Poisons and Poisoning

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Poisons and Poisoning

farmakon
pharmakon

Medicine Poison Magic Spell

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

Diagnosis

- 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

Diagnosis

- ECG
  - Long PR – Calcium Channel
    - Verapamil
  - Wide QRS – Sodium Channel
    - Amitriptyline
  - Long QT – Potassium Channel
    - Amiodarone

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)

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
- Fomepizole
  » ethylene glycol, methanol

Note also fomepizole may be used to treat ethylene glycol and methanol poisoning ([https://en.wikipedia.org/wiki/Fomepizole](https://en.wikipedia.org/wiki/Fomepizole)).
Specific Antidote

- **Chelation**
  - desferrioxamine (iron)
  - edetate (lead)
  - penicillamine (copper, mercury)
  - hydroxocobalamin (cyanide)

- **Atropine/pralidoxime**
  - anti-cholinesterases

- **Phytomenadione (vitamin K1)**
  - warfarin

- **Antibody**
  - digoxin F(ab) and digoxin
  - idarucizumab and dabigatran
  - andexanet and rivaroxaban/apixaban

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**Anti Factor Xa Activity**

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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
  - UK guidelines (2014) for treatment shown to be cost-ineffective

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“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].”


A “two bag” 12 h administration of acetylcysteine appears to be safer.

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