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QUESTION 04

Describe the factors which are important when interpreting plasma drug concentrations

Clinical relevance

Drug plasma concentrations are relevant when certain criteria are met;
- demonstrated relationship between drug concentration and therapeutic or toxic effect (digoxin)
- narrow therapeutic window (carbemazapine)
- variability in plasma level such that response cannot be predicted from dose alone (warfarin)
- drug produces effects, intended or unwanted, that are difficult to monitor (heparin)

Pharmacokinetic factors

Absorption enables an appreciation of bioavailability and variation in different routes
heparin is an example, there is reduced absorption SC due to endothelial protein binding

Distribution highly lipid soluble drugs generally have a high volume of distribution
plasma levels will therefore appear markedly decreased when compared to dose
the pKa may be relevant as the amount ionised may be more important in determining effect rather than the total plasma level (ability to cross membranes)

Metabolism drugs may have saturatable metabolic pathways such that even at high doses the drug will be cleared at a fixed rate (phenytoin)
co-administration of drugs may upregulate metabolic catalysts (eg CYP450s) increasing metabolism, or compete for substrate/catalyst decreasing metabolism

Excretion drugs with that are excreted renally may have much higher plasma concentration if there is impairment or oliguria.

Pharmacodynamic factors

Drug action receptor sensitivity
action at the sensor (eg. competitive antagonist vrs non competitive antagonist)

Appreciation of reference values for plasma concentration levels
- To check therapuetic effect
  - antimicrobials -minimal inhibitory concentration levels
- To monitor side effects
  - local anaesthetic agents -CNS:CVS ratios

Patient factors

Age (decreased sedative concentrations required in elderly)

Lean body mass vrs toal body mass (lipid soluble versus small Vd drugs)

Renal and hepatic function (may prolong and elevate plasma concentrations)

Pharmacogenetic factors - abnormalities in CYP450 (eg variable codiene metabolism)
abnormal plasma esterases - suxmethonium metabolism