Poisons and Poisoning

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Poisons and Poisoning

ϕαρμακον
pharmakon

Medicine    Poison    Magic Spell

Objectives

- Learn some typical signs of acute drug poisoning
- Understand the pharmacological basis for enhancing elimination of drugs
- Understand the pharmacological basis for the use of specific antidotes

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’)

Diagnosis

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

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

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

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Treatment

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

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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.
**Increase Elimination**

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

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 Antidotes**

- N-acetylcysteine
  - paracetamol
- Naloxone
  - morphine
- Flumazenil
  - benzodiazepines
- Ethanol
  - methanol
- Fomepizole
  - ethylene glycol, methanol


**Specific Antidotes**

- Chelation
  - desferrioxamine iron
  - edetate lead
  - penicillamine copper, mercury
  - hydroxocobalamin cyanide
- Atropine/pralidoxime
  - anti-cholinesterases
- Phytomenadione (vitamin K1)
  - Warfarin
- Protein Binding Agent
  - digoxin F(ab) digoxin
  - idarucizumab F(ab) dabigatran
  - andexanet apixaban, rivaroxaban

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].”


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
N-Acetylcysteine Treatment Nomogram 
for Paracetamol Overdose in Adults

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

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

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

Assessment Short Answer Question Examples

1. Give an example of a physical sign of drug poisoning and a medicine causing this.
2. Explain how activated charcoal may enhance the elimination of drugs.
3. What specific antidote may be used to treat cyanide poisoning?