First 2011
VIVA 3

Describe the factors that affect ORAL drug absorption

This viva explored basic pharmacology, dose response curves and poisoning as it related to paracetamol, aspirin and organophosphates. Areas of weakness included the depth of knowledge regarding basic pharmacology as it related to concepts such as clearance and bioavailability and first pass metabolism.

"How might organophosphate poisoning occur, what is the mechanism and what is the symptoms?"

Present in insecticides, herbicides and chemical warfare agents
Absorbed following oral ingestion or via skin (lipid soluble)
Mechanism
- inhibits acteylcholinesterases
- resulting in excessive acteylcholine and symptoms of cholinergic excess

Symptoms
- SLUDGEM salivation, lacrimation, urination, defecation, gastro motility, emesis, miosis
- bradycardia, hypotension, respiratory failure (secretions and delayed neurotoxicity)

"Discuss the changes that occur with aspirin overdosage"

requires a large dose of 10 - 30g
mechanisms are complex, aspirin demonstrates zero order metabolism in increased doses
It will increase respiratory drive and cause a respiratory alkalosis,
whilst also causing a wide anion gap metabolic acidosis due to lactate and ketone build up in addition to the salicylic acid.
it is a direct neurotoxic.
early symptoms of acute aspirin toxicity include tinnitus, fever, vertigo, nausea, vomiting, and diarrhea;
later signs include altered mental status, noncardiac pulmonary edema, coma, and death.
treatment is direct at decontamination via charcoal or hemodilasis and HCO3 treatment to raise pH

"What is a toxic dose of paracetamol, what is the mechanism and what are the symptoms"

Results from ingestion of doses inexcess of 15mg/kg/QID
Mechanism
- metabolised by three pathways, gluconoridation (65%), sulfation (35%), and NAPQI (1%)
- NAPQI is toxic and usually converted quickly by glutathione
- inexcess, glutathione is overwhelmed leading to excess NAPQI - hepatic necrosis

Symptoms
- abdominal pain, deranged hepatic synthetic function
- ALT is most sensitive marker

"Please discuss bioavailability, how it is measured, and what affects it"

Bioavailability is defined as the fraction of unchanged drug reaching the systemic circulation following administration by any route. The area under the blood concentration-time curve (AUC) is a common measure of the extent of bioavailability for a drug given by a particular route. For an intravenous dose of the drug, bioavailability is assumed to be equal to unity. For a drug administered orally, bioavailability may be less than 100% for two main reasons—incomplete extent of absorption and first-pass elimination