Q13 Outline the effects of critical illness on drug pharmacokinetics. Give examples (March 2013)

ABSORPTION

- Routes of administration other than IV will be impaired in the presence of a low cardiac output (and thus low regional blood supply) state
    - Eg, poor PO absorption if impaired GIT motility and blood supply; poor absorption of subcutaneous medications (eg, insulin, enoxaparin) due to poor circulation in peripheral tissues
- Low cardiac output state will influence time to onset (and offset) requiring adjustment of dose

DSITRIBUTION

- Protein binding
    - Low albumin and plasma protein stores in the critically ill alter drug binding (low protein levels → less binding → more free drug available). Important for highly protein bound drugs such as propofol
    - Protein binding creates a larger central compartment in multicompartment models → decreased protein in critically ill will alter this

- Volume of distribution
    - Low cardiac output state will affect distribution (eg, hypovolaemia)
    - Derangement of pH leads to altered ionisation depending on pKa
    - Variation in lean body mass:total body mass for different drugs (loss of muscle mass in critically ill)
    - Renal and hepatic disease can increase the Vd

METABOLISM

- Hepatic impairment due to primary disease or low cardiac output state may alter metabolism, altering drug half life and plasma concentrations
- Interactions with other medications used in critically ill (may potentiate the effect of an agent, add to its effect, act synergistically, produce idiosyncratic reactions or antagonize):
    - Inducing CYP enzymes - phenytoin, carbamazepine
    - Inhibiting CYP enzymes - amiodarone, metronidazole

EXCRETION

- Renal impairment may increase plasma concentration and prolong the half life of renally excreted agents or their active metabolites (eg, barbituric acid, a metabolite of thiopentone, gentamicin)