Q5 List the antiplatelet agents and outline their mechanisms of action, adverse effects, mode of elimination and duration of action (Sept 2010)

	Aspirin	Dipyridamole	Clopidogrel	Tirofiban	Abciximab
Mechanism of action	Irreversible inhibition of cyclooxygenase-1 and 2 (COX-1 and 2) enzymes via acetylation of serine residues, resulting in decreased formation of prostaglandin precursors. Irreversibly inhibits formation of thromboxane A2 in platelets, thus inhibiting platelet aggregation for the life of that platelet cohort. Also inhibits PGI2 production in vascular endothelial cells, however they are nucleated and can regenerate COX, whilst platelets cannot	Phosphodiesterase inhibition in the platelet increases cAMP and reduces intracellular calcium. It reduces the platelet's ability to adhere to damaged vascular endothelium by inhibiting adenosine uptake, potentiates the effects of prostacyclin and interferes with adhesion more than aggregation. Also causes potent coronary vasodilatation	Clopidogrel's active metabolite is a thiol derivative formed by oxidation and hydrolysis. It irreversibly prevents ADP from binding to its receptor (P2Y12) at the platelet surface, thus inhibiting the transformation of GpIIb/IIIa to its active form.	Antagonises the GpIIb/IIIa receptor, preventing the binding of fibrinogen and platelet crosslinking and aggregation.	Similar mechanism as tirofiban but monoclonal antibody
Adverse effects	Haemorrhage (especially GI bleed), caution in asthmatics (risk of bronchospasm), renal toxicity, caution in use with other anticoagulants eg warfarin, rash, dermatitis	Haemorrhage, may cuase hypotension, thrombocytopenia and myalgias. Dipyridamole can be incorporated into gallstones.	Haemorrhage, neutropenia secondary to bone marrow toxicity. Potential for significant drug interactions as requires activation by CYP450	Haemorrhage Difficulty reversing agent Dose adjustment in renal impairment	Hemorrhage, thrombopenia, human antichimeric antibody development, allergic reaction
Mode of elimination	Converted to salicylic acid mainly in GI mucosa and liver. Metabolism of salicylate occurs primarily by hepatic conjugation; metabolic pathways are saturable. Excreted in urine mainly as salicylate	Undergoes hepatic conjugation to glucuronide. Mainly excreted as glucuronides in bile, 5% excreted in urine	Two main metabolic pathways – one mediated by esterases to inactive metabolites, and one mediated by CYP450 enzymes ELIMINATION - Excreted urine and faeces.	Limited metabolism in humans. Excreted in urine and faeces, mostly unchanged	
Duration of action	4-6 hours. Effects on platelet aggregation will last until the cohort of platelets is replaced in 7-10 days	10-12 hours	Half life of parent drug 6hrs, active metabolite 30min. Effect on platelet aggregation will last until the cohort of platelets is replaced in 7-10 days	Half life ranges from 1.9-2.2 hours	Platelet function typically returns to normal 24-48 hours after infusion ceases