2009b(4): Describe the effect of obesity on pharmacokinetics and the potential clinical implications, providing relevant examples

General: Obesity
- body mass index >30kg/m2
- often associated with comorbidities including
  - IHD
  - Diabetes
  - GORD
- Drug doses are usually calculated on total body weight which in non-overweight individuals is close to lean body mass and ideal body weight
- In obese individuals TBW>> LBM>IBW
  - Doses must be adjusted
  - Target controlled infusion devices may produce variable results

Absorption
- ↓ FRC → increased uptake of volatile anaesthetic agents
- transdermal, IM and subcutaneous absorption variable

Distribution
Volume of distribution
- increased for highly lipophilic drugs eg. Barbiturates and benzodiazepines
  - ↑ dose initially
  - exception- remifentanil highly lipophilic but no ↑Vd- dose on IBW
- no sig change in Vd for less lipophilic drugs-dose on LBM

Increased Total body water
- total body water increases 2ndry to ↑LBM
- NDMB (hydrophilic) → modest ↑ Vd
- Add 20% dose to hydrophilic medication

Examples
- Propofol – does not accumulate in morbidly obese pts. Dose on LBW
- Sufentanil – lipophilic: Vd ↑ and prolonged elimination half life
- Volatiles – low blood:gas solubility → rapid onset and offset (eg. Sevo, des)
  - Desflurane has the lowest solubility in fat tissue→ rapid and consistent recovery

Metabolism
- Halothane- ↑ risk of reductive hepatic metabolism in the obese
- Increased risk of halothane hepatitis
- Comorbidities
  - Renal impairment
  - Hepatic dysfunction
  - Impair metabolism and excretion of drugs

Excretion
- Paracetamol → ↑ clearance in obese
- Residual neuromuscular blockade can be lethal in obese patients therefore antagonism may be indicated

By Alison Main