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

**DISTRIBUTION**

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