Q17 Compare and contrast the mechanism of action, pharmacokinetics, and side effects of adrenaline, steroids, and antihistamines when used for the treatment of anaphylaxis (March 2013)

Anaphylaxis – a Type 1 hypersensitivity response characterized by IgE mediated mast cell degranulation in response to an allergen. Potential to be life threatening as may cause airway oedema, bronchospasm and severe hypotension.

	Adrenaline	**Steroids**	**Antihistamines**
Description	An endogenous catecholamine released from the mammalian post ganglionic sympathetic nerve terminals.	Hydrocortisone and prednisone most common in treating anaphylaxis. Pharmacokinetics of hydrocortisone will be discussed here	Range of sedating and nonsedating agents. Fexofenadine will be discussed here.
Mechanism of action	Adrenaline typically exerts is effects through beta agonism at low doses (increasing inotropy and chronotropy) and causing smooth muscle relaxation (including bronchorelaxation). At higher doses it displays alpha effects and causes vasoconstriction. It also stabilises mast cells to prevent degranulation.	Work by binding to the cell nucleus and switching off the transcription of various genes which encode for inflammatory mediators such as cytokines, chemokines, adhesion molecules and arachadonic acid. They also activate anti-inflammatory genes such as MAP (mitogen activated protein) and increase the expression of beta 2 receptors.	Binds to H1 receptors to block the effects of the histamine released from mast cells – namely, inhibition of vasodilatation, increased vascular permeability, and contraction of nonvascular smooth muscle
Side effects	May cause HTN, tachycardia and arrhythmias, metabolic SE (glycogenolysis, lipolysis, gluconeogenesis) and can increase BMR. Can worsen PHTN (causes pulm vasoconstriction) and glaucoma.	Single dose – minimal side effects. Repeated dosing – multiple effects on virtually every organ system. CNS – psychosis, mood disorders. CVS – HTN. GIT – gastric ulcers, pancreatitis. Haem – leukocytosis. ID – increased risk of infection. MSK – osteoporosis, weakening of proximal muscles, abdominal striae, easy bruising, thin skin	May cause headache or drowsiness
PHARMACOKINETICS			
Absorption	Route - IV, IM, S/C, NEB, ETT Dose - 1mg ALS, 0.1mg anaphylaxis, titrated dose for haemodynamic instability (commence at 0.01mcg/kg/min, increase for alpha effects) Bioavailability - 100% Onset to action - seconds, duration 2 mins	Route - PO, IV, inh, neb Dose – usually 200mg IV for anaphylaxis. May require repeat dosing.	Route - PO Dose - 60-240mg daily in divided doses Bioavailability - 33%
Distribution	Does not cross the BBB 50% protein bound	90% protein bound at low concentrations, only 60-70% bound at higher. Vd 0.3-0.5L/kg	Protein binding 70%
Metabolism	Taken up by the sympathetic nerve terminals and metabolised via COMT and MAO, circulating Adr metabolised via COMT	Hepatic to tetrahydrocortisone	Negligible metabolism in humans.
Elimination	Via urine as inactive metabolites (half life 2 min)	Elimination half life 1.2-1.8hrs	Terminal half life 14-15 hours