Clinical toxicology:
*common poisonings in the ED*

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Poisoning & the ED

- Epidemiology
  - Great differences
  - Influences: society - culture

- Categories
  - Main diagnosis/ concomitant diagnosis
  - Accidental/ intentional
  - Acute/ sub-acute/ chronic

Poisoning & ED: Why challenges & controversies?

- Multiple ingestion = different challenge
- Limited evidence-based therapeutic approach
  - Toxicology literature = cases & uncontrolled studies
  - Ethical issues for studies
    - Design: double blinded
    - Informed consent
Poisoning & the ED

- Toxidrome recognition
- Assessment
- Management
  - Stabilisation - supportive therapy
  - Decontamination
  - Enhance elimination of the toxins
  - Antidote administration
  - Psychosocial support

Recognition of poisoning

- Major determinant is clinical experience

- Preformatted admission charts
  - facilitate clinical assessment
  - guarantee completeness of examination data
  - computerisation for research, quality management, epidemiology, ...

Recognition of poisoning

- Dissociation between typically paired changes
- Cluster of symptoms and signs

  = Toxidromes

  = fingerprints of a group of products/ poisons
Recognition = “detective work”

Recognition of the risk = suspicion

- History of suicide or psychiatric pathology
- Coma e causa ignota
- Cardiac arrhythmia in patients < 40 years
- Metabolic acidosis
- Victims of fire
- Lethargy or coma in children
- Heterogenic symptomatology without a clear uniform clinical diagnosis

Recognition = “detective work”

History

- Patient related factors
  - Access to products & medication
  - Prescriptions to other family members
  - Gender, age, work or leisure conditions (epidemiology)
  - History of event
  - Medical history

Recognition = “detective work”

History

- Circumstance related factors
  - Containers, suicide notes,
  - Absence of personal identification
  - Location
Clinical assessment

1. central nervous system
2. pupil diameter
3. respiration
4. heart and circulation
5. gastro-intestinal system
6. temperature
7. diuresis
8. general examination

Clinical assessment

1. Central nervous system
   - GCS
   - Fasciculations - myoclonus
   - excitation - convulsions
   - hyper / hyporeflexia

2. Pupil diameter
   - myosis
   - mydriasis
   - blurred vision

Clinical assessment: coma

L  Lead, lithium
E  ethanol, ethylene glycol,...
T  tricyclic antidepress., thallium, toluene
H  heroin, hemlock, hepatic encephalopathy,
   heavy metals, hydrogen sulfide, hypoglycemics
A  arsenic, antidepress., anticonvuls., antipsych.,
   antihistamines
R  rohypnol (hypnotics), risperidone
G  GHB
I  isoniazid, insulin
C  carbon monoxide, cyanide, clonidine
Clinical assessment: seizures

- organophosphates, oral hypoglycemics
- tricycl. Antidepressants
- isoniazid, insulin
- sympathomimetics, strychnine, salicylates
- camphor, cocaine, CO, HCN, chlor. hydrocarbon
- amphetamines, anticholinergics
- methylxanthines (theophylline, caffeine), methanol
- PCP, propranolol
- benzo withdrawal, botanicals (hemlock), GHB
- ethanol withdrawal
- lithium, lidocaine, lead, lindane

Clinical assessment: pupil size

- Miosis (COPS)
  - cholinergics, clonidine, carbamates
  - opiates, organophosphates
  - phenothiazines, pilocarpine, pontine hemorrhage
  - sedatives-hypnotics
- Mydriasis (SAW)
  - sympathomimetics
  - anticholinergics
  - withdrawal

Clinical assessment

3. Respiration

- Breathing pattern
  - hyperpnoea = correction metabolic acidosis
  - superficial breathing (resp. freq.↑ and resp. vol.↓)
  - breathing depression (resp. freq.↓ and resp. vol.↓)
- Lung auscultation
- Breath odour
Clinical assessment: RR

- Rapid respiration (PANT)
  - P PCP, paraquat, (chemical) pneumonitis, phosgene
  - A ASA & other salicylates
  - N noncardiogenic pulm oedema, nerve agents
  - T toxin-induced metabolic acidosis

- Slow respiration (SLOW)
  - S sedative-hypnotics
  - L liquor (alcohol)
  - O opioids
  - W weed (marijuana)

Clinical assessment

4. Heart and circulation

- ECG: arrhythmias / conduction abnormalities
- CVP (vasodilatation - intravascular volume deficit)
- Blood pressure: hypotension - hypertension

Clinical assessment: brady-tachy

- Bradycardia (PACED)
  - P propranolol (β blockers), poppies (opiates), physostigmine
  - A anticholinesterase drugs, antiarrhythmics
  - C clonidine, calcium reentry blockers
  - E ethanol
  - D digitalis

- Tachycardia (FAST)
  - F free base (cocaine)
  - A antichol, antihist, antipsych, amphetamine, alc withdrawal
  - S sympathomimetics (cocaine, caffeine, …), solvent, strychnine
  - T theophylline, TCA, thyroid hormones
Clinical assessment: hypo-hypertension

- Hypotension (CRASH)
  - C clonidine, calcium reentry blockers
  - R rodenticides (arsenic, cyanide)
  - A antidepressants, aminophylline, antihypertensives
  - S sedatives-hypnotics
  - H heroin or other opiates

- Hypertension (CT SCAN)
  - C cocaine
  - T thyroid supplements
  - S sympathomimetics
  - C caffeine
  - A anticholinergics, amphetamine
  - N nicotine

Clinical assessment

5. Gastro-intestinal system

- Vomiting - diarrhoea
- hypo- / hyperperistalsis

Clinical assessment

6. Body temperature
- hypothermia - hyperthermia

7. Diuresis
- prerenal kidney insufficiency
- acute tubular necros - rhabdomyolysis

8. General examination
- injection points, petechia, bullae
- icterus, methaemoglobinemia-cyanose
- compartment syndrome
Clinical assessment: hypo-hyperthermia

- Hypothermia (COOLS)
  - C: opioids
  - O: oral hypoglycemics, insulin
  - L: liquor (alcohol)
  - S: sedatives-hypnotics

- Hyperthermia (NASA)
  - N: neuroleptic malignant syndrome, nicotine
  - A: antihistamines, alcohol withdrawal
  - S: salicylates, sympathomimetics, serotonin syndrome
  - A: anticholinergics, antidepressants, antipsychotics

Clinical assessment

= the key for recognition

- dissociation between usually paired changes
- + abnormalities in organ function

= the key for toxidrome recognition

= classifying the toxin

Toxidromes

agitation, aggression, hallucinations, coma, hypertonia, hyperreflexion, myoclonus, strabismus, mydriasis, hyperpnea, tachycardia, QT-time prolongation (ECG), cardiac arrhythmia, hyperperistalsis, constipation, urine retention, hyperthermia, flush, dry skin & mucosa

anticholinergic syndrome

Anticholinergics, antihistaminics, anti-Parkinson, spasmodics, antipsychotics, tricyclic antidepressants, datura stramonium (Jimson weed)
Anticholinergic toxidrome

- Hyperthermia  HOT as a hare
- Flushed  RED as a beet
- Dry skin  DRY as a bone
- Dilated pupils  BLIND as a bat
- Delirium  MAD as a hatter
- Tachycardia
- Urinary retention

Toxidromes

- muscle fasciculations, coma, pinpoint-pupils, bronchorhea, superficial breathing, hyperperistalsis, intestinal spasm, diarrhoea, hypersalivation, flood of tears

cholinergic syndrome

Cholinesterase - inhibiting insecticides
amanita-mushrooms

Cholinergic toxidrome

- DUMBELS
  - Diarrhea, diaphoresis
  - Urination
  - Miosis
  - Bradycardia, bronchosecretions
  - Emesis
  - Lacrimation
  - Lethargic
  - Salivation
Toxidromes

extrapyramidal movements, rigidity, torticollis, trismus dysphonia, dysphagia, tremor, opisthotonus, laryngospasm

extrapyramidal syndrome

Neuroleptics (phenothiazines, butyrophenons)

Toxidromes

Agitation, fear, restlessness, paranoia, trembling, convulsions, epilepsy, hyperreflexion, mydriasis, tachycardia, cardiac arrhythmia, hypertension, hyperthermia, hyperperistalsis, dry mouth

sympathomimetic syndrome

Excitatory drugs, decongestiva (ephedrine, epinephrine), sympaticomimetics, aminophylline

Toxidromes

nausea, vomiting, tinnitus, transpiration, hyperpnea, vasodilatation

Salicylate intoxication

Sedation à coma, pinpoint pupils, depressed breathing

Morphinomimetics
Toxidromes

coma (ev. hallucinations, agitation), hypotonia, hyporeflexion, supressed breathing, hypotension, vasoplegia, oliguria, shock, hypothermia

*Hypnotics, sedatives, ethanol*

Toxidromes

confusion, myoclonus, hyperreflexia, diaphoresis, tremor, facial flushing, diarrhoea, fever, trismus

*serotonergic syndrome*

*SSRI and drug combinations as MAO-inhibitors with L-Tryptophan or Paroxetine*

Figure 2: Findings in a Patient with Moderate Severe Serotonin Syndrome.
Hypertensive myocardial findings of tremor or clonus and hyperreflexia should lead the decision to consider the diagnosis of the serotonin syndrome.
Toxidromes pitfalls

No toxidrome = No poisoning? NO

No toxidrome “yet”
- delayed toxicity or delayed toxidrome
  → delayed onset of toxicity
  → delayed deterioration

mechanisms:
- delayed absorption of the toxin
- distribution factors
- metabolic factors
- cellular and organ capacity effects

Toxidromes pitfalls

No toxidrome “at all”
- very mild poisoning
- very serious poisoning + immediate fatal
- symptom free interval
  • Paracetamol
  • Paraquat
  • Hydrocarbons
Toxidromes pitfalls

Multiple compound ingestion

toxidrome (1) of TCAD - history of only a TCAD intake - ready for dismissal
toxidrome (2) of β-blocker - denial of intake
toxidrome of TCAD - acetominophen not mentioned

Toxidromes pitfalls

One patient with simultaneous disorders

Accident because of an overdose (ethanol, drugs, ...)
(1/3 of major trauma victims BAC > 0.5 pro mille)

Psychiatric patient with an overdose may have a head injury

Patient with an overdose may develop a diabetic ketoacidosis

Toxidromes pitfalls

A toxidrome with a “missing” sign or an “unexpected” symptom

f.i. organophosphate poisoning = bradycardia versus tachycardia
Toxidromes pitfalls

Toxidrome recognition is of major help to the clinician in finding the diagnosis

However

Toxidrome phenomenon is not exclusive

Additive diagnostic protocol

- Substance determination
  - NO screening
  - Selective clinically driven

- Biochemical evaluation
  - Osmolality
  - Electrolytes - rhabdomyolysis
  - Acid-base + anion gap
  - Baseline organ parameters

Additive diagnostic protocol: biochemical evaluation

- Osmolality - osmotic gap
  - Methanol: (OG x 0.030) g/L
  - Ethanol: (OG x 0.046) g/L
  - Isopropanol: (OG x 0.056) g/L
  - Aceton: (OG x 0.055) g/L
  - Ethyleneglycol: (OG x 0.053) g/L
Additive diagnostic protocol: biochemical evaluation

- Osmolar gap (ME DIE)
  - M methanol
  - E ethylene glycol
  - D diuretics (mannitol), diabetic ketoacidosis (acetone)
  - I isopropyl alcohol
  - E ethanol

Additive diagnostic protocol: biochemical evaluation

- Osmolality - osmotic gap

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<th>Aceton</th>
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<tr>
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<td>Ethylene-glycol</td>
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Additive diagnostic protocol: biochemical evaluation

- Electrolytes

  - Na⁺
    - Dehydration - H₂O poisoning
    - Thiazide diuretic = H₂O and excess Na⁺
  - K⁺
    - Diuretics - laxativa
    - Spironolactone - ACE inhibitor
    - Insuline
    - β₂ agonist
Additive diagnostic protocol: biochemical evaluation

- Acid - base
  - Respiratory origin
    - Breathing centre (opioids)
    - pCO₂ receptor (salicylates)
    - Muscles (organophosphates, curares)
  - Metabolic origin
    - Generation of organic acids (methanol, EG)
    - pKa of toxin (barbiturates)
    - Renal toxicity

- Elevated anion gap (METAL ACID GAP)
  - methanol, metformin, massive overdoses
  - ethylene glycol
  - toluene
  - alcoholic ketoacidosis
  - lactate
  - acetaminophen (large overdose)
  - cyanide, CO, colchicine
  - isoniazid, iron, ibuprofen
  - diabetic ketoacidosis
  - generalized seizure producing toxins
  - ASA & other salicylates
  - paraldehyde, phenformin

Additive diagnostic protocol: imaging

- X-ray thorax
  - Pneumonia?

- X-ray abdomen
  - Visible
  - Body packers

- CT abdomen
  - Body packers
Additive diagnostic protocol:

- Imaging
  - Agents visible on abdominal X-ray (COINS)
    - C: chloral hydrate, cocaine packets, calcium
    - O: opium packets
    - I: iron & other heavy metals: lead, arsenic, mercury
    - N: neuroleptic agents
    - S: sustained-release or enteric-coated agents

Therapeutic protocol

- Supportive therapy
- Reducing absorption
  - Vomiting (ipecac) - gastric emptying
  - Gastric lavage - whole bowel irrigation
  - Activated charcoal
- Increasing elimination
  - Activated charcoal
  - Forced diurese - extracorporeal drug removal
- Antidotes
- Psychosocial therapy

Therapeutic protocol

- Toxic agent
  - Reducing absorption
  - Circulation
  - Inhibition of metabolism
  - Metabolism
  - Desintoxification
  - Target organ: specific actions:
    - Receptor
    - Enzyme
  - Toxic symptoms: supportive therapy
Therapeutic protocol reducing absorption

- Vomiting (ipecac) - gastric emptying
- Gastric lavage - whole bowel irrigation
- Activated charcoal

Therapeutic protocol reducing absorption: gastric lavage

**Evidence:**
- Removed marker is highly variable and time dependent
- Lack of beneficial effects
- Serious risks: aspiration, fluid & electrolyte abnormalities, laryngospasm,...

**Consideration**
- Early GI decontamination (< 1 h)
- High amount of potential toxic substance
Therapeutic protocol reducing absorption: gastric lavage

**Contraindicated:**
- Loss of protective airway reflexes
- Ingestion of acid or alkali
- Ingestion of hydrocarbon
- Risk of GI haemorrhage

*J Toxicol, Clin Toxicol 2004; 42(7): 933-943*

Therapeutic protocol reducing absorption: whole bowel irrigation

**Evidence:**
- Decreased bio-availability in volunteer studies
- No controlled trials on outcome of the poisoned patient

**Consideration:**
- Sustained-release & enteric-coated, potentially toxic
- Iron ingestion
- Ingested packets of illicit drugs

Therapeutic protocol reducing absorption: whole bowel irrigation

**Contraindicated:**
- Bowel obstruction, perforation, ileus
- GI haemorrhage
- Haemodynamic unstable
- Unprotected airway, intractable vomiting

**Caution:**
- Specific medical conditions
- Concurrent administration of activated charcoal

*J Toxicol, Clin Toxicol 2004; 42(6): 843-854*
Therapeutic protocol
reducing absorption: single dose activated charcoal

Evidence:
- Effectiveness decreases with time
- No benefit on outcome

Consideration:
- Ingestion of a potentially toxic amount up to 1 hour or longer (=7)
- Known to adsorb to charcoal

Caution:
- Intact or protected airway


Adsorption to activated charcoal

Well adsorbed:
- Amphetamine, Antidepressants, Antiepileptics, Antihistamines
- Barbiturates, Benzodiazepines, B-blocking agents
- Chloroquine and primaquine, Cimetidine
- Dextropropoxyphene and other opioids, Digitalis glycosides
- Ergot alkaloids
- Phenothiazines, Phenylbutazone, Phenylpropanolamine
- Strychnine, Tetracyclines, Theophylline

Moderately adsorbed:
- Aspirin and other salicylates,
- Malathion,
- Many ‘high dose’ non-steroidal anti-inflammatory drugs,
- Paracetamol (acetaminophen)
Adsorption to activated charcoal

Poorly or clinically inadequately adsorbed:
- Cyanide
- Ethanol, Ethylene glycol, Methanol
- Iron, Lithium
- Strong acids and alkalis

Therapeutic protocol
Increasing elimination: Multiple-dose AC

**Theoretical rationales: pro's**
- Sustained-release products
- Enterohepatic circulation
- Actively secreted in GI tract
- “GI dialysis”

**Theoretical rationales: con's**
- Given within one hour following ingestion
- Side effects (aspiration, constipation, ...)
- No evidence of improvement in outcome

Therapeutic protocol
Increasing elimination

**Extracorporeal drug removal techniques**
- Haemodialysis - haemoperfusion
- Molecular Adsorbent recycling system (MARS)

- Limited indications - severe cases
- Poor tolerance in haemodynamically compromised patient
Therapeutic protocol
Increasing elimination

- Toxins accessible to hemodialysis (UNSTABLE)
  U uremia
  N no response to conventional therapy
  S salicylates
  T theophylline
  A alcohols (isopropanol, methanol)
  B boric acid, barbiturates
  L lithium
  E ethylene glycol

Therapeutic protocol
Antidotes

- Binding to non-toxic complex (chelator)
- Inhibition on metabolism
- Competitive receptor binding
- Physiological antidote (atropine vs. overdose acetylcholine)

Therapeutic protocol
Antidotes

- More benefit from attentive supportive care than from a specific antidote
- Side effect profile of the antidote itself may be threatening
- Poisons & antidotes possess their own pharmacokinetic & dynamic properties
- Limited evidence & experience
  - USA: 43,278 specific antidote administration on 2.4 million cases
Therapeutic protocol antidotes

- Hyperbaric oxygen for CO poisoning
  - Lost consciousness
  - Pregnant patient
  - Neurological & ECG changes

- Cyanide & hydroxocobalamin
  - Not toxic
  - Prehospital use

Therapeutic protocol antidotes

- 4-methylpyrazole & methanol/ethylene glycol
  - Alcohol dehydrogenase inhibitor
  - No blood concentration monitoring
  - No "ethanol" like side effects (hypoglycaemia, pancreatitis, ...)
  - No haemodialysis - critical care facilities
  - Expensive

"American Academy of Clinical Toxicology. Practice guidelines on the treatment of methanol poisoning." Clinical Toxicology, Volume 40, number 4, 2002, p 415-446
Octreotide & sulfonylurea class poisoning

- Glucose infusion: central access/ rebound hypoglycaemia
- Long acting somatostatin analogue - blocks insulin release
- Adverse effects:
  - Vomiting, diarrhea, steatorrhea
  - Cardiac conduction abnormalities
  - Biliary tract disease

Psychosocial support

- Task of each ED collaborator
- Task social worker
- Task Emergency psychiatry
Conclusions

- Recognition = cornerstone
- Therapy = combination of
- Be careful with antidotes
- “Primum non nocere”

Conclusions

- Teach me, I will forget
- Show me, I will probably remember
- Involve me, I will understand