Poisons and Poisoning

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Objectives
• Appreciate the difference between acute overdose and chronic exposure
• Learn some typical signs of drug poisoning
• Understand the pharmacological basis for enhancing elimination of drugs
• Understand the pharmacological basis for the use of specific antidotes
Poisoning

- Types
  - Acute Overdose
  - Chronic Exposure

Diagnosis

- History
  - Patients rarely lie
  - But may be unreliable
    - Sedation
    - Amnesic drug effects

- Pupils
  - Constricted
    - opiates (morphine)
    - clonidine
    - anti-cholinesterases (neostigmine)
  - Dilated
    - atropine
    - tricyclic antidepressants (amitriptyline)
    - amphetamine/MDMA (‘ecstasy’)/BZP (‘party pills’)

MDMA 3,4-Methylenedioxymethamphetamine
http://en.wikipedia.org/wiki/MDMA
BZP benzylpiperazine
http://en.wikipedia.org/wiki/Benzylpiperazine
Diagnosis

- Skin
  - Sweating
    - Increased amphetamine
    - Decreased atropine
  - Bullae
    - carbon monoxide
    - [barbiturates]

Diagnosis

- Odour
  - ethanol
  - garlic
    - arsenic
    - organophosphates (anti-cholinesterase)
  - almonds
    - cyanide

Diagnosis

- Clinical Chemistry
  - Blood
    - salicylate
    - paracetamol
    - ethanol
    - carbon monoxide
    - tricyclics
    - digoxin
    - theophylline
Diagnosis

- Clinical Chemistry
  - Urine
    - salicylate
    - opioids
    - tricyclics

Treatment

- General Supportive
  - A Airway
  - B Breathing
  - C Circulation

Decrease Absorption

- emesis
  - syrup of ipecac
- gastric lavage
  - must have reflexes
  - not for corrosives/hydrocarbons
- activated charcoal - IMPORTANT
  - 50g every 4 h
- Fuller’s Earth (or activated charcoal)
  - Paraquat (herbicide)

Note that treatment of paraquat poisoning seems to be rarely effective.

http://en.wikipedia.org/wiki/Activated_charcoal
http://en.wikipedia.org/wiki/Fuller%27s_earth
### Increase Elimination

- **Activated Charcoal**
  - "enteral dialysis"
- **Haemoperfusion**
  - charcoal, theophylline
  - ion exchange, salicylate
- **Haemodialysis**
  - methanol (wood alcohol)
  - ethylene glycol (anti-freeze)
- [Diuresis]

### Specific Antidote

- **N-acetylcysteine**
  - paracetamol
- **Naloxone**
  - morphine
- **Flumazenil**
  - benzodiazepines
- **Ethanol**
  - methanol

### Specific Antidote

- **Chelation**
  - Desferrioxamine (iron)
  - Succimer (lead)
  - D-Penicillamine (copper, mercury)
  - Hydroxycobalamin (cyanide)
- **Atropine/pralidoxime**
  - anti-cholinesterases
- **Antibody**
  - Fab fragments (digoxin)
  - idarucizumab (dabigatran)
  - andexanet (rivaroxaban/apixaban)

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Specific Antidote

- Paracetamol Hepatotoxicity
  - Minor metabolite is NAPQI (N-acetyl-p-benzoquinoneimine)
    - Formed by CYP2E1
    - Ethanol induces CYP2E1
  - NAPQI inactivated by glutathione
  - Liver damage caused by NAPQI
  - Glutathione reserves used up by large doses (> 15 grams of paracetamol)

- Acetylcysteine supplies SH to make more glutathione
- Recent UK guidelines for treatment shown to be cost-ineffective

“Paracetamol poisoning is the most common acute overdose seen in industrialized countries [1, 2]. It is estimated that between 82 000 and 90 000 patients present in the UK each year with paracetamol overdose [3–5]. Between 150 and 250 deaths occur annually, the vast majority in patients who have presented late, after a staggered overdose or after unintentional therapeutic excess [6–9]. Deaths or episodes of liver failure in patients [10] who present and are treated within 8 h of a single acute ingestion are extremely rare [1, 5, 11].”


N-Acetylcysteine Treatment Nomogram for Paracetamol Overdose in Adults

Children: 225 mg/L at 2 hours
Anderson et al. 1999 [Auckland]

Specific Antidote […] but no effect on NPD

Clinical Applications

- Approach to Poisonings
  » ABC and General Support
  » Specific antidotes are uncommon

- Use physiology and pharmacology to assist in diagnosis

- Consider factors affecting drug clearance if enhanced elimination procedures are used

NPD=NeuroPsychological Development
TREATMENT OF LEAD EXPOSED CHILDREN TRIAL. GROUP THE EFFECT OF CHELATION THERAPY WITH SUCCIMER ON NEUROPSYCHOLOGICAL DEVELOPMENT IN CHILDREN EXPOSED TO LEAD N Engl J Med 2001;344:1421-6