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SYMPATHOMIMETICS

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DRUG	EFFECT SITE	MECHANISM	PHYSIOLOGICAL RESULTS	KINETICS
ADRENALINE	**α + β ACTIVATION**	α2 coupled to Gi receptors that inhibit adenyl cyclase, leading to increase in cAMP	Low Dose = β1 = ↑CO, ↑Myocardial O2 Consumption ↑Coronary Artery Dilation, ↓Arrhythmia Threshold High Dose = α1 = ↑SVR RESP = ↑MV, ↑Bronchodilation, ↑PVR METABOLIC = ↑BMR, ↑Glyconeogenesis, ↑Lipolysis, ↑Gluconeogenesis, ↑Glucagon, ↑Plasma Lactate β2 causes K+ shift into cells, after an initial temporary rise as K+ is released from the liver CNS = ↑MAC RENAL = ↓Renal Blood Flow (slight), ↑Bladder Tone	Metabolised by MAO/COMT within liver, kidney and blood. Short half-life of 2 minutes
NORADRENALINE	**α1+ β ACTIVATION**	Used to ↑SVR Caution with MAOI's	Peripheral Vasoconstriction, ↑systolic, ↑diastolic, reflex bradycardia, ↓CO can occur, ↑Myocardial O2 Consumption, ↑Coronary Blood Flow (via vasodilation), ↑Venous Return, ↑PulmVR. In excess it causes hypertension, bradycardia, headache and excessive vasoconstriction. Endogenously Released Noradrenaline causes = Tachycardia and ↑CO ↓Splanchnic Renal and Hepatic Flow ↓Blood Flow to Uterus, can cause foetal ↓HR	"Uptake 1"= Re-uptake into nerves to be metabolised by MAO or recycling. 2 minute half life 25% uptake when passes lungs
DOPAMINE	**α + β + $D_{1\&2}$ ACTIVATION**	Historically used to promote urine output and haemodynamics by α + β + D activity. Uses Gs & Gi coupled adenylate cyclase leading to ↑↓cAMP Also stimulates the release of norad.	Varies by rate of infusion. Low = ↑CO, ↑Contractility, ↑Myocardial O2 Consumption ↑Coronary Flow. Higher = α effects = ↑SVR and ↑Venous Return. Less arrhythmogenic than adrenaline. Resp = ↓PulmVR, Reduce carotid body response to hypoxia. Splanchnic = Dilates mesenteric vessels via D1. CNS = Inhibits secretion of prolactin. ↑N&V. ↑Gastric transit time.	Metabolised by MAO/COMT in liver, kidneys and plasma. Inactive metabolites. 25% of administered dose converted to noradrenaline. Half life = 3mins. Acts in 5m.
PHENYLEPHRINE	**α1 AGONIST**	Direct acting sympathomimetic amine with potent α1 agonism. It has no β effects.	Rapid ↑SVR and ↑BP. Reflex bradycardia is common. Causes a ↓CO. No CNS effects. Renal blood flow falls in a manner similar to noradrenaline. Favourable cord-gas profile in obstetrics.	Metabolised in liver by MAO. IV lasts 5-10 mins, SC could last 1h.
ISOPRENALINE	**β AGONIST**	Highly potent synthetic catecholamine with β1 + 2 Action. NO ALPHA effects. No longer used to treat reversible airway diseases = increased mortality. **It is used IV to treat severe bradycardia associated with AV block or β-blockers.**	↑HR, ↑Myocardial Contractility, ↑CO, ↑Automaticity (from β1 effects). β2 effects may drop the SVR so that increase in CO may not be enough to maintain BP. Myocardial Oxygen Consumption increases significantly when tachycardia reduces diastolic coronary filling time - but coronary vasodilation occurs to offset this a bit. It is a potent bronchodilator. Inhibits histamine release in the lungs, improving mucous flow. Anatomical deadspace and VQ mismatch increase leading to hypoxaemia. CNS stimulant. Splanchnic - ↑mesenteric and renal BF β-effects lead to raised BM's and free fatty acid	Rapidy metabolised by COMT Extensive FPM if oral Significant fraction excreted unchanged in urine along with conjugated metabolites.
DOBUTAMINE	**β1 AGONIST (+ some β2)**	Direct acting synthetic catecholamine derivative of isoprenaline. Mostly β1 effects, but some β2 retained. Used to augment low CO states assoc. with MI, cardiac surgery and cariogenic shock. Can be used in cardiac stress testing.	↑HR, ↑Myocardial Contractility, ↑CO. BP usually increased despite small β2 related ↓ in SVR. Can precipitate arrhythmias including an ↑ventricular rate in pt's with AF, flutter due to ↑AV conduction. AVOIDED in aortic stenosis or cardiac outflow obstruction. It has no effect on the splanchnic system, though urinary output can ↑ due to better CO!	COMT metabolism to inactive metabolites that are conjugated and exerted in urine. HL 2 mins.
DOPEXAMINE	**β2 + D1 AGONIST**	Synthetic Analogue of Dopamine May inhibit reuptake of noradrenaline Minimal D2 and β1 effect - no α effect.	↑inotropy due to cardiac β2 - reduced afterload contributes due to peripheral β2 which may ↓BP. Small increase in coronary blood flow, with no change in myocardial oxygen extraction. Only rarely precipitates arrhythmias. ↑Blood flow to gut and kidneys increase. ↑Urine Output. ↑N&V. ↑Bronchodilation. Headache	Cleared rapidly and has a half-life of 7mins
SALBUTAMOL SALMETEROL	**β2 AGONIST**	Synthetic sympathomimetic amines. Long non-polar side chain for salmeterol increases its duration. Used in reversible airway disease and preterm labour. Tocolytic.	Bronchodilator. Reverses HPV = ↑shunt = hypoxaemia. Adequate O2 is administered with salbutamol. β1 effects can stimulate a tachycardia. Lower doses associated with β2 vasodilation = ↓BP. Can precipitate arrhythmias especially in presence of hypokalaemia. Na/K/ATP-ase is stimulated and K+ goes intracellularly = hypokalaemia. BM's rise especially in diabetics. Relaxation of the gravid uterus - a small amount crosses the placenta. Direct skeletal muscle effect causes tremor.	If oral- would have high FPM Rapid onset. 10% Protein Bound HL of 4-6h Hepatic metabolism. Inactive metabolites.
RITODRINE	**β2 AGONIST**	Premature Labour. Tocolytic.	Tachycardia due to β1 effects. Crosses placenta and can cause ↑foetal HR. Associated with foetal maternal pulmonary oedema. Causes hypokalaemia, ↑BM, ↑N&V, Restlessness & Seizures	-
TERBUTALINE	**β2 AGONIST (+ some β1)**	Premature Labour. Tocolytic. Asthma.	Similar side effect profile to salbutamol.	-
EPHEDRINE	**MIXED α + β AGONIST**	Direct and indirect sympathomimetic actions. It also inhibits actions of MAO on noradrenaline.	It causes the release of noradrenaline from the sympathetic nerves. ↑CO, ↑HR, ↑BP, ↑Coronary Blood Flow, ↑Myocardial O2 consumption, ↑Arrhythmias. ↑Bronchodilation, ↑Respiratory Stimulation ↓Renal Blood Flow and GFR falls Use in caution with patients on MAOI's.	Well absorbed, PO, IM and SC. HL 4hours. 65% excreted unchanged in urine, the rest hepatic metabolism. *(NOT metabolised by COMT/MAO)*
METARAMINOL	**α1 AGONIST (+ some β)**	Synthetic amine with direct and indirect sympathomimetic actions.	↑SVR = ↑BP. Despite some β activity, the CO often drops in the face of ↑SVR. There is ↑Coronary Artery Flow via indirect mechanism. ↑Pulmonary Vascular Resistance = raised pulmonary artery pressures.	-
AMINOPHYLLINE	**PDE Inhibitor (All 1-5)**	Non-selective inhibitor of ALL 5 phosphodiesterase isoenzymes that hydrolyse cAMP and possibly cGMP - increasing their intracellular levels.	Bronchodilation, ↑Contractility of Diaphragm, ↑Sensitivity to CO2. Works well in combo with βagonists. Mild ↑inotropic/chronotropic effects. ↑Coronary/Peripheral Vasodilation. CNS - stimulant (caffeine derivative), ↓seizure threshold. It has weak diuretic effects. Drugs that inhibit p450 delay elimination of aminophylline-(cimetidine, erythromycin, ciprofloxacin + OCP).	High oral bioavailability. 50% protein bound. P450 to inactive metabolites. 10% excreted unchanged in urine. First change to Zero order kinetics
ENOXAMINE	**PDE 3 Inhibitor (Selective)**	Imidazolone derivative. Yellow liquid with pH 12 used to treat low cardiac output states associated with cardiac surgery. Prevents degradation of cAMP + cGMP	By increasing cAMP in the myocardium, it increases the slow calcium inward current during action potential and an increase in calcium in the vicinity of contractile proteins = positive inotrope. It is an INODILATOR due to its positive inotropic and vasodilator effect. In heart failure, CO can increase up to 30% and end diastolic filling pressures decrease by 35%. Myocardial oxygen extraction ratio unchanged. Shortens atrial, AV node and ventricular refractoriness. Agranulocytosis has been reported. Beware in IHD as it may reduce coronary perfusion pressure.	Extensive FPM, but good PO absorption. 70% protein bound. Liver metabolism, active metabolite with 10% of activity. Infusion HL = 4.5h. Wide therapeutic ratio, low toxicity risk. Reduce dose in renal failure.
MILRINONE	**PDE 3 Inhibitor (Selective)**	Bipyridine Derivative	Similar effect to enoxamine, but associated with increased mortality when given orally to those with severe heart disease.	70% protein bound. Elimination HL of 1- 2.5h. 80% excreted in the urine unchanged. Reduce dose in renal failure.
GLUCAGON	**Polypeptide**	Pancreatic α-cell.	The activation of glucagon receptors via G-proteins stimulated adenyl cyclase and increases intracellular cAMP. **Used in beta-blocker overdose.**	-
CALCIUM	**Cation**	Improves intracellular calcium availability to contractile proteins.	Short lived effects on bolus. Use is restricted to circulatory collapse secondary to hyperkalaemia and calcium channel antagonist overdose.	-
T3	**Hormone**	Not used to increase BP.	T4 and T3 both have positive inotropic and chronotropic effects via intracellular mechanisms.	-

ALPHA 1 = VASOCONSTRICTION, GUT SMOOTH MUSCLE RELAXATION, INTERNAL BLADDER & GUT SPHINCTER CLOSURE, SALIVARY SECRETIONS, GLYCOGENOLYSIS, UTERINE CONTRACTION

ALPHA 2 = CENTRAL VASODILATION, PERIPHERAL VASOCONSTRICTION, GUT SMOOTH MUSCLE RELAXATION, CNS SEDATION, INSULIN INHIBITION

BETA 1 = POSITIVE INOTROPY AND CHRONOTROPY, INCREASE MYOCARDIAL OXYGEN DEMANDS, RENIN RELEASE AND RAAS STIMULATION

BETA 2 = BRONCHODILATION, VASODILATION IN MUSCLE, GUT AND KIDNEY, PUPILS DILATE, GLYCOGENOLYSIS (MUSCLE & LIVER), GLUCAGON RELEASE

DOPAMINE = will work mainly by action on alpha 1, beta 1 and beta 2. Dopamine receptors when stimulated will cause increase & decrease of adenyl cyclase via cAMP.