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-Methylenedioxyamphetamine
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

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

- Chelation
  - Desferrioxamine (iron)
  - Succimer (lead)
  - D-Penicillamine (copper, mercury)
  - Hydroxycobalamin (cyanide)

- Atropine/pralidoxime
  - anti-cholinesterase

- 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
- 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


http://www.merck.com/mmpe/sec21/ch326/ch326c.html