



## 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



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## 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



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## Poisoning & the ED

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

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## Recognition of poisoning

- Major determinant is clinical experience  
*Nice A. and Leikin J., Ann Emerg Med 1988, 17(7): 676-680*
- Preformatted admission charts
  - facilitate clinical assessment
  - guarantee completeness of examination data
  - computerisation for research, quality management, epidemiology, ...*Buckley N. and Whyte I., Ann Emerg Med 1999, 34: 476-482*

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## Recognition of poisoning

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

= *Toxidromes*

= fingerprints of a group of products/poisons

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## 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

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## 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



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## Recognition = "detective work"

- *History*
  - Circumstance related factors
    - Containers, suicide notes,...
    - Absence of personal identification
    - Location



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## 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

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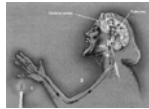
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## Clinical assessment

### 1. Central nervous system

- GCS
- Fasciculations - myoclonus
- excitation - convulsions
- hyper / hyporeflexia



### 2. Pupil diameter

- myosis
- mydriasis
- blurred vision

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## 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

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**Clinical assessment: seizures**

- O** organophosphates, oral hypoglycemics
- T** tricycl. Antidepressants
- I** isoniazid, insulin
- S** sympathomimetics, strychnine, salicylates
  
- C** camphor, cocaine, CO, HCN, chlor. hydrocarbon
- A** amphetamines, anticholinergics
- M** methylxanthines (theophylline, caffeine), methanol
- P** PCP, propranolol
- B** benzo withdrawal, botanicals (hemlock), GHB
- E** ethanol withdrawal
- L** lithium, lidocaine, lead, lindane
- L**

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**Clinical assessment: pupil size**

- **Miosis (COPS)**
  - C** cholinergics, clonidine, carbamates
  - O** opiates, organophosphates
  - P** phenothiazines, pilocarpine, pontine hemorrhage
  - S** sedatives-hypnotics
  
- **Mydriasis (SAW)**
  - S** sympathomimetics
  - A** anticholinergics
  - W** withdrawal

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**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**

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## 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)

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## Clinical assessment

### 4. Heart and circulation

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

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## Clinical assessment: brady-tachy

### ■ Bradycardia (PACED)

- P propranolol ( $\beta$  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

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### 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

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### Clinical assessment

#### 5. Gastro-intestinal system

- Vomiting – diarrhoea
- hypo- / hyperperistalsis

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### Clinical assessment

#### 6. Body temperature

- hypothermia - hyperthermia

#### 7. Diuresis

- prerenal kidney insufficiency
- acute tubular necrosis - rhabdomyolysis

#### 8. General examination

- injection points, petechia, bullae
- icterus, methaemoglobinemia-cyanose
- compartment syndrome

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## Clinical assessment: hypo-hyperthermia

### ■ Hypothermia (COOLS)

- C CO
- O 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

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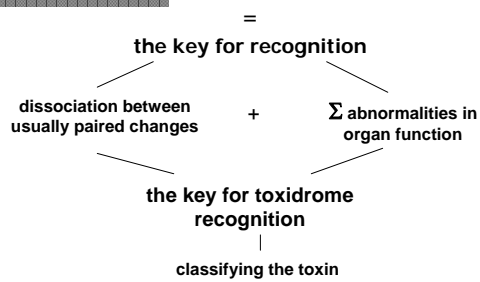
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## Clinical assessment



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## Toxidromes

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

### *anticholinergic syndrome*

*Anticholinergics, antihistaminics, anti-Parkinson, spasmolitics, antipsychotics, tricyclic antidepressants, datura stramonium (Jimson weed)*

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## 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

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## Toxidromes

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

### *cholinergic syndrome*

*Cholinesterase – inhibiting insecticides  
amanita-mushrooms*

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## Cholinergic toxidrome

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

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**Toxidromes**

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

*extrapyramidal syndrome*

*Neuroleptics*  
*(phenothiazines, butyrophenons)*

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**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*

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**Toxidromes**

nausea, vomiting, tinnitus, transpiration,  
hyperpnea, vasodilation

*Salicylate intoxication*

*Sedation à coma, pinpoint pupils, depressed  
breathing*

*Morphinomimetics*

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## Toxidromes

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

*Hypnotics, sedatives, ethanol*

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## 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*

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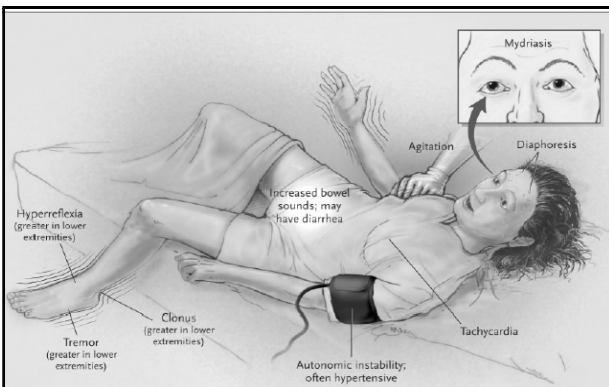


Figure 2. Findings in a Patient with Moderately Severe Serotonin Syndrome. Hyperkinetic neuromuscular findings of tremor or clonus and hyperreflexia should lead the clinician to consider the diagnosis of the serotonin syndrome.

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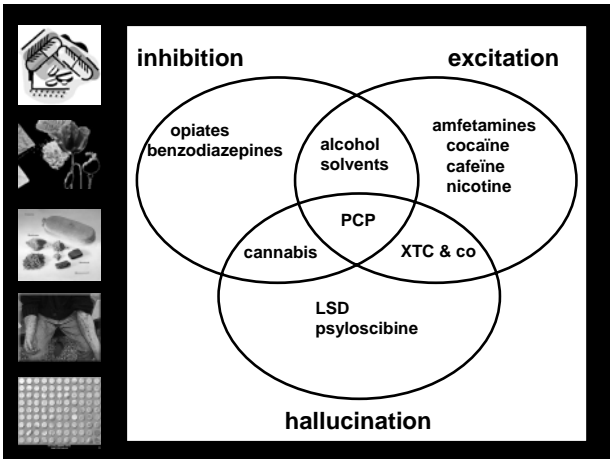
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### Toxidromes pitfalls

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**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

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### Toxidromes pitfalls

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***No toxidrome "at all"***

- very mild poisoning
- very serious poisoning + immediate fatal
- symptom free interval
  - Paracetamol
  - Paraquat
  - Hydrocarbons

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## Toxidromes pitfalls

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### *Multiple compound ingestion*

toxidrome (1) of TCAD – history of only a TCAD intake – ready for dismissal  
toxidrome (2) of  $\beta$ -blocker – denial of intake

toxidrome of TCAD – acetaminophen not mentioned

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## Toxidromes pitfalls

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### *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 keto-acidose

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## Toxidromes pitfalls

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### *A toxidrome with a "missing" sign or an "unexpected" symptom*

f.i. organophosphate poisoning  
= bradycardia versus tachycardia

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## Toxidromes pitfalls

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

*However*

Toxidrome phenomenon is not exclusive

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## Additive diagnostic protocol

### ■ *Substance determination*

- NO screening
- Selective clinically driven

### ■ *Biochemical evaluation*

- Osmolality
- Electrolytes - rabdomyolysis
- Acid-base + anion gap
- Baseline organ parameters



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## 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

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**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

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**Additive diagnostic protocol:  
biochemical evaluation**

■ Osmolality – osmotic gap

	Osmolal gap	Acidose + anion gap	Aceton	oxalaat
Ethanol	+	-	-	-
Methanol	+	+	-	-
Isopropanol	+	-	+	-
Ethylene-glycol	+	+	-	+

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**Additive diagnostic protocol:  
biochemical evaluation**

■ Electrolytes

- Na<sup>+</sup>
  - Dehydration – H<sub>2</sub>O poisoning
  - Thiazide diuretic = H<sub>2</sub>O and excess Na<sup>+</sup>
  
- K<sup>+</sup>
  - Diuretics – laxativa
  - Spironolactone –ACE inhibitor
  - Insuline
  - β<sub>2</sub> agonist

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### Additive diagnostic protocol: biochemical evaluation

#### ■ Acid – base

##### ■ Respiratory origin

- Breathing centre (opioids)
- pCO<sub>2</sub> receptor (salicylates)
- Muscles (organophosphates, curares)

##### ■ Metabolic origin

- Generation of organic acids (methanol, EG)
- pKa of toxin (barbiturates)
- Renal toxicity

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### Additive diagnostic protocol: biochemical evaluation

#### ■ Elevated anion gap (METAL ACID GAP)

- M methanol, metformin, massive overdoses
- E ethylene glycol
- T toluene
- A alcoholic ketoacidosis
- L lactate
  
- A acetaminophen (large overdose)
- C cyanide, CO, colchicine
- I isoniazid, iron, ibuprofen
- D diabetic ketoacidosis
  
- G generalized seizure producing toxins
- A ASA & other salicylates
- P paraldehyde, phenformin

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### Additive diagnostic protocol: imaging

#### ■ X-ray thorax

- Pneumonia?

#### ■ X-ray abdomen

- Visible
- Body packers

#### ■ CT abdomen

- Body packers



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## 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

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## Therapeutic protocol

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

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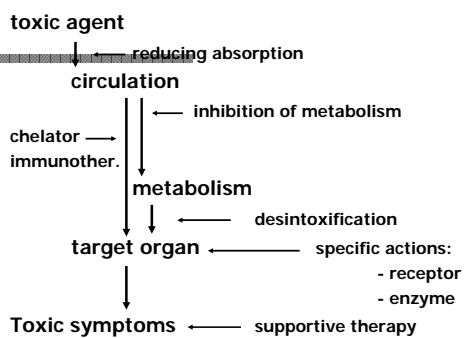
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## Therapeutic protocol




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**Therapeutic protocol  
reducing absorption**

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

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**Therapeutic protocol  
reducing absorption**



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**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

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**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*

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**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



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**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*

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**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 (=?)
- Known to adsorb to charcoal

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**Therapeutic protocol**  
reducing absorption: single dose activated charcoal

■ **Caution:**

- Intact or protected airway

*J Toxicol, Clin Toxicol 2005; 43(2): 61-87*

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**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)

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## Adsorption to activated charcoal

### Poorly or clinically inadequately adsorbed:

- Cyanide
- Ethanol, Ethylene glycol, Methanol
- Iron, Lithium
- Strong acids and alkalis

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## 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

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## 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



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## 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

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## Therapeutic protocol antidotes

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

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## 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

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### Therapeutic protocol antidotes

#### ■ Hyperbaric oxygen for CO poisoning

- Lost consciousness
- Pregnant patient
- Neurological & ECG changes

#### ■ Cyanide & hydroxocobalamin

- Not toxic
- Prehospital use



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### 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*

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## Therapeutic protocol antidotes

### ■ Octreotide & sulfonyleurea 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

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## Therapeutic protocol

### ■ Psychosocial support

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

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## Conclusions

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

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## Conclusions

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



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