JULY 2008
QUESTION 23

Describe the factors which contribute to inter-individual variability in drug response seen with an induction dose of an intravenous anaesthetic drug

- Amount of drug reaching the receptor
  - Pharmacokinetic factors
    - Absorption
      - IV dose so should be 100%
      - dose variability between patients
    - Distribution
      - Volume of distrib — Body mass and ratio of fat:muscle differences; pregnancy, cardiac output states
      - Protien binding — low albumin states, other protien bound drugs; propofol has 98% protien binding and will be influenced
      - Blood pH — affects degree unionised which can cross lipid membranes; eg alkalotic state with thiopentone pKa 7.6
    - Metabolism
      - Hepatic factors — liver disease may reduce metabolism; CYP enzymes (inhibited or upregulated) eg Ketamine
    - Excretion
      - Renal impairment — offset of effect more dependent of redistribution, but can be prolonged if renally excreted
- Presence of endogenous or exogenous ligands
  - Endogenous — increased catecholamines may necessitate a higher induction dose
  - Exogenous — medications which potentiate sedation opioids, benzodiazepines, volatiles; medications which reduce sedation - amphetamines
- Variation in the number of receptors
  - Extremes of age
  - Previous exposure to the drug or similar - tolerance, tachyphylaxis
- Variability in the response distal to the receptor
  - Phramocogentic factors
    - idiosyncracy
    - anaphylaxis
  - Pathological and physiological factors
    - sepsis
    - CNS function