Q13 Describe the effects of obesity on drug pharmacology (70% of marks). Give examples of drugs that illustrate those effects (30% of marks) (Sept 2012)

Obesity: BMI >30
Affects all aspects of pharmacology.
Dosage often requires calculation of ideal body weight (males: height – 100, females: height – 110) or lean body weight (males: 50 + 0.9kg for every cm over 150cm, females: 45 + 0.9kg for every cm over 150cm)

EFFECTS ON ABSORPTION

- Increased gastric emptying in the obese (increasing absorption)
- Decreased subcut absorption due to poor subcutaneous blood supply
- IM administration may fail if needles are too short
- Difficult IV access in the obese

EFFECTS ON DISTRIBUTION

- Increase of body fat relative to lean body mass → increase in volume of distribution for lipid soluble drugs (eg, midazolam). Hence lipid soluble drugs (eg, midazolam) should be dosed based on actual body weight, whereas dosing for non lipid soluble drugs (eg, rocuronium) should be based on ideal body weight
- Increase in blood volume and cardiac output →may require an increased loading dose for therapuetic effect (eg, thiopentone)
- Plasma protein binding may be decreased due to increased binding of lipid to proteins →increased free fraction of highly protein bound drugs (eg, warfarin, phenytoin)

EFFECTS ON METABOLISM

- Plasma and tissue esterase levels are increased → increased clearance of drugs by these enzymes eg, remifentanil.
- Increase in pseudocholinesterase levels in obesity → base suxamethonium doses on total body weight
- Hepatic enzyme function may be impaired due to disease associated with obesity (non alcoholic fatty liver disease) → prolonged half life of drugs normally metabolised hepatically eg, haloperidol

EFFECTS ON ELIMINATION

- Half life of lipid soluble drugs increased due to accumulation
- Renal clearance often increased in obesity due to increased cardiac output and renal blood flow → may require increase in dosage of drugs cleared renally (eg, gentamicin)
- Renal clearance may be impaired if diabetes coexists with obesity → monitoring of eGFR required and dose adjustments as indicated