FEB 2011
QUESTION 01

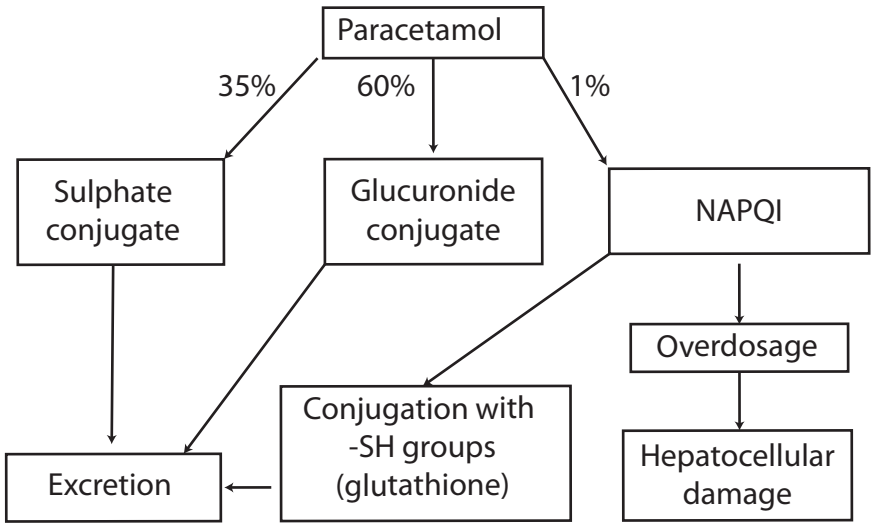
Describe the pharmacological effects of paracetamol. Outline its toxicity and management.

Paracetamol

little effect on extracerebral COX-1 or COX-2, although it inhibits central COX-3. \
it reduces prostaglandin E2 in the hypothalamus during pyrexia, reducing fever
It has similar effects to aspirin on non-specific pain
synergistic with opioid medications (20-30% reduction)

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 heaptocellular 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-acetylcystiene infusions which most toxicologists agree replaces glutathione
Monitor
ALT is generally to most sensitive marker of liver damage.