Toxicology: Basic concepts and toxidromes
Acute intoxications

Definition

Acute exposition to an overdose of drugs or substances not intended for human use
Belgian Poison Control Centre

Number of calls in 2004
Types of acute poisoning

- Auto-intoxication
- Accidental
- Homicide, Münchhausen-syndrome
- Bioterrorism
- Alcohol and illicit drugs
Intoxications in the emergency department

Auto-intoxication = most frequent

- Parasuicidal: "cry for help" in the context of a psychological crisis
- Suicidal: intention to die

difficult to distinguish → always psychiatric evaluation!
Self-harm

The short-term physical and psychological management and secondary prevention of self-harm in primary and secondary care

Clinical Guideline 16
July 2004
Developed by the National Collaborating Centre for Mental Health

NHS
National Institute for Clinical Excellence

Developed by the National Collaborating Centre for Mental Health
Types of acute poisoning

• Auto-intoxication

• Accidental
  ▶ most frequently carbon monoxide
  ▶ therapeutic mistakes (children / elderly patients)
  ▶ errors

• Homicide, Münchhausen-syndrome

• Bioterrorism

• Alcohol and illicit drugs
Types of acute poisoning

- Auto-intoxication
- Accidental
- Homicide, Münchhausen-syndrome
- Bioterrorism
- Alcohol and illicit drugs
Acute ethanol intoxication (1)

• Very frequent!

• Symptoms vary according to degree of intoxication with possible coma

Caveat: interpretation of breath odour
Acute ethanol intoxication (2)

- Be aware of "hidden" clinical and metabolic disturbances:
  - hypoglycemia
  - head and neck trauma
  - Wernicke encephalopathy (thiamine deficiency)
  - acid-base disturbances
  - cardiomyopathy, gastro-intestinal bleeding
  - cardiac rhythm disturbances
  - infections (pneumonia, ...)
  - intake of ethylene glycol, methanol
Interventions for preventing injuries in problem drinkers

The Cochrane Database of Systematic Reviews, 2005

Action with problem drinkers can cut risk of injury. Several different approaches were evaluated, the most common being brief counseling by health workers. The evidence from these studies suggests that action with problem drinkers is effective in reducing both injuries and events that lead to injury (such as falls, motor vehicle crashes, and suicide attempts). However, more research is needed to calculate the level of effectiveness accurately and to determine which type of program works best.
Preventing acute intoxications

• "Child resistant" containers
• Warning of parents for the danger of medications for children
• Legibility of prescriptions
• Controlling medications and substances at home
• Avoiding prescription of large quantities
• ...
General approach in acute intoxication (1)

- Phases of intoxication: preclinical, toxic and resolution
- Initial evaluation and treatment:
  - brief screening examination to identify immediate measures required to stabilize and prevent deterioration (vital signs, mental status, cardiac monitoring, ...)
  - supportive care, antidotes (glucose, thiamine, naloxone, ...)

General approach in acute intoxication (2)

• Diagnosis of intoxication:
  ▶ history
  ▶ physical examination
  ▶ electrocardiography
  ▶ X-ray
  ▶ toxicological screening / laboratory

• Evaluation of severity and predicting expected toxicity

• Treatment
Acute intoxication and physical examination (1)

- Mental status, vital signs and pupillary examination allow distinction between:
  - physiological excitation: e.g. by anticholinergic, sympathomimetic or central hallucinogenic agents, drug withdrawal state
  - physiological depression: e.g. by cholinergics, sympathicolytics, opiates, sedative-hypnotics or alcohols
Acute intoxication and physical examination (2)

- mixed physiological effects: e.g. polydrug overdoses, certain metabolic poisons (hypoglycemic agents, salicylates, cyanide, ...), membrane-active agents (e.g. antiarrhythmics, local anesthetics, ...), agents with multiple mechanisms of action (e.g. tricyclic antidepressants)

- Other physical findings:
  odor, neuromuscular abnormalities, skin findings, temperature alterations, ...

Toxic syndromes (toxidromes)
## Toxidromes (1)

<table>
<thead>
<tr>
<th>Toxidrome</th>
<th>Mental status</th>
<th>Pupils</th>
<th>Vital signs</th>
<th>Other manifestations</th>
<th>Examples of toxic agents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sympathomimetic</td>
<td>Hyperalert, agitation, hallucinations, paranoia</td>
<td>Mydriasis</td>
<td>Hyperthermia, tachycardia, hypertension, widened pulse pressure, tachypnea, hyperpnea</td>
<td>Diaphoresis, tremors, hyperreflexia, seizures</td>
<td>Cocaine, amphetamines, ephedrine, pseudoephedrine, phenylpropanolamine, theophylline, caffeine</td>
</tr>
<tr>
<td>Anticholinergic</td>
<td>Hypervigilance, agitation, hallucinations, delirium with mumbling speech, coma</td>
<td>Mydriasis</td>
<td>Hyperthermia, tachycardia, hypertension, tachypnea,</td>
<td>Dry flushed skin, drymucous membranes, decreased bowel sounds, urinary retention, myoclonus, choreoathetosis, picking behavior, seizures (rare)</td>
<td>Antihistamines, tricycl. antidepress., cyclobenzaprine, orphenadrine, antiparkinson agents, antispasmodics, phenothiazines, atropine, scopolamine, belladonna alkaloids (eg. Jimson Weed)</td>
</tr>
</tbody>
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(Uptodate, 2007)
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<tr>
<td>Hallucinogenic</td>
<td>Hallucinations, perceptual distortions, depersonalization, synesthesia, agitation,</td>
<td>Mydriasis (usually)</td>
<td>Hyperthermia, tachycardia, hypertension, tachypnea</td>
<td>Nystagmus</td>
<td>Phencyclidine, LSD, mescaline, psilocybin, designer amphetamines (eg. MDMA, MDEA)</td>
</tr>
<tr>
<td>Opioid</td>
<td>CNS depression, coma</td>
<td>Miosis</td>
<td>Hypothermia, bradycardia, hypotension, hypopnea, bradypnea</td>
<td>Hyporeflexia, pulmonary edema, needle marks</td>
<td>Opiates (eg. heroin, morphine, methadone, oxycodone, hydro-morphone), diphenoxylate</td>
</tr>
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(Uptodate, 2007)
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<tbody>
<tr>
<td>Sedative-hypnotic</td>
<td>CNS depression, confusion, stupor, coma</td>
<td>Miosis</td>
<td>Hypothermia, bradycardia, hypotension, hypopnea, bradypnea</td>
<td>Hyporeflexia</td>
<td>Benzodiazepines, barbiturates, carisoprodol, meprobamate, glutethimide, alcohols, zolpidem</td>
</tr>
<tr>
<td>Cholinergic</td>
<td>Confusion, coma</td>
<td>Miosis</td>
<td>Bradycardia, hypertension, or hypotension, tachypnea or bradypnea</td>
<td>Salivation, urinary and fecal incontinence, diarrhea, emesis, diaphoresis, lacrimation, GI cramps, bronchoconstriction, muscle fasciculations and weakness, seizures</td>
<td>Organophosphate (insecticides) and carbamate, nerve agents, nicotine, pilocarpine, physostigmine, edrophonium, bethanechol, urecholine</td>
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(Uptodate, 2007)
### Toxidromes (4)

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<tr>
<td>Serotonin syndrome</td>
<td>Confusion, agitation, coma</td>
<td>Mydriasis</td>
<td>Hyperthermia, tachycardia,</td>
<td>Tremor, myoclonus, hyperreflexia, clonus, diaphoresis, flushing, trismus, rigidity, diarrhea</td>
<td>MAOIs alone or with: SSRIs, meperidine, dextromethorphan, TCAs, L-tryptophan</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>hypertension, tachypnea</td>
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<tr>
<td>Tricyclic antidepressant</td>
<td>Confusion, agitation, coma</td>
<td>Mydriasis</td>
<td>Hyperthermia, tachycardia,</td>
<td>Seizures, myoclonus, choreoathetosis, cardiac arrhythmias and conduction disturbances</td>
<td>Amitriptyline, nortriptyline, imipramine, clomipramine, desipramine, doxepine</td>
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<tr>
<td></td>
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<td>hypertension then hypotension,</td>
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<td></td>
<td>hypopnea</td>
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(Uptodate, 2007)
General approach in acute intoxication

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General approach in acute intoxication

- Phases of intoxication: preclinical, toxic and resolution
- Initial evaluation and treatment
- Diagnosis of intoxication:
  - history
  - physical examination
  - electrocardiography
  - X-ray
  - toxicological screening / laboratory
- Evaluation of severity and predicting expected toxicity
- Treatment
Toxicological investigations

- **Screening**
  - e.g. acetaminophen and salicylates in cases of auto-intoxication or uncertainty in history
  - immunoassay: fast, simple
  - qualitative screening (GC or MS) e.g. in cases of severe toxicity or unexplained toxic symptoms

- **Quantitative determination**
  - e.g. acetaminophen, carboxyhaemoglobin, methanol, ...
Treatment of acute intoxications

1. Supportive therapy
2. Decontamination
3. Antidotes
4. Enhanced elimination techniques
Decontamination in acute intoxications

- For topical exposures:
  copious water / saline irrigation

- For oral ingestions:
  ‣ activated charcoal
  ‣ syrup of ipecac, gastric lavage, whole bowel irrigation, endoscopy, surgery, dilution, cathartics
Problems with obtaining "evidence" for the utility of gastro-intestinal decontamination in acute intoxication

- Large variability in intoxications (dose, time since ingestion, multiple substances, ...)
- Problem with reliability of the patient history
- Problem of informed consent in suicidal patients
- Low mortality (1%)

(Smilkstein, 2002)
Position statements: Gut decontamination

- Published in 1993 with updates in 2004-2005
- The American Academy of Clinical Toxicology (AACT)
- European Association of Poison Centers and Clinical Toxicology (EAPCCT)

http://www.clintox.org/Pos_Statements/Intro.html
Click below for position statements on the following topics in PDF format:

- Ipecac Syrup
- Single-Dose Activated Charcoal
- Multi-Dose Activated Charcoal
- Cathartics
- Whole Bowel Irrigation
- Gastric Lavage
- Urine Alkalization

Activated charcoal

- Not absorbable, fine black powder
- Adsorbs chemical substances in the pores within minutes of contact
- Surface: 950 to 2000 m² per gram
Activated charcoal

Adsorptive capacity varies according to
- molecular weight
- structure
- ionisation
- solubility of the toxic substance
### Agents not well adsorbed by activated charcoal

<table>
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<tr>
<th>Heavy metals</th>
<th>Corrosives</th>
</tr>
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<tbody>
<tr>
<td>Arsenic</td>
<td>Acids</td>
</tr>
<tr>
<td>Lead</td>
<td>Alkali</td>
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<tr>
<td>Mercury</td>
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<tr>
<td>Iron</td>
<td>Hydrocarbons</td>
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<tr>
<td>Zinc</td>
<td>Alkanes</td>
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<tr>
<td>Cadmium</td>
<td>Alkenes</td>
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<td></td>
<td>Alkyl halides</td>
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<tr>
<td>Inorganic ions</td>
<td>Aromatic hydrocarbons</td>
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<tr>
<td>Lithium</td>
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<tr>
<td>Sodium</td>
<td>Alcohols</td>
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<td>Calcium</td>
<td>Acetone</td>
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<tr>
<td>Potassium</td>
<td>Ethanol</td>
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<tr>
<td>Magnesium</td>
<td>Ethylene glycol</td>
</tr>
<tr>
<td>Fluoride</td>
<td>Isopropanol</td>
</tr>
<tr>
<td>Iodide</td>
<td>Methanol</td>
</tr>
<tr>
<td>Boric acid</td>
<td>Essential oils</td>
</tr>
</tbody>
</table>

(Uptodate, 2007)
Indications for single dose activated charcoal

- Volunteer studies suggest that activated charcoal is more likely to reduce poison absorption if it is administered within one hour of ingestion.

- In the absence of satisfactorily designed clinical studies demonstrating benefit from its use, the administration of activated charcoal may be considered if a patient has ingested a potentially toxic amount of a poison up to one hour following ingestion.

- The potential for benefit after one hour cannot be excluded.

Position paper AACT/EAPCCT (Clinical Toxicology 2005; 43: 61-87)
Contraindications for single dose activated charcoal

- The patient has an unprotected airway.
- Its use increases the risk and severity of aspiration (e.g. a hydrocarbon with a high aspiration potential)
- Patients who are at risk of gastrointestinal hemorrhage or perforation due to pathology, recent surgery or medical conditions.
- Presence of activated charcoal in the gastrointestinal tract may obscure endoscopic visualization, but a corrosive is not a contraindication when charcoal is used for co-ingested agents that are systemic toxins.
Complications of single dose activated charcoal

Majority of adverse events not related to appropriate use:

• Aspiration pneumonitis
• Vomiting (5 – 15%)
• Corneal abrasions
Decontamination in acute intoxications

• For topical exposures :
copious water / saline irrigation

• For oral ingestions :
  ▸ activated charcoal
  ▸ syrup of ipecac, gastric lavage, whole bowel irrigation, endoscopy, surgery, dilution, cathartics:

  see “Position Paper ACCT/EAPCCT”
Gastrointestinal decontamination
Treatment of acute intoxications

1. Supportive therapy
2. Decontamination
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Poison control centre