharmacokinetics of metoprolol? *Prompt: What's the bioavailability? Why is this so?*	Oral or IV, Well absorbed Bioavailability 50% due to **first-pass effect** **Large volume of distribution** (>200L) Half-life, 3-4 hours Metabolised in the liver	Bold and 2 others to pass
	What are the cardiovascular effects of metoprolol?	1 **Negative inotropic and chronotropic effects** 2 Slow a-v node conduction with increased PR on ECG 3 decrease BP by a mechanism not fully understood but probably includes suppression of renin release and CNS effects	Bold and 1 to pass
	How does metoprolol differ from propranolol in its action at beta receptors?	B1 equipotent B2 50-100 fold less potent ie **metoprolol is B1 specific and propranolol is not** (equipotent at B1 and B2) metoprolol at higher doses is less specific	Bold to pass

Metoprolol 2014-2-A

Stem: His heart rate is 40 beats per minute and he takes metoprolol.			
Question 2 **Subject**: Pharm Metoprolol / Beta blockers (Ch 10) LOA: 1	1. Describe the pharmacokinetics of metoprolol **Prompt** what is its bioavailability and why? 2. How does metoprolol differ from propranolol in its action at beta receptors? 3. How do BB control hypertension?	Oral or IV, Vd – large, T ½ 3 – 4 hrs, Metabolised in liver Bioavailability 50% due to 1st pass effect. Beta 1 – full agonist Beta 2 - 50 – 100 fold less potent Negative **inotropic and chronotropic** effects Slow a-v node conduction Antagonises release of renin/not fully understood.	**Oral & IV & 1st pass** Or **3/5** **B1 Selective** **Negative inotropic & chronotropic effect**

Metoprolol 2010-1

Question 4: Metoprolol P147-55, 169	1. Describe the pharmacokinetics of metoprolol *What's the bioavailability?* *Why is this so?* 2. How does metoprolol differ from propranolol in its action at beta receptors? 3. How do B Blockers control hypertension?	Oral or IV, Well absorbed Bioavailability 50% due to first-pass effect Large volume of distribution Half-life, 3-4 hours Metabolised in the liver B1 equipotent B2 50-100 fold less potent Not fully understood Negative inotropic and chronotropic effects Slow a-v node conduction Antagonises release of renin caused by sympathetic nervous system	Large Vd + first pass B1 selective Negative inotrope/chronotrope
Question 5:	1. During clinical drug trials, what factors might	1. variable natural history of most disease	B'

Propranolol 2013-1

Question 2 **PROPRANOLOL** LOA: 1	Describe the pharmacodynamics of propranolol.	B antagonist; competitive; non-selective CV ↓BP if high -ve inotrope –ve chronotrope ↑PR interval ↓renin release Resp bronchospasm Eye ↓pressure (↓humour production) Metabolic ↓glycogenolysis ↑VLDL ↓HDL	2 CV + 1 other
	What are the potential adverse effects?	Bradycardia; ↑CCF; ↑PVD ↓hypoglycaemia response Bronchospasm Sedation/depression Abrupt withdrawal effects Exacerbate Ca channel blocker effects	Bradycardia, bronchospasm and 1 other

Propranolol 2004-2

Beta receptor antagonists	Describe the pharmacokinetics of propanolol Describe the cardiovascular effects of beta blockers	High 1st pass, liver metabolism, lipid solubility high B blockade with variable selectivity, negative intropic and chronotropic	

Calcium Channel Blockers 2011-2

Question 2: Calcium channel blockers	a) What are the effects of Ca channel blockers on smooth muscle? *(Prompt: tissue level)* b) By what mechanisms do Ca channel blockers control angina? c) Why is verapamil more efficacious than dihydropyridines in the treatment of arrhythmias?	a) **Relax smooth muscle esp vascular smooth muscle** Arterioles more sensitive than veins Does effect bronchiolar GIT and uterine b) **Decrease myocardial contractility** Decrease oxygen demand **Decrease afterload by relaxing vascular smooth muscle** Verapamil/ diltiazem have a non-specific antiadrenergic effect and decrease heart rate Relieve and prevent coronary artery spasm c) Blockade of L-channels more marked in tissues that fire frequently More marked effects on tissues that depend on Ca channels for activation, SA & AV nodes More marked on tissues with tissues less polarised at rest	Bolded Bolded Supplementary

Calcium Channel Blockers 2009-2

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

	• What are the toxic effects of CCB's	• Cardiovascular: cardiac arrest; bradycardia; AV block; heart failure, hypotension • Minor: flushing, dizziness, nausea, constipation, peripheral oedema	2 cardiovascular

Calcium Channel Blockers 2006-2

2. Ca Channel Blockers	**At a cellular level describe the action of calcium channel blockers.** **What are the differences in pharmacodynamics between dihydropyridines and other Ca channel blockers?** **How are these differing pharmacodynamics reflected in their side effect profile?**	**Bind at intracellular L type calcium channel** **Dihydropyridines are vascular smooth muscle selective** **Verapamil / Diltiazem greater effect on cardiac/conducting tissue** **Dihydropyridines cause flushing, headache & tachycardia** **Verapamil causes bradycardia** **Both can cause hypotension**	

Verapamil 2017-2-C

Stem: An 85 year old man presents with heart failure. He is on verapamil. We will start with Pharmacology.			
TOPIC	QUESTIONS	KNOWLEDGE **(essential in bold)**	NOTES
Question 1 **Subject: Pharm** Verapamil LOA: 1	Describe the mechanism of action of verapamil.	**Blocks** voltage gated L-type **calcium channels** (α1 subunit), reduced frequency of opening when depolarized resulting in decreased transmembrane calcium current and calcium in-flux.	**Bold** + concept of blocking Ca influx
	Describe the effects of verapamil on the heart and blood vessels.	**Reduced contractility/CO**, oxygen demand, Reduced impulse generation/**AVN conduction block**. **Vascular smooth muscle relaxation** (less than dihydropyridines) or reduced coronary artery spasm.	2 of 3 bold
	What are the adverse effects of verapamil?	CVS; **bradycardia/AV block**, cardiac arrest, **heart failure**, **hypotension** Minor: flushing, dizziness, nausea, constipation, peripheral oedema.	2 of 3 bold

Verapamil 2013-1

Question 2 **VERAPAMIL** LOA: 1	Describe the effects of verapamil on the heart.	Binds to α1 receptor L-type Ca channel **Blocks Ca influx** **Reduced contractility** CO, O_2 demand **Reduced** impulse generation/**conduction AV node** Reduced coronary artery spasm	**Bolded**
	What are the indications for verapamil?	**Angina; hypertension; atrial arrhythmias** migraine	**2 bolded**
	Name some clinical adverse effects	Extensions of therapeutic action (exacerbated by β blockers) **Bradycardia; AV block; CCF; hypotension** Other Constipation; peripheral oedema; dizziness; flushing; nausea	**2 bolded**

Acetazolamide 2007-2

3.4 Acetazolamide (SB)	What are the actions of acetazolamide What are the toxic effects of acetazolamide? (at least one) PROMPT: Can renal &/or hepatic disease increase the risk of adverse effects?	**Carb anhydrase inhibitor**, ciliary body, choroid plexus, prox. renal tubules (plus one organ) , • Hyperchloraemic metabolic acidosis • Renal stones (PO_4, Ca) • Renal K^+ wasting • Drowsiness, parasthesia • Increased risk of neurological toxicity with renal failure (reduced renal elimination) • Hepatic encephalopathy in patients with cirrhosis (reduced renal excretion of NH_4^+)	/2

Frusemide 2017-1-B

Stem: Moving onto Pharmacology. He is on frusemide			
Question 3 Frusemide **Subject:** Pharm LOA: 1	a) What class of drug is it? b) What are the pharmacokinetics of frusemide?	**Loop diuretic** Absorption: Well absorbed / variable oral bioavailability /10-100%. Onset post oral is 1-3 hour. Post IV is 15-30 mins. Duration post oral is 2-6 hours. Post IV 2 hours. Distribution: highly albumin bound. Metabolism: Liver (small amount). Elimination: Renal.	Bold 3 of 6
	c) What are the adverse effects?	orthostatic hypotension, dehydration Hyponatremia, hypokalemia, hypomagnesemia, metabolic alkalosis - ototoxicity, tinnitus, vertigo - GIT: pancreatitis, jaundice, N&V Raised uric acid- causing gout - thrombocytopenia - hypersensitivity reactions – rash	1 electrolyte abnormality and CVS effect (the other ones are quite rare)
	d) What are the possible drug interactions?	- NSAID, aminoglycosides - anticoagulants - digoxin, lithium, propranolol, probenecid, thiazides, amphotericin B , cisplatin	1 to pass

Frusemide 2014-2-B

Stem: We will now move on to pharmacology. Treatment is commenced with normal saline and frusemide.			
Question 3 Frusemide (pp 258-260) **Subject**: Pharm LOA: 1	1. How does frusemide exert its action?	**Selectively inhibits Na+-K+-2Cl- transporter in thick ascending limb of loop of Henle thus preventing resorption of Na+ & Cl-** Abolishes counter-current concentrating mechanism leading to dilute urine. Increased prostaglandin synthesis -> inhibition of salt transport in thick ascending limb -> increased renal blood flow, decreased pulmonary congestion, decreased LV filling pressures	Bold to pass
	2. What are the pharmacokinetic properties of frusemide?	• Rapid absorption after oral admin • Oral bioavailability 50% (range 10 –100%) • Highly protein-bound (>95%) • 50% conjugated in kidney & 50% excreted in urine unchanged (tubular secretion) • Elimination t1/2 1.5 – 2 hours • Peak effect 30 minutes IV / 1 hour oral	List 3

	3. What are the potential adverse effects of frusemide?
	
	PROMPT:
	What are the electrolyte disturbances?
		• Electrolyte disturbances
		  • **hypokalaemia**,
		  • hyponatraemia,
		  • hypomagnesaemia,
		  • hyperuricaemia
		
		• Postural **hypotension** & dizziness
		• Metabolic Alkalosis
		• Allergy - rash, eosinophilia, interstitial nephritis
		• Increased LDL & triglycerides, decreased HDL
		• Hyperglycaemia
		• Ototoxicity (high dose IV)
			Bold plus 2

Frusemide 2011-2

Question 2 Loop Diuretics	a) What are the mechanisms of action of FRUSEMIDE?	a) • inhibits NKCC2 = a luminal $Na^+/K^+/2Cl$ co-transporter of **thick ascending limb of Loop of Henle** => **decreased reabsorption of NaCl** => diuresis • increased prostaglandin synthesis => a) inhibition of salt transport in thick ascending limb => b) increased renal blood flow, decreased pulmonary congestion, decreased LV filling pressures	**bold** to pass
	b) What are the toxic effects of FRUSEMIDE?	b) • **decreased K** metabolic alkalosis • ototoxicity • hyperuricaemia • hypomagnesaemia • Allergy - rash, eosinophilia, interstitial nephritis • dehydration • hyponatraemia	4+ to pass - must include **decr K** & one non-electrolyte

Frusemide 2010-2

2. a. What are the pharmacokinetic properties of frusemide?	• Rapid absorption after oral admin • Oral bioavailability 50% (range 10 –100%) • Highly protein-bound (>95%) • 50% conjugated in kidney & 50% excreted in urine unchanged (tubular secretion) • Elimination $t^1/_2$ 1.5 – 2 hours • Peak effect 30 minutes IV / 1 hour oral	Must list 3 properties
b. What are the site and mechanism of action of frusemide ?	• Actively secreted into lumen of nephron from proximal tubule cells via organic-base pump • Inhibits Na^+-K^+-$2Cl^-$ transporter in **thick ascending limb of loop of Henle** thus **preventing resorption of Na^+ & Cl^-** • Abolishes counter-current concentrating mechanism leading to a dilute urine	Must mention thick ascending limb of loop of Henle and reduced resorption of Na and Cl.
C. What are the adverse effects of the frusemide?	• Electrolyte disturbances – **hypokalemia**, **hyponatraemia**, hypomagnesaemia, hyperuricaemia • Postural **hypotension** & dizziness • Increased LDL & triglycerides, decreased HDL • Ototoxicity (high dose IV) • Drug interactions	Must list • Hypokalemia • Hyponatremia • Hypotension or dizziness • 1 other

Frusemide 2008-1

Loop Diuretics	How does frusemide exert its action ? What are the adverse effects of frusemide? (Are any other organ systems effected ?)	Selective inhibition of NaCl reabsorption in the thick ascending loop of Henle Hypokalemic Metabolic Alkalosis Ototoxicity Hyperuricemia Hypomagnesemia . Allergy Skin rash Eosinophilia Interstitial nephritis Hyponatremia Pass – Na & loop of Henle, 4 adverse effects incl hypokalaemia & one non electrolyte	

Frusemide 2004-2

Loop diuretics	Describe the mechanism of action of Frusemide What effects do they have on renal handling of Ca and Mg ?	Na/K/ 2Cl pump, thick ascending limb loop Henle Excretes calcium	

Mannitol 2015-2-D

Stem: Moving onto Pharmacology. He is given Mannitol.			
Question 4 Mannitol **Subject:** Pharm LOA: 2	Why is mannitol used in the management of head injury?	Mannitol is used to **reduce intracranial pressure** after head injury.	**Bold** to pass
	What is the mechanism of action of mannitol?	Mannitol is an osmotic diuretic, it alters Starling forces as it does not cross the intact blood-brain barrier and thus **draws water out of cells** and **reduces intracellular volume** (hence reduces intracranial volume and intracranial pressure)	**Bold** to pass
	What are the other clinical effects?	Reduces intraocular pressure Diuresis / dehydration / hypovolaemia Hypernatraemia Hyperkalaemia	2/4 to pass
	Supplemental Question; What is an appropriate dose of mannitol in this clinical situation?	1-2g/kg as an IV bolus over 15 mins (**0.25-2g/kg IV bolus**).	

Osmotic Diuretics 2007-1

2.4 Osmotic diuretics (including mannitol)	How are osmotic diuretics handled by the kidney? What are the clinical uses of Mannitol? What are the toxic effects of Mannitol?	Freely **filtered** by glomeruli. **Not reabsorbed**, causes water retention in the freely permeable sections of the nephron = proximal tubule and descending loop of Henle IV dose 0.5-1-2 g/kg for **raised intracranial pressure**. Rarely for intraocular pressure and diuresis in haemolysis or rhabdomyolysis Extracellular volume expansion, Hypernatraemia **(must get 1)**	/2

Thiazide Diuretics 2015-2-D

Stem: Moving onto Pharmacology. His regular medications include hydrochlorothiazide			
Question 3 Thiazide diuretics **Subject:** Pharm LOA: 2	Describe the mechanism of action of thiazides?	**Inhibition of Na/Cl transporter in the distal convoluted tubule** leading to increased NaCl excretion and **diuresis**	**Bold to pass**
	What are the major clinical indications for thiazide diuretic use?	**Hypertension** **Heart failure** Nephrolithiasis Nephrogenic Diabetes Insipidus Generalised oedema Nephrotic syndrome cirrhosis	**2 bold to pass**
	What are the potential adverse effects of thiazide diuretics?	**Hypokalaemia** **Dehydration/post hypotension/hypovolaemia** **Hyponatraemia** Metabolic alkalosis Hyperuricaemia Hyperlipidaemia Allergic Reactions – x- reactivity with sulphonamides Impaired carbohydrate tolerance – Hyperglycaemia Hypercalcaemia Pancreatitis	**2 bold plus 1 other**

Thiazide Diuretics 2006-2

2. Thiazide Diuretics	**1. How do thiazides exert their diuretic action** **2. What are the adverse effects of thiazides?** (3/6 FOR PASS)	**Inhibition of NaCl reabsorption in the distal convoluted tubule** **1. Hypokalaemic metabolic alkalosis and hyperuricaemia** **2. Impaired carbohydrate tolerance** **3. Hyperlipidaemia** **4. Hyponatraemia** **5. Allergic reactions (sulphonamides)** **6. Weakness, fatigue, paraesthesia (like carbonic anhydrase inhibitors)**	

Antiplatelet agents 2003-2

4. Anti-platelet agents	1.What is the mechanism of aspirin's antiplatelet action?	Irreversible inhibition of COX Inhibits synthesis of thromboxane A2	Needs Irreversible inhibition of COX	
	2. What other types of anti-platelet agents are there?	Inhibitors of ADP pathway 2b,3a blockers beta blockers Other NSAIDs	The first two, others bonus. Can give name or example	
	3. What are the clinical indications for anti-platelet agents?	IHD TIA/CVA Pregnancy: prophylaxis pre-eclampsia Post acute coronary intervention	3 out of 4	

Clopidogrel 2017-1-A

Stem: Moving on to Pharmacology. He is on clopidogrel.			
Question 3 Clopidogrel **Subject:** Pharm LOA: 1	a) What is the mechanism of action of clopidogrel?	a) Anti-platelet effect by **inhibiting ADP pathway** (irreversible blockade ADP receptor on platelet for life of platelet).	**Bold** to pass
	b) Describe the pharmacokinetics of clopidogrel.	b) A **prodrug**, metabolised to a pharmacologically active metabolite and inactive metabolites. **Activated in liver by cyto P450** (including CYP2C19). 80% platelet activity inhibited within 5 hrs oral dose. **Elimination t ½** ~ 0.5 to 1.0 h. **Effects last life of platelet** Following an oral dose: 50% excreted in the urine and 46% in the faeces in next five days. **Loading dose 300 - 600mg** or **75mg daily**	**2/6 Bold** to pass
	c) What are the adverse effects?	c) - **bleeding,** rash**,** (rarely **-** pancytopaenia & TTP) - diarrhoea, abdominal pain, reflux, gastric ulcers - sensation of tingling, numbness	**Bold** plus 2 others

Clopidogrel 2006-2

4. Clopidogrel	**1. What is the mechanism of action of clopidogrel?** **2. How long is this effect** **3. What are the indications for clopidogrel** (1/2 for pass)	**Irreversible blockade of platelet ADP receptors, leading to inhibition of platelet activity** **Note there is no anti-prostaglandin effect cf aspirin** **7-10 days** **IHD – pre/post stent, stroke prevention**	

Clopidogrel 2005-1

Antiplatelet agents	Describe the mechanism of action of clopidogrel. How does it differ from aspirin? What other types of anti platelet agents are there?	**Irreversibly blocks the ADP receptor on platelets to inhibit platelet aggregation.** **Asprin inhibits the synthesis of Thromboxane A2** within platelets by the **irreversible acetylation of cyclooxygenase. (1 of 2)** **Phosphodiesterase inhibitors (dypridamole)** **Glycoprotein IIb/IIIa inhibitors (abciximab)** **(1 of 2)**	Thienopyridine derivative. Unlike asprin has no effect on PG metabolism

Heparin 2014-2-B

Stem: We will now move on to Pharmacology. A heparin infusion is commenced.			
Question 3 Heparin (pp 604-607) **Subject:** Pharm LOA: 1	1. How does heparin act?	Heparin binds endogenous **antithrombin and enhances its activity. Antithrombin inhibits factors IIa, IXa and Xa** by complexing with them and inducing a conformational change.	Bold to pass
	2. How may heparin be administered?	**IV vs SC.** Continuously (following bolus) vs intermittent. Therapeutic vs prophylactically	Bold to pass
	3. What are the potential adverse effects?	**Bleeding,** allergy, alopecia, osteoporosis, **HIT,** mineralocorticoid deficiency	Bold + 1 to pass
	4. What are the advantages of low molecular weight heparins compared to unfractionated heparin?	Have equal efficacy, increased SC bioavailability, require less frequent dosing, and less monitoring. Shorter chain heparin with less effect on thrombin (IIa).	Demonstrates understanding

Heparin 2012-1

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

Heparin 2008-1

LMWH	What are the pharmacodynamic differences between low molecular weight and unfractionated heparin? What are the advantages of low molecular weight heparin over unfractionated heparin?	Enoxaparin predominantly binds and inhibits factor Xa function, UFH binds to AT that inhibits factors II, IX, X Single daily or divided subcutaneous doses – facilitates patient mobility and OPD management. Routine monitoring not required (not mentioned in book) Reduced bleeding risk. Lower incidence of HITP. Improved efficacy over unfractionated heparin in ACS. Increased bioavailability (Pass – dosage differences and bleeding risk as well as factors II and IX less inhibited by LMWH (or at least that APTT is not accurate measurement of anticoagulation)	

Heparin 2006-1

heparins	Describe the mechanism of action of heparin?	**Binds to Antithrombin III** and accelerates its inhibition of clotting factor proteases (1000 fold).	Heparin binds to endothelial cell surfaces. About 1/3 of heparin molecules have a unique polysaccharide needed for high affinity binding to AT III, which then causes a conformational change to expose the active site of AT III for more rapid interaction with the proteases (activated clotting factors). Heparin catalyzes the AT III-protease reaction without being consumed and can move on to bind more AT III.
	How can heparin be reversed? *Prompt* *What dose of protamine should be used?*	• stop the drug • **Administration of antagonist – protamine** sulphate For every 100 Units Heparin need 1mg Protamine, but excess protamine must be avoided as can have anticoag effect	Protamine binds with heparin to form stable complex devoid of anticoagulant activity
	What are the potential adverse effects of heparin? *Prompt* *"what are the different types of TCP seen in patients on heparin?*	• Bleeding • **Thrombocytopaenia**	Elderly and pts with renal impairment more prone; contraindicated in pts with bleeding disorders, GIT ulcers, infective endocarditis and active TB, etc Transient in 25% patients ?due to heparin induced aggregation - benign
			5% severe due to antibody-mediated cause – antibody generated against heparin-platelet factor 4 complex causing aggregation and paradoxical thromboembolism; may be aggravated by warfarin

Heparin 2003-1

FIRST QUESTION	How does unfractionated heparin work?	
	Heterogenous mixture of sulfated mucopolysaccharides which binds to endothelial cell surfaces **Binds to ATIII** – conformational change so active site exposed for more active interaction with proteases to inhibit them from clotting (VIIa, IX a, Xa, II a) Heparin speeds up process 1000x. Heparin not consumed in process	
SECOND QUESTION	How does the mechanism of action of LMW heparins differ?	
	Inhibit activated factor X but less effect on AT and coagulation Increased bioabilability from SQ site of injection Need less frequent dosing (1-2/day) Don't need to follow APTT	
THIRD QUESTION	What is the adverse effects?	
	Bleeding – incr. in elderly, renal failure Transient **thrombocytopenia** 25% patients, severe in 5% Heparin induced thromocytopenia – heparin induced Ab against heparin platelet factor 4 complex Long term – osteoporosis, spontaneous fractures, mineralocorticoid deficiency	
FOURTH QUESTION	What is the clinical advantage of LMW over unfractionated heparin	BONUS
	Ease of administration – IV/SQ; timing; place question	

Rivaroxaban 2016-1-A

Stem: Moving onto Pharmacology. The patient is commenced on oral anticoagulants.			
Question 5 Rivaroxaban – mechanism of action Pharmacokinetics **Subject**: Pharm LOA: 1	a) Describe the mechanism of action of rivaroxaban.	Inhibits both free and prothrombinase-bound forms of activated factor X.	Inhibits factor Xa
	b) Describe the pharmacokinetics of rivaroxaban.	Oral bioavailability >80% Maximal plasma levels 3 hours post-ingestion Small volumes of distribution (<50L) Highly protein bound Elimination renal (predominant) and hepatic (CYP3A4) with steady state half-life 5-14 hours and prolonged with renal impairment.	2 things including predominant renal excretion to pass
	c) What clinical advantages does rivaroxaban offer over warfarin?	More rapid onset/offset of action More predictable effect = easier dosing, wider therapeutic index INR monitoring not required Fewer drug and dietary interactions	2 to pass. Better candidates will be able to correlate differing MOA and pharmacokinetics to advantages
	Extra Q: Do the pharmacokinetics of rivaroxaban present any clinical disadvantages relative to warfarin?	Predominant renal excretion means dose must be adjusted in renal failure and not suitable for dialysis patients.	Supplementary question, only use if sufficient time.

Thrombolytics 2017-2-A

Stem: Moving on to Pharmacology. The patient becomes haemodynamically unstable and he is to be thrombolysed.			
Question 4 Thrombolytics **Subject:** Pharmacology LOA: 1	a) What are the classes of thrombolytic agents? Prompt: What are the 2 classes? b) What is the mechanism of action of tissue plasminogen activator (t-PA)? c) What are the adverse effects of thrombolytic agents?	a) **t-PA** (tissue plasminogen activator e.g. alteplase, tenecteplase, reteplase) and **streptokinase** (a protein synthesized by streptococci). b) t-PA is an enzyme that directly converts **plasminogen to plasmin**. Plasmin is the major fibrinolytic enzyme. c) **Bleeding** – cerebral haemorrhage, gastrointestinal, previous surgery/wounds Allergy (especially streptokinase)	Bold to pass. Candidates may draw diagram (Katzung, 11th Ed, fig 34-2, p280). Bold to pass. Bold to pass.

Tissue Plasminogen Activator 2012-2

Question 4 Tisssue Plasminogen Activator LOA 1	Describe the mechanism of action of tissue plasminogen activator (tPA)?	Activates **plasminogen to form plasmin**, resulting in fibrin digestion. Preferentially activates plasminogen bound to fibrin by several hundred fold therefore is considered **clot specific.** Short half life therefore heparin is essential adjunct. Naturally occurring.	Bold
	What are the clinical uses of tPA? *Prompt: Are there are any other time-critical indications?*	**AMI, unstable PE, acute ischaemic stroke**, severe DVT, intra arterial peripheral limbs	First 3 to pass
	What are the complications of tPA?	**Haemorrhage.** Physiological hemostatic thrombi at site of vascular injury eg GIH, or systemic lytic state resulting from formation of plasmin, producing fibrinogenolysis and destruction of other coagulation factors esp V and VIII.	Must give more than one site.

Tissue Plasminogen Activator 2009-2

Question 4: **TPA**	(a) How does TPA work?	• Fibrinolytic. Binds to fibrin in a thrombus and converts entrapped inactive plasminogen to active plasmin to initiate local fibrinolysis	Definition
	(b) What are the indications for TPA use?	• STEMI • PE with haemodynamic instability • Acute Ischaemic Stroke: • Severe DVT	AMI, stroke and 1 other

Tissue Plasminogen Activator 2007-1

1.4 tPA	How does tPA work. How does tPA differ from streptokinase?	**tPA activates plasminogen already bound to fibrin, to form plasmin.** Plasmin degrades fibrin to fibrin split products. This *theoretically* confines fibrinolysis to formed thrombus. **Short half life** means **heparin** is an essential adjunct. **tPA** is a **naturally occurring human enzyme. Streptokinase** is not an enzyme itself- it is a **bacterial product** that combines with plasminogen to form an enzymatic complex catalyses conversion of plasminogen to plasmin. **Long half life** means that heparin is not required (and may increase bleeding risk). **Prior streptococcal infection** may result in antibodies that cause fever, allergic reactions and therapeutic resistance. **Prompts (if needed):** - *"compare and contrast the methods of administration and the adjunctive use of heparin"* - *When might streptokinase be ineffective?"*	/2

Warfarin 2012-2

Question 4 Warfarin Interactions LOA: 1	Describe the mechanisms by which drugs interact with Warfarin. *Prompts* *Please describe pharmacokinetic interactions* *Please describe pharmacodynamic interactions*	**PK - Enz inhibition** (majority), **Enz induction**, altered, plasma protein binding, altered abs **PD** – Synergism (**impaired haemostasis)** Competitive antagonism (**clotting factor synthesis/concentration**)	Must get one example of PK and PD
	Give some examples of drugs that increase the INR.	↑ **INR**: aspirin, heparin, corticosteroids metronidazole, fluconazole, trimethoprim-sulfamethoxazole, third generation cephalosporins, macrolides, amiodarone, SSRIs, tramadol	Must give at least 1 example of each
	Give some examples of drugs that decrease the INR.	↓ **INR:** Vit K, diuretics, barbiturates, phenytoin, carbamazepine, rifampicin, diclox, azathioprim	

Warfarin 2012-1

Question 4 LOA: 1 **WARFARIN**	What is the mechanism of action of warfarin?	Warfarin **inhibits reduction of inactive Vit K** epoxide (KO) to active hydroquinone (KH_2) form. Blocks γ-carboxylation of glutamate residues in **prothrombin (Factor II) and factors VII, IX and X** ,as well as endogenous anticoagulant protein C and S.	Need to know role of vitamin k
	Why is there a delay in the onset of action of warfarin?	8-12 hr delay due to partially inhibited synthesis and unaltered degradation of 4 vit k dependent clotting factors and depends on **degradation ½ life** in circulation eg factor VII- 6 hrs, IX 24-hrs, X - 40 hrs and II- 60 hrs)	Need to have some idea of delay in onset
	What pharmacological agents are used in the reversal of warfarin?	Vitamin K. FFP. Prothrombin Complex. Recombinant FVIIa	
	Optional: Describe the mechanisms of drug interactions with warfarin	Pharmacokinetic: Enzyme induction + inhibition. Altered protein binding Pharmacodymanic: Synergism. Competitive antagonism (Vitamin K)	3 required

Warfarin 2011-1

Warfarin-pharmacokinetics and drug interactions	Describe the mechanisms for drug interactions with warfarin and give examples. *Prompts:* *Please describe a pharmacokinetic interaction with warfarin* *Please describe a pharmacodynamic interaction* *What drugs could increase the INR* *What drugs could decrease the INR*	**PK - enz inhibition** (majority), **Enz induction**, altered plasma protein binding, altered abs (cholestyramine p 157) **PD** – bioavailability of Vit K, **influencing Vit K dependant clotting factors**, drugs affecting haemostasis (**1 eg**) ↑ INR: Amiodarone, aspirin, azitrhomycin, cephalosporins, cimetidine, erythromycin, phenytoin, quinidine, SSRI, valproate, metronidazole, hyperthyroid ↓ INR: AZT, barbs, carbamazepine, haloperidol, rifampicin, Vit K, St Johns Wort p159, hypothyroid, cabbage	Must get bold items Must give at least 1 example of each

Warfarin 2009-2

Question 4: **Warfarin**	(a) What is the mechanism of action of warfarin?	• Blocks synthesis of Clotting Factors II, VII, IX, X and Anticoagulant proteins C and S • Coupled to Deactivation of Vitamin K	Blocks factors II, VII, IX, X

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

	(c) How is the action of Warfarin reversed?	• Vitamin K: FFP:Prothrombin complex – Prothrombin X: Recombinant Factor VIIa	2 of 4

Warfarin 2006-1

Warfarin interactions	Describe the pharmacokinetic mechanisms for drug interaction with oral anticoagulants? Describe a pharmacodynamic interaction with warfarin?	**Enzyme induction or enzyme inhibition** **-reduced plasma protein binding (all 3)** -competitive antagonism Vit K Pharmacodynamic: aspirin, heparin, 3rd gen cephalosporin -altered physiologic control loop - hereditary resistance -clotting factor conc-spironolactone	Pharmacokinetic: amiodarone, metronidazole, trimethoprim **At least 2 examples** *Prompt "what happens to a patient on warfarin who is given Vit K"* *"why does the INR alter?"*