Q15 Describe the pharmacology of naloxone (March 2013)

Naloxone is an opioid antagonist used in the management of opioid overdose and respiratory depression associated with opioid use, and in managing the pruritus and nausea associated with opioid use.

PHARMACEUTICAL - solution for injection (400mcg/ml). Also available as a minijet (2 or 5ml).

PHARMACODYNAMICS
MECHANISM OF ACTION → naloxone is a competitive antagonist at mu, kappa, delta, and sigma opioid receptors (highest affinity for mu receptors).

SIDE EFFECTS → short duration of action means duration of effect may be shorter than the opioid it needs to counteract - repeated doses may be needed. May cause ventricular dysrhythmias in patients with irritable myocardia. May also cause tachycardia, hypo- or hypertension, and severe withdrawal symptoms.

PHARMACOKINETICS
ADMINISTRATION
Route - IV/IM/SC
Dose - 0.4-2mg for OD, start at 0.1mg for resp depression. 1mg of naloxone IV blocks the effects of 25mg of diacetylmorphine (heroin)
Onset of action – within 1-2 min (IV) or 2-5 min (SC/IM)
Bioavailability - extensive first pass metabolism so bioavailability only 2% when given PO

DISTRIBUTION
Vd - 2L/kg
Protein binding - 50%

METABOLISM - conjugation to glucuronide in liver

ELIMINATION - urine. Plasma half life 30-80 minutes (mean ~60 minutes)