

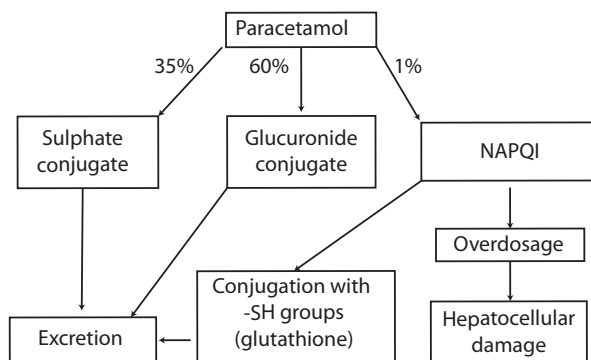
List the functions of the liver (60% marks). Discuss the metabolism of paracetamol in toxicity and the pharmacologic management of this overdose (40% marks).

Liver functions

- carbohydrate metabolism
- protein metabolism
- lipid metabolism
- immunological and filtration functions
- storage - blood, iron, copper, vitamins and glycogen
- bile production and bilirubin metabolism
- EPO, renin, coagulation factor production
- drug and hormone metabolism - phase 1 and 2 reactions
- endocrine functions - vitamin D activation, thyroxine conversion

Pathogenesis

At normal therapeutic dosages (15mg/kg QID) primarily hepatic metabolism to sulfate and glucuronide conjugates, a small amount is metabolized by CYP2E1 to a highly reactive intermediate, (NAPQI), it is conjugated rapidly with glutathione and inactivated to nontoxic conjugates at toxic doses glutathione conjugation becomes insufficient causing an increase in NAPQI concentrations, leading to hepatocellular damage



Management

ABCs

Assess

- preliminary investigations (history, examination, bloods, ECG)
- plot paracetamol level on a nomogram to assess intervention strategy

Prevent

- further absorption with activated charcoal
- paracetamol is absorbed in the small intestine (80% bioavailability)

Supportive management

- replenish glutathione
- N-acetylcysteine infusions which most toxicologists agree replaces glutathione

Monitor

- ALT is generally the most sensitive marker of liver damage.
- Renal damage may also be prominent.