CVS VIVAs (Pharmacology)

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2015.1A

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

2015.1B

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

2015.1C

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**

2014.2A

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

2014.2B

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

2014.1A

Question 4 Compound Sodium Lactate (MIMs & product information) Constitution, Indications, Adverse effects. Comparison to other crystalloids and colloids **Subject:** Pharm LOA: 1	(a) How does Hartmann's solution differ from normal saline?	Addition of **Sodium Lactate, Potassium** Chloride**, Calcium** Chloride (+pH adjustment) Na 131, K 5, Cl 112, Ca 2, Lactate/Bicarb 28 mmol Compare Normal Saline Na 150 Cl 150)	Bold
	(b) What are the potential advantages of Hartmann's solution in resuscitation?	Closer to physiologic – potassium, calcium **Less Hyperchloraemia** **Effective bicarbonate – some (slow) good effect on acidosis** (proof of superiority lacking)	Bold
	(c) What are the potential complications of IV fluid therapy?	overload/under resuscitation, hypothermia, extravasation, acidosis, electrolyte abnormalities, osmo changes, air embolism, infection, cerebral oedema, haemodilution	Bonus

2014.1A

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

2013.2A

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.

2013.2C

Question 2 **PHARMACOLOGY GTN** LOA: 1	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
Katzung 12th ed Chapter 12) MoA, principles of tachyphylaxis	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

2013.1.1

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**

2013.1.2

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

2013.1.3

Question 2 **GLYCERYL TRINITRATE (GTN)** LOA: 1	How does Glyceryl Trinitrate (GTN) exert its effect on smooth muscle?	Nitrate→**Nitric Oxide→↑cGMP→** relaxation→**vasodilation** Also involves Prostaglandin E or prostacyclin	**Nitric Oxide , cGMP/second messenger, vasodilation**
	Describe the Pharmacokinetics of GTN **Prompt**: How is GTN given?	**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	**Low Bioavailabilty** **Short halflife**

2012.1.3

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

2012.2.3

Question 2 adenosine LOA: 1	What are the indications for use of Adenosine?	**Conversion of paroxysmal SVT to sinus rhythm.**	Bold to pass
	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

2011.1.1

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

2011.1.3

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

2011.1.3

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.

2011.1.3

Drugs used in hypertensive emergencies	List some drugs used in hypertensive emergencies.	GTN , nifedipine , diazoxide , hydrallazine , nitroprusside , esmolol , labetalol	At least 3 drugs 2/4 Bold
	Tell us about the pharmacokinetics of Na nitroprusside .	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	
	What are the potential toxicities of Na nitroprusside?	**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	Both bolded categories and 1 example of each.

2011.2.2

Question 2: Calcium channel blockers	a) What are the effects of Ca channel blockers on smooth muscle? *(Prompt: tissue level)*	a) **Relax smooth muscle esp vascular smooth muscle** Arterioles more sensitive than veins Does effect bronchiolar GIT and uterine	Bolded
	b) By what mechanisms do Ca channel blockers control angina?	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	Bolded
	c) Why is verapamil more efficacious than dihydropyridines in the treatment of arrhythmias?	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	Supplementary

2011.2.2

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

2011.2.3

Question 2 Loop Diuretics	a) What are the mechanisms of action of FRUSEMIDE? b) What are the toxic effects 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 b) • **decreased K** metabolic alkalosis • ototoxicity • hyperuricaemia • hypomagnesaemia • Allergy - rash, eosinophilia, interstitial nephritis • dehydration • hyponatraemia	**bold** to pass 4+ to pass - must include **decr K** & one non-electrolyte

2010.1.1

Question 4: Amiodarone P228-9	1. What are the cardiac effects of amiodarone at a cellular level? 2. What are the mechanisms of pharmacokinetic drug interaction with Amiodarone and give two examples.	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 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	K block and 1 other Enzyme induction/inhibition + 1example of either

2010.1.2

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

2010.1.3

Question 4: Atropine P108-9, 114-6	1. Describe the pharmacokinetics of atropine	Oral or IV (usually), neb, topical; Well absorbed orally Widely distributed (including CNS) Half-life 2 hours Elimination: 60% excreted renally unchanged 40% phase I and phase II metabolism and renally excreted	Wide distribution + short t1/2
	2. At which receptors does atropine act?	Muscarinic (equipotent at M1, M2 and M3) Nicotinic (minimal potency)	Predominant Muscarinic
	3. What are the effects of atropine on heart rate?	Lower doses often an initial bradycardia, (Blocks prejunctional M1 receptors); Tachycardia	Dose dependant

2010.2.1

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

2010.2.2

2.
a. Describe the mechanism of action of ACE inhibitors
	• competitive **block conversion of angiotensin I to II** ⇒
	  o **decreased vascular tone** from prevention of vasoconstrictor effects of Ang II (main effect)
	  o **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

2010.2.3

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

2009.2.3

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

2009.1.1

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

2009.1.2

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	

2009.1.3

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.

2008.2.3

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

2008.1.1

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.)	

2008.1.1

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)	

2008.1.2

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	

2008.1.3

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

Older

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

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

3.2 Atropine	What is the mechanism of action of atropine? Give examples of organ effects What are the features of atropine poisoning	Reversible block of **cholinergic muscarinic** receptors 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)** Agitation and delerium Raised temp Blurred vision / mydriasis Dry mouth / flushed skin Tachycardia **(must get 4)**	/4

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

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)
		Electrical: (i) Direct: **Shortening of action potential** and ∴ shortened atrial and ventricular refractoriness	Follows early brief prolongation of AP Probably due to ↑K+conductance
		At toxic levels, resting membrane potential reduced, then as toxicity progresses depolarizing afterpotentials	Overloaded intracell Ca+ stores
	PROMPT for autonomic effects: What are the autonomic effects of digoxin?	(ii) Autonomic- at lower doses **parasymp effects** predominate	Atropine –blockable effects: sensitization of baroreceptors, central vagal stim, facilitation of muscarinic transmission (mainly atria and AV node where rich cholinergic innerv'n)
		At toxic levels sympathetic outflow increased	Sensitizes myocardium and exaggerates all

	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 convulsions Gynaecomastia **1 GIT and 1 CNS example** (*prompt allowed*) Hyperkalaemia	toxic effects 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

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)

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

2. Thiazide Diuretics	1. How do thiazides exert their diuretic action	Inhibition of NaCl reabsorption in the distal convoluted tubule	
	2. What are the adverse effects of thiazides? (3/6 FOR PASS)	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)	

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)	a, b, c	
	What are their different effects on the action potential	1a: prolong, 1b: nil, 1c: minimal	

Beta blockers (carvedilol)	Describe the pharmacodynamics of 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).**	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.
	How does carvedilol differ from propranolol?	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)**	

Lignocaine	What are the pharmacodynamic effects of lignocaine on the heart? What features distinguish lignocaine from other Class 1 Antiarrythmics? What are the clinical uses of lignocaine?	• **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)** • **Does not prolong the duration of the AP.** • Dissociates from the channel with rapid kinetics • Has no effect on normal cells. **(1 of 3)** • **Type 1B Antiarrhythmic** • **Local Anaesthetic** • Post herpetic neuralgia **(2 of 3)**	Type 1B antiarrhythmic. Affects cells with the longest APs, such as purkinje and ventricular cells as opposed to the atrial cells.

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	

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	

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	

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	

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	

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.**	

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

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