JULY 2008
QUESTION 07

Describe five (5) potential mechanisms by which poisoning can be fatal and provide one specific example for each mechanism.

- Respiratory failure
  - Organophosphate poisoning
    - 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)

- Cellular hypoxia
  - Cyanide posioning
    - Present in industrial settings, older paints, sodium nitroprusside
    - Absorbed from smoke inhalation, intentional ingestions, iatrogenic
    - Mechanism
      - inhibits final step in mitochondrial oxidative phosphrylation'
      - despite adequate oxygenation it is unable to be utilised
    - Symptoms
      - dyspnoea despite normal saturations
      - may also act to reduce GABA and therefore seizure threshold

- Hepatic failure
  - Paracetamol poisoning
    - 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

- Acidemia / Renal Failure
  - Ethylene glycol / methanol poisoning
  - Mechanism
    - development of toxic metabolites, methanol - formate, ethylene glycol - glycolate
    - formate leads to retinal injury and basal ganglia haemorrhage, glycolate to tubular necrosis
    - both can lead to a profound increased anion gap acidosis
  - Symptoms
    - intoxication, n+v, then increased RR, tachycardia, high BP (acidosis), then anuria, death

- CNS depression/seizures
  - TCA overdose
  - Mechanism
    - inhibits norad, serotonin reuptake, blocks sodium channels, muscarinic receptors, GABA, H1
  - Symptoms
    - antimuscarinic - atropine like effects, vasodilation, decreased secretions, tachycardia, myosis
    - cardiac abnormalities (sodium channels and vagalytic),
    - CNS seizures (GABA), coma, respiratory depression