ACUTE INTOXICATIES

BREVET ACUTE GENEESKUNDE

Dr. Agnes Meulemans
UZ Leuven

Definitie :

Elke stof die in contact met een levend organisme dit organisme schade toebrengt = een GIF

o.w.v.
- **aard**
- **in overmaat aanwezig zijn**

“Dosis sola facit venenum” (Paracelsus)

Blootstelling via:

- **huid**
- **slijmvliezen**
- **ademhalingswegen**
- **spijsverteringsstelsel**
- **bloedbaan**

Omstandigheden:

intentionele - accidentele intoxicatie

Aantal intoxicaties stijgt :

- **beschikbaarheid / aantal toxische en farmaceutische producten nemen toe**
- **incidentie (illegale) drugabusus neemt toe**
- **incidentie van intentionele intoxicatie neemt toe**
- **blootstellingsrisico in het milieu stijgt**

Belgian PCC - data 1993 - 1996

- 217 575 calls 83 % = poisoning
  15 % = information
- Victims: children: 52 % adults: 48 %
  71 % of the children were < 4 years old
- Products involved: pharmaceuticals: 41 %
  householdproducts: 31 %
- Suggested solutions: do nothing: 65 %
  GP: 23 %
  hospital: 12 %

Acute intoxicaties - BAG

B – Flanders - Health - indicators 1999

- 1.121 death due to suicide
  75% male - 47 years
- men : suicide by 1. Strangulation (59%)
  2. Fire arms
  3. Poisoning

  women : suicide by 1. Strangulation
  2. Drowning
  3. Poisoning
- if poisoning: 1. Pharmaceuticals
  85% women 72% men
  2. Agro-chemicals
  men > women

Acute intoxicaties - BAG

Emergency medicine and clinical toxicology

- **Poisoning as main reason for admission or main diagnosis on dismission**

  B - Poisoning registry Leuven

- **Poisoning as concomitant diagnosis**

  Belgian Trauma and Toxicology Study

B - Poisoning registry - Leuven 1/1/93 - 31/7/96

- **Admissions for poisoning: 2.32 %**

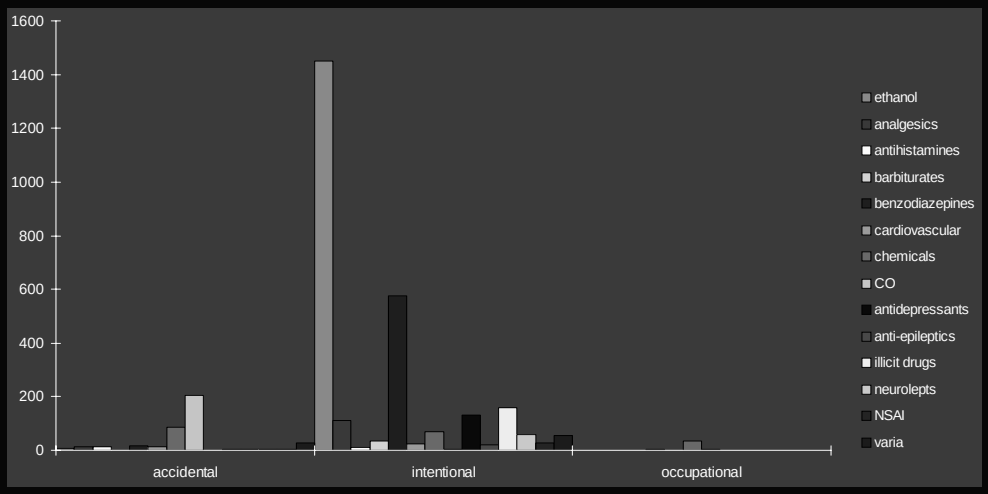
  N poisonings = 3 306
  N admissions ED = 142 449

- **Circumstances:** **accidental: 13 %**
  intentional: 85.5 %
  occupational: 1.5 %

- **Exposure :**

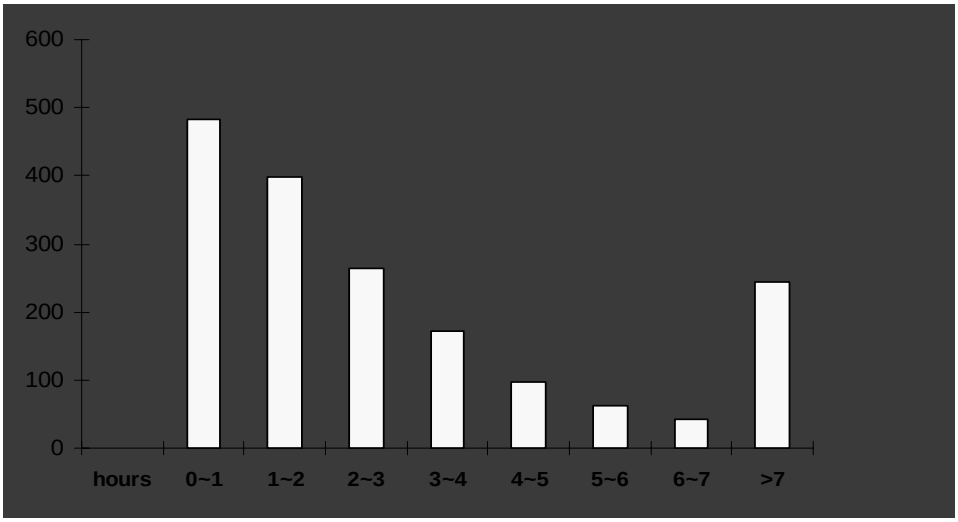
	ingestion	inhalation
accidental:	41%	54 %
intentional:	97 %	1.5 %
occupational:	1.2 %	36 %

Nature of the poison - circumstances

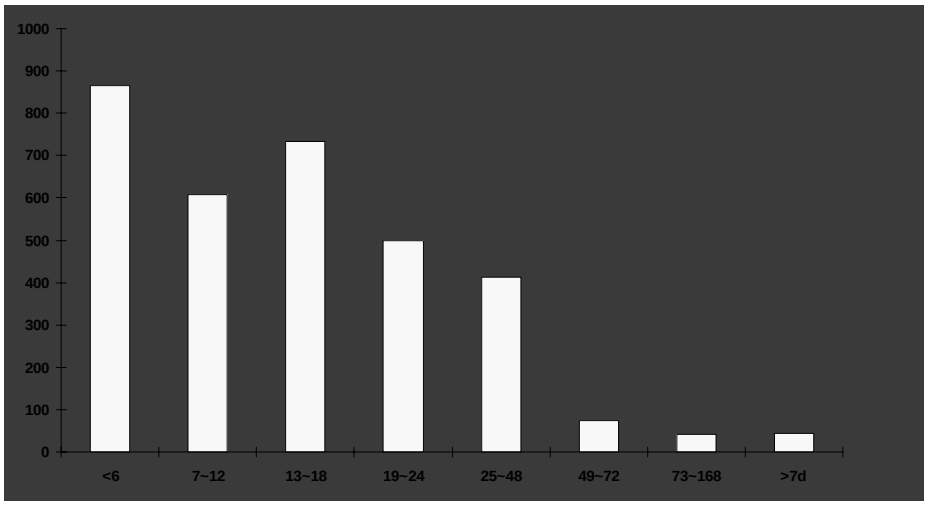


Acute intoxicaties - BAG

Delay poisoning - admission



Length of stay



B - Poisoning registry - Leuven 1/1/93 - 31/7/96

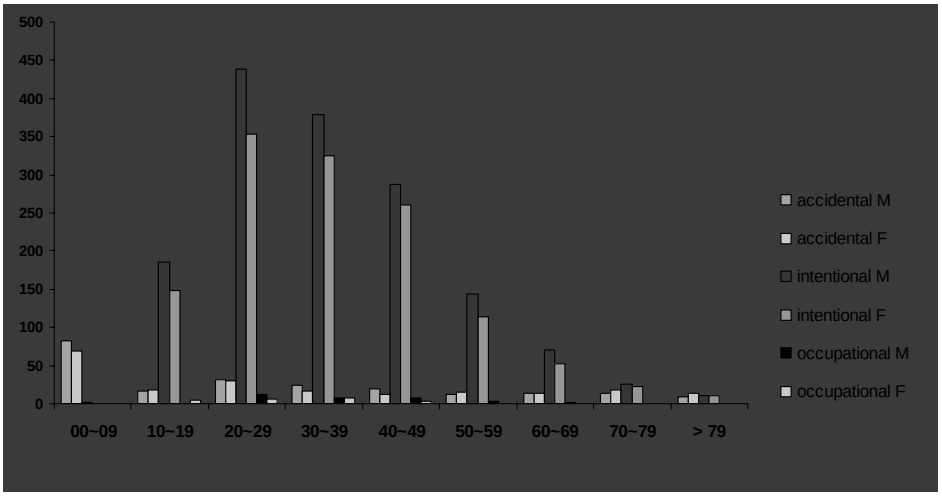
- **Transport mode ? 69 % ambulance**
- **Referred by ? intentional poisoning**
  - **a MD: 27.5 %**
  - **own initiative: 14.5 %**
- **First treatment ? accidental: 60 % none**
  intentional: 93 % none
  occupational: 43 % none

if referred by a MD: only 6 % gets first treatment

Accidental Poisoning N = 428

- **CO - intoxications: 204 = 48 %**
- **Others: 224 = 52 %**
  - **male: 54 % female: 46 %**
  - **0 - 9 years: 56 %**
    0 - 4 years: 79 %
    4 - 10 years: 21 %

Circumstances - age - sex



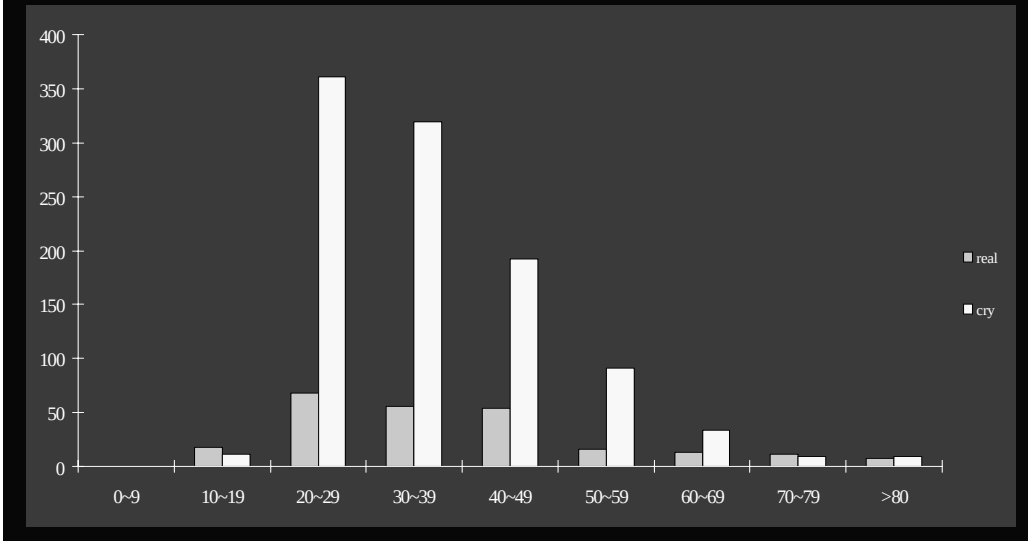
Acute intoxicaties - BAG

Intentional poisoning N = 2827 = 85.5 %

- **Major products:**
  ethanol: 51 % **benzodiazepines: 20 %**
  illicit drugs: 5.7 % **antidepressants: 4.7 %**
- **Number of products / patient: 2.4**
- **Real suicidal attempt: 17 % Cry for help: 83 %**
- **NOT the first attempt: 62 %**

Acute intoxicaties - BAG

Intentional poisoning: real suicide - cry for help



Acute intoxicaties - BAG

Intentional poisonings N = 2827 = 85. 5 %

- **if pharmaceuticals were used**

  38 % was not prescribed for the patient

  62 % was prescribed (GP - Psychiatrist)

if pharmaceuticals were prescribed

20 % was started < 1 month before

49 % < 6 months before

suicidal attempt - previous therapy ?

43 % no 57 % yes

Acute intoxicaties - BAG

Intoxicatieregister Spoedgevallendienst U.Z. K.U.Leuven (B):
1-1-1993 - 31-7-1996 N=3306

- **Symptomen:**

	accidentele	intentionele
nihil	25%	13,5%
CZS depressie	63%	84%
CZS+AH+CV depressie	4%	2,5%

- **Outcome: overlijden voor of bij opname in de SPGD**
  N = 7 (intentionele): 2 x methanol ; 2 x paraquat;
  2 x organofosfaten ; 1 x white spirit

Acute intoxicaties - BAG

B - Poisoning registry Leuven 1-1-93 - 31-7-96

- **death = found dead, dead on arrival at the ED, dead in spite of intensive treatment (CPR, antidotes, ...)**
  N = 7 2 x methanol 2 x paraquat
  2 x organophosphates 1 x white spirit

- **death = dead from late complications indirectly related with the poisoning**
  N = 8 1 x organophosphates
  3 x benzodiazepines 4 x ethanol

B - Poisoning registry Leuven 1-1-93 - 31-7-96
Death due to intentional poisoning

N = 15 / 2827 = 0,53 % **median age = 43 yrs** **13 men 2 women**

- **Chemicals :**
  death caused by the poison itself : nature of product, quantity taken, delay ingestion-medical support
  = paraquat, cholinesterase-inhibitors, methanol **LOS = 3,7 d**
- **Ethanol :**
  death caused by concomitant pathology - trauma lesions following fall, road accidents, ... - due to alcohol (mean BAL = 2,43 g/L) induced risky behaviour **LOS = 6,7 d**
- **Benzodiazepines :**
  death caused by medical complications and comorbidity - coma, hypothermia, aspiration, pneumonia, rhabdomyolysis, compartment syndrome, renal insufficiency, MOF, sepsis - and delay ingestion-medical support **LOS = 4,27 d**

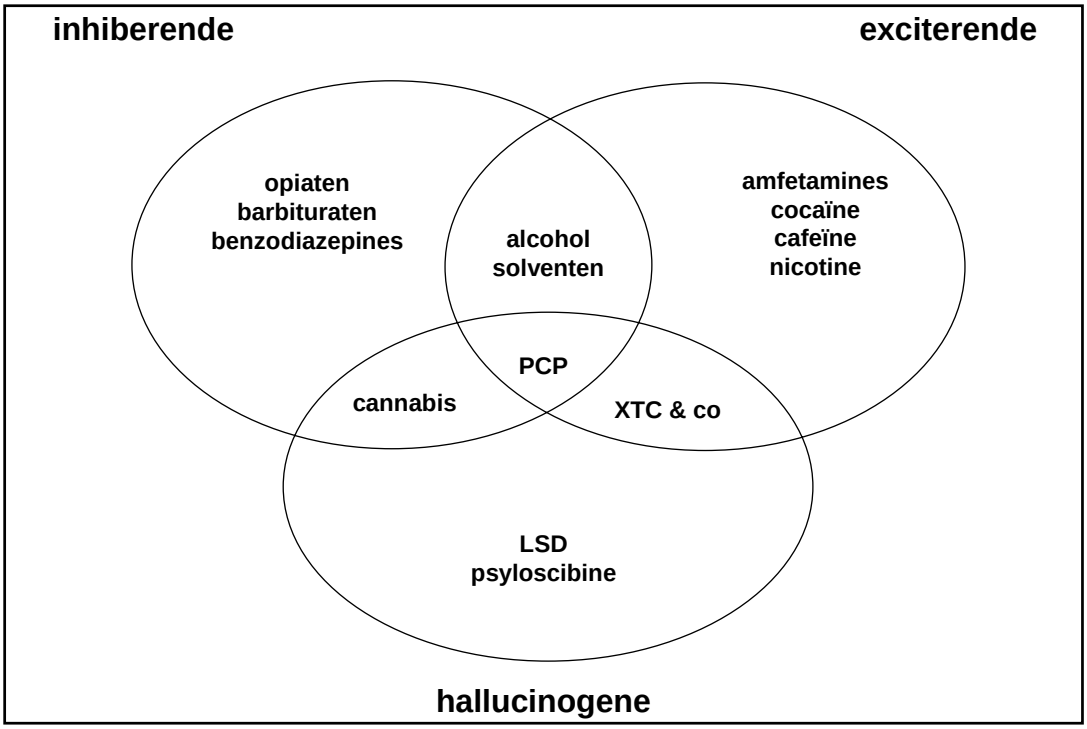
Belgian Toxicology and Trauma Study :
A study on the presence of alcohol, medicines and illegal drugs in <u>drivers</u> who were victim of a <u>traffic accident</u> and the relationship between these substances and the accidents

- **16-1-95 - 15-6-96**
- **UZ RUGent, UZ KULeuven, UZ VUBrussel CHR Namur, CHU Liège**
- **drivers (motorized vehicles + bikes) - traffic accident victims - > 14 yrs - primary admission - > 24 hrs hospital stay or death - severe trauma**
- **N = 2053** **n = 0,81 / hospital / 24 h**
- **men = 74%** **women = 26%**
- **14-24 yrs = 34%** **+ 65 yrs = 10%**

Wat is een drug ?

- elke enkelvoudige of samengestelde stof die, zonder ernstige reden ingenomen, de gevoelens, het waarnemingsvermogen, het gedrag en het bewustzijn kan wijzigen en die direct of op lange termijn schadelijk kan zijn voor het individu en/of de maatschappij

- soorten: 3 grote groepen



Belgian Toxicology and Trauma Study (BTTS)
15-1-1995 - 15-06-1996 N = 2053

- **28% BAC > 0,5 pro mille**

  2/3 van deze 28% BAC > 1,5 pro mille

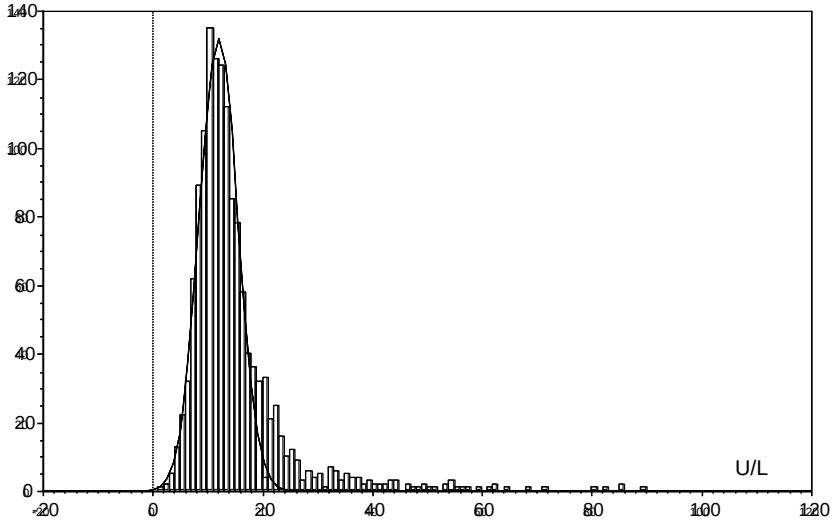
  1/3 van deze 28% BAC > 2 pro mille

- **8,5% benzodiazepines**

  7,5% opiaten

  6% cannabis

Frequency distribution of CDT (U/L) values for men BTTS



men

The objective of assessment of the poisoned patient is:

- **to identify the need for live-saving intervention**
- **to confirm a diagnosis of poisoning**
- **to identify the poison or poisons**
- **to anticipate the development of toxic features**
- **to determine the prognosis in respect of the time course and outcome**
- **to assess its psychiatric seriousness**

Patient is
- conscious
- aware of the possibility of being intoxicated
- co-operative

1. **supportive therapy for vital functions if necessary**
2. **history : what ? how much ? way of exposure ? time of exposure ? symptoms developped since exposure**
3. **clinical evaluation, biochemical and toxicological investigation, aiming at**
   - **confirmation or negation of diagnosis**
   - **estimation of seriousness of intoxication**
   - **formulating a prognosis**
4. **start therapy**
   - **stop the absorption of the toxic agent**
   - **elimination**
   - **eventually antidotes**

Patient is
- **unconscious**
- **not aware of the possibility of being intoxicated**
- **not co-operating**

Diagnosis of poisoning = “detective work”

1. **awareness – suspicion**
2. **clinical evaluation aiming at the composition of a toxidrome**
3. **biochemical and toxicological investigation to confirm the clinical suspicion**

Diagnosis of poisoning according to Sherlock Holmes

1. Awareness - suspicion = recognition of the risk

Circumstances which stand for intoxication until the contrary has been proven

- **history of suicide or psychiatric pathology**
- **coma e causa ignota**
- **cardiac arrythmia in patients < 40 yrs**
- **victims of fire**
- **metabolic acidosis**
- **lethargy or coma in children**
- **heterogenic symptomatology without a clear uniform clinical diagnosis**

Diagnosis of poisoning according to Hercule Poirot

2. **History**

   (directed search via family, ambulance crew, GP, …)

- **Patient related factors**
  - **to which substances had the patient access ?**
  - **which medication has been prescribed to the patient or other family members ?**
  - **gender, age and related social-cultural, work or leisure conditions (epidemiology)**
  - **history of the event**
  - **past medical history and risk factors in the patients health**

Diagnosis of poisoning according to Hercule Poirot

2. **History**

   (directed search via family, ambulance crew, GP, …)

- **Circumstantial evidence**
  - **poison containers**
  - **suicide notes**
  - **location of the patient found**
  - **absence of personal identifying items …**
- **Circumstance related factors**
  - **environment**
  - **demographic / social factors (local epidemiology)**

Diagnosis of poisoning according to Agatha Christie

3. Clinical evaluation aiming at the composition of a toxidrome

Why : acute toxicology theorems

- **routine biochemical and haematological investigations rarely suggest a diagnosis of acute poisoning**
- **an unexpected dissociation between typically paired changes (BP ↓ and pols ↑) points to only a few toxicologic etiologies**
- **a single or isolated symptom or sign is seldom of diagnostic value; clinical features tend to occur in clusters; constellations of symptoms and signs are of diagnostic value since clusters tend to occur consistently with particular toxins.**

These clusters of symptoms and signs

=

toxic symptom complexes

=

TOXIDROMES

(Mofenson and Greensher, 1974)

=

pathognonomic fingerprints of a group of products or poisons

Toxidromes

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

anticholinergic syndrome

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

Toxidromes

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

cholinergic syndrome

Cholinesterase – inhibiting insecticides (organo-phosphates, carbamates), amanita-mushrooms

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 arrhytmia, hypertension, hyperthermia, hyperperistalsis, dry mouth

sympathomimetic syndrome

Cocaine, caffeine, amphetamines, decongestiva (ephedrine, epinephrine), sympaticomimetics, aminophylline

Toxidromes

nausea, vomiting, tinnitus, transpiration, hyperpnea, vasodilation

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

serotoninergic syndrome

Sentraline, Paroxetine, Fluoxetine, L-Tryptophan and drug combinations as MAO-inhibitors with L-Tryptophan or Paroxetine and dextro-methophan

How ? Systematic almost algorhythmic clinical assessment of organs and systems

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**
   - **coma : Glasgow Coma Scale : EMV … / 15**
   - **fasciculations (OP), myoclonus (chloralhydrate)**
   - **exitation à convulsions (TCAD, CO, ethanol, phenothiazines, …)**
   - **hyper / hyporeflexia**

2. **Pupil diameter**
   - **myosis (opiates, OP, phenothiazines)**
   - **mydriasis (anticholinergics, amphetamines, TCAD, …)**
   - **blurred vision (quinines, methanol, ethyleenglycol, …)**

Clinical assessment

3. **Respiration**
   - **Breathing pattern**
     - **hyperpnea (resp. freq.↑ and/or resp. volume ↑)**
       = Kussmaul respiration = correction metabolic acidosis (KUSMALE)
     - **superficial breathing (resp. freq.↑ and resp. vol. ↓)**
       (deep coma, OP, curarisation)
     - **breathing depression (resp. freq. ↓ and resp. vol.↓)**
       (opiates)
   - **Lung auscultation**
   - **Breath odour**

Clinical assessment

4. **Heart and circulation**
   - **ECG : arrhythmias / conduction abnormalities**
     (amphetamines, CO, digitalis, cocaine bêta-blocking agents, quinine, TCAD, …)
   - **CVP (vasodilation – intravascular volume deficit)**
   - **blood pressure : hypotension**
     hypertension (amphetamines, cocaine, sympaticomimetis)

5. **Gastro-intestinal system**
   - **Vomiting – diarrhoea (Fe, Hg-salts,OP, mushrooms, colchicine, …)**
   - **hypo- / hyperperistalsis**

COMMON TOXIC CAUSES OF CARDIAC ARRHYTMIA

Amphetamine	**Phenol**
Arsenic	**Phenothiazines**
Carbon monoxide	**Physostigmine**
Chloral hydrate	**Propranolol**
Cocaine	**Quinine, quinidine**
Cyanide	**Succinylcholine**
Digitalis	**Theophylline**
Dinitrophenols	**Tricyclic antidepressants**

Clinical assessment

6. **Body temperature**
   - **hypothermia** (ethanol, barbiturates, coma with vasodilation)
   - **hyperthermia** (salicylates, phenothiazines, butyrophenons, amphetamines, …)

7. **Diuresis**
   - **prerenal kidney insufficiency** (coma with dehydration)
   - **acute tubular necrosis** (diquat, Hg-salts, …)
   - **rhabdomyolysis** (CO,ethanol, barbiturates, …)

8. **General examination**
   - **injection points, petechia, bullae**
   - **icterus, methaemoglobinemia-cyanose**
   - **compartment syndrome**

COMMON TOXIC CAUSES OF HYPERTHERMIA

Acetylsalicylic acid
Amphetamines
Anesthetics (induction)
Arsenic
Butyrophenones
Cadmium (oxide)
Coffee
Cinchopheen
Cobalt (oxide)
Convulsants
Curares
Copper
Dinitrocresol
Dinitrophenol
Hexachlorophenol
IMAO
Imipramines
Lead (oxide)
Nickle (oxide)
Pentachlorophenol
Phenothiazines
Theophylline
Tin
Xanthines
Zinc (oxide)

Systematic clinical assessment

=

the key for recognition

dissociation between usually paired changes + **Σ abnormalities in organ function**

the key for toxidrome recognition

classifying the toxin

Het diagnostisch protocol

3. Biochemische en RX-onderzoeken

3.1. Routine labo

BGW - glycemie - electrolyten - ureum - creatinine

* aniongap [(Na^++ K^+) - (Cl^- + bicarbonaat)]

A.G. > 13 = High aniongap acidose

KUSMALE

* osmolaliteit

osmotic gap = gemeten - berekende osmolaliteit = > 10

||

$$2 \times Na^+ + \frac{Glyc}{18} + \frac{Ureum}{6}$$

3.2. RX thorax - RX abdomen enkel

Het diagnostisch protocol

4. Toxicologische investigaties

- Kwalitatieve / Kwantitatieve resultaten

  ↓ ↓

  urine bloed

  maagvocht speeksel

  oogvocht

  = hulpmiddel ter bevestiging van de klinische diagnose
- Toxicologische qualitatieve drugscreening
- Toxicologische drugmonitoring

Advies:

Betrouw op klinisch oog en oordeel. Start steeds supportieve therapie zonder wachten op resultaten van toxicologische analyses. Behandel de patiënt, niet de druglevel.

Toxidrome use

1. **Key for the diagnosis of a poisoning**
   Key for the start of the specific treatment
   (decontamination – antidote – elimination)
2. **Allows assessment of severity and evolution**
3. **Allows determination of the appropiate LOS – observation period – observation area in the ED**
4. **Allows increasing efficiency of laboratory use by ordening tests only for the clinically suspected drugs**
   = decrease of the number of unnecessary tests = cost effectiveness effect
5. **Education**
   f.i. 5 most commonly seen intoxications in the ED
   5 where toxidrome recognition = avoidable death

Toxidromes pittfalls

No toxidrome = No poisoning ? NO

1. **No toxidrome "yet"**

   = delayed toxicity or delayed toxidrome

   → delayed onset of toxicity (f.i. symptom free interval of acetaminophen poisoning)

   → delayed deterioration (f.i. malathion, parathion versus fenthion, dimethoate : immediate versus gradual and late onset of symptoms)

   mechanisms :

   - delayed absorption of the toxin (cfr. composition of the toxic agent – dose – concentration – route of administration – environmental factors)

   - distribution factors

   - metabolic factors

   - cellular and organ capacity effects (f.i. state of health – medication – age – maturity)

Toxidromes pittfalls

2. **No toxidrome "at all"**

   - very mild intoxication

   - very serious intoxication with immediate fatal issue

   - symptom free interval

   Paracetamol Paraquat

   Hydrocarbons

Toxidromes pittfalls

3. **One toxidrome in a multiple compound ingestion**

f.i.

toxidrome (1) of TCAD – history of only a TCAD intake – ready for dismission
toxidrome (2) of β-blocker – denial of intake

f.i.

toxidrome of TCAD – acetominophen ingestion not mentionned

Toxidromes pittfalls

4. **One patient with simultaneous disorders**

f.i.

an accident victim may have the accident because of an overdose (ethanol, drugs, …)
(1/3 of major trauma victims BAC > 0.5 pro mille)

f.i.

a psychiatric patient with an overdose may have a head trauma

f.i.

a patient with an overdose may develop an acute episode of diabetic ketoacidosis

Toxidromes pittfalls

5. **A toxidrome with a “missing” sign or an “inexpected” symptom**

f.i. organophosphate poisoning

= bradycardia versus tachycardia

02 depletion **nicotinic effect**

Therapeutisch protocol

“Primum non nocere”

1. **Ondersteunende therapie**
2. **Stoppen van verdere absorptie van het toxisch agens**
3. **Bevorderen van de eliminatie van het toxine**
4. **Antidota**

(mortaliteit < 1%)

Therapeutisch protocol

1. Supportieve therapie

1.1. Vrije ademweg

– **stabiele zijligging**

– **OTT/NTT zo: GCS < 8/15 - shock**

1.2. Kunstmatige ventilatie zo:

coma, hypercapnie of hypoxie, shock

+ hyperventilatie tot pCO2 ± 32 mm Hg als alkalose = proteïnegebonden fractie ↑ en vrije toxische fractie ↓

1.3. Circulatie

= optimale orgaanperfusie onder monitoring ECG, CVD, BD ...

= R/ correctie circulerend volume, inotropie, ...

1.4. Correctie lichaamstemperatuur

Therapeutisch protocol

2. Vermijden verdere absorptie toxisch agens

2.1. Evacuatie van de maaginhoud

2.1.1. Emesis

- ***spontaan***
- **mechanische faryngeale stimulatie**
- **medicamenteuze inductie = Ipecac**

Absolute contraïndicaties:

- **gedaald bewustzijn**
- **inname van een caustische stof**
- **de aard van de ingenomen stof laat een snel optreden van neurologische symptomen veronderstellen**
- **ingestie van koolwaterstof**

Relatieve contraïndicaties:

- **baby's minder dan 6 maanden oud**
- **oude of verzwakte personen met verhoogd risico op aspiratie**
- **gevorderde zwangerschap**
- **zware cardiale of respiratoire aandoening of ongecontroleerde hypotensie**

Therapeutisch protocol

2. Vermijden verdere absorptie toxisch agens

2.1. Evacuatie van de maaginhoud

2.1.2. Maaglediging - maagspoeling

- **effectiviteit = relatief aan**
  - **aard van het toxine**
  - **dosagevorm**
  - **hoeveelheid toxine**
  - **latentietijd**
  - **lavagetechniek**
- **Fauchersonde**
  Trendelenburg + Li zijde
  kinderen : NaCl 0,9% 15 ml/kg/cyclus
  volwassenen : 200-400 ml/cyclus
- **Contraïndicaties: cfr. emesis**

Cave: GCS < 8 ! eerst OTT / NTT

POSITION STATEMENT: IPECAC SYRUP

SYRUP OF IPECAC SHOULD NOT BE ADMINISTERED ROUTINELY in the management of poisoned patients. In experimental studies the amount of marker removed by ipecac was highly variable and diminished with time. THERE IS NO EVIDENCE FROM CLINICAL STUDIES THAT IPECAC IMPROVES THE OUTCOME OF POISONED PATIENTS AND ITS ROUTINE ADMINISTRATION IN THE EMERGENCY DEPARTMENT SHOULD BE ABANDONED. There are insufficient data to support or exclude ipecac administration soon after poison ingestion. Ipecac may delay the administration or reduce the effectiveness of activated charcoal, oral antidotes, and whole bowel irrigation. Ipecac should not be administered to a patient who has a decreased level or impending loss of consciousness or who has ingested a corrosive substance or hydrocarbon with high aspiration potential.

Journal of Toxicology, Clinical Toxicology, volume 35 (7), 1997

(The official journal of the American Academy of Clinical Toxicology and the European Association of Poisons Centres and Clinical Toxicologists)

Includes the AACT/EAPCCT position statements on gastrointestinal decontamination

POSITION STATEMENT: GASTRIC LAVAGE

GASTRIC LAVAGE SHOULD NOT BE EMPLOYED ROUTINELY IN THE MANAGEMENT OF POISONED PATIENTS. **In experimental studies, the amount of marker removed by gastric lavage was highly variable and diminished with time. There is no certain evidence that its use improves clinical outcome and it may cause significant morbidity. GASTRIC LAVAGE SHOULD NOT BE CONSIDERED unless a patient has ingested a potentially life-threatening amount of a poison and the procedure can be undertaken within 60 minutes of ingestion. Even then, clinical benefit has not been confirmed in controlled studies. Unless a patient is intubated, GASTRIC LAVAGE IS CONTRAINDICATED if airway protective reflexes are lost. It is also contraindicated if a hydrocarbon with high aspiratioin potential or corrosive substance has been ingested.**

Journal of Toxicology, Clinical Toxicology, volume 35 (7), 1997

(The official journal of the American Academy of Clinical Toxicology and the European Association of Poisons Centres and Clinical Toxicologists)

Includes the AACT/EAPCCT position statements on gastrointestinal decontamination

Therapeutisch protocol

2. Vermijden verdere absorptie toxisch agens

2.2. Adsorptie door actieve kool

- **Actieve kool = onoplosbaar zwart poeder**
  "pyrolyse" organisch materiaal - "activated"
- **Adsorptie-efficiëntie = afhankelijk van**
  - adsorptieoppervlakte > 1500 m2/gr
    poriëngrootte 10 Å $\leftrightarrow$ 100 Å
  - farmaceutische formule:
    watersuspensie - droog/donker bewaren - geen additieven
  - aard van de stof die moet geadsorbeerd worden:
    goede - middelmatige - slechte adsorptie
  - hoeveelheid toegediende actieve kool:
    R/ 10 x hoeveelheid ingenomen produkt
    = 1 gr / kg / lichaamsgewicht
  - (de maag pH + voedsel in maag)
  - de stabiliteit van het kool-toxinecomplex

Adsorption of drugs and other substances to activated charcoal in vitro

Well adsorbed: Alfatoxins, Amphetamine, Antidepressants, Antiepileptics, Antihistamines, Atropine, Barbiturates, Benzodiazepines, B-blocking agents, Chloroquine and primaquine, Cimetidine, Dapsone, Dextropropoxyphene and other opioids, Digitalis glycosides, Ergot alkaloids, Frusemide, Glibenclamide and glipzide, Glutethimide, Indomethacin, Meprobamate, Nefopam, Phenothiazines, Phenylbutazone, Phenylpropanolamine, Piroxicam, Quinidine and quinine, Strychnine, Tetracyclines, Theophylline

Moderately adsorbed: Aspirin and other salicylates, DDT, Disopyramide, Kerosene, benzene and dichlorethane, Malathion, Many 'high dose' non-steroidal anti-inflammatory drugs, e.g. tolfenamic acid, Mexiletine, Paracetamol (acetaminophen), Polychlorinated biphenyl-compounds, Phenol, Syrup of ipecacuanha, Tolbutamide, Chlorpropamide, carbutamide, tolazamide.

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

Therapeutisch protocol

Stoppen van verdere absorptie van het toxisch agens

Besluit

- uit het milieu verwijderen
- "spoelen" van de huid
- spontaan braken
- ~~emesisinductie~~
  ~~maagspoeling~~: uitz.: cyaniden, ethanol, ethyleenglycol, ijzer, lithium, methanol
  activated charcoal: 1 gr/kg lichaamsgew.

  CAVE: caustische slokdarmverbrandingen

Therapeutisch protocol

3. Eliminatie van het toxisch agens

“elk” product heeft “zijn” meest effectieve + efficiënte methode

3.1. Kunstmatige ventilatie

3.2. Geforceerde diurese

3.3. Hemodialyse-hemoperfusie

3.4. Wisseltransfusie

3.5. Repetitieve doses actieve kool

Therapeutisch protocol

3. Eliminatie van het toxisch agens

3.1. Kunstmatige ventilatie
- stoffen die via de AH geëlimineerd worden
- gewilde respiratoire alkalose-inductie

TOXINS PULMONARY ELIMINATED

Aceton
Alcohols
Benzeen
Carbon monoxide
CCL_4
Chloroform
Cyanide
Ethanol

Ether
Ether
Fluothane
Fuel
Menthol
Methanol
Solents
Trichlorethyleen
Xyleen

Therapeutisch protocol

3. Eliminatie van het toxisch agens

3.2. Geforceerde diurese

- **indicaties: barbituraten, salicylaten, bromiden, alcoholen, amfetamines, lithium, paraquat**
  = zeldzaam
- **mechanisme: GFR doen ↑ , tubulaire reabsorptie doen ↓**
  = f (vrije fractie toxine)
  (wateroplosbaarheid toxine)
  (hoeveelheid vloeistof tubuli)
  (urine pH)
- **3 L + electrolyten i.v./4-6 u max 12 L/24 u**
  onder vochtbalans/CVD
- **contraïndicaties : NI - cardiaal falen**
- **+ aanzuren**
  + alkalinisatie

Therapeutisch protocol

3. Eliminatie van het toxisch agens

3.3. Hemodialyse-hemoperfusie

- **Indicaties dialyse**
  - **primair :**
    lithium, bromiden, methanol, ethyleenglycol, glycolen
  - **secundair : bij NI, hoge ‰ alcohol, hypothermie**
    ! MG <1500
    klein distributievolume
    lage proteïnebinding
- **Hemoperfusie :**
  - **op koolfilter**
  - **op resinepartikels**

3.4. Wisseltransfusie

Therapeutisch protocol

3. Eliminatie van het toxisch agens

3.5. Repetitieve doses actieve kool mechanisme

- **onderbreking van de entero-hepatische cyclus**
- **onderbreking van de entero-enterische cyclus**
- **ondervangen van het desorptiefenomeen**

- **indicaties:**

  theophyline, digitalis, dapsone, phenytoine, cyclosporines, methotrexate, phenobarbital, meprobamaat, benzodiazepines, bêtablokkers, ...

- **0,5 gr/kg lichaamsgewicht / 4-6 u**

Brand – brandwonden - antidotum ?

? → CO-intoxicatie : O_2
? → CN-intoxicatie : Hydroxocobolamin

BWZ ↘ of confusie + roetneerslag
+ + +
BP ↘ à shock RR ↘ à apnee lactaat-acidose
+ cardiopulmonary arrest

R/ Cyanokit® (Hydroxocobalamin)

SNRI

Serotonin noradrenaline re-uptake inhibitors
(Prozac®, Seroxat®, Serlain®, Cipramil®, …)
Serotonin Syndrome
Cardiovascular shock – respiratory failure
Convulsions – cardiac rhythm disturbances
HYPERTHERMIA
Death

R/ aggressive treatment
anti shock therapy O2 fluids
COOLING ice
sedation-narcosis-curarisation - artificial ventilation

! + 42° C → < 39.5° C
20’

Therapeutisch protocol

4. Antidota

Werkingsmechanisme

1. **Binding aan het toxisch agens om aldus een niet-toxisch complex te vormen**
2. **Neutralisatie van het toxisch agens of zijn metaboliet**
3. **Competitieve inhibitie door receptorbinding, waardoor verhinderd wordt dat het toxisch agens zich met de receptor bindt**
4. **Ofwel werken ze als een fysiologisch antidotum**

Therapeutisch protocol

Antidota te voorzien voor prehospitaalgebruik

O2	**CO - Cyaniden**
Alcohol 94°	**Methanol - Ethyleenglycol**
Atropine	**Organofosfaten**
(Naloxone	**Opiaten)**

Intoxicatie met TCAD

Ritmestoornissen / convulsies

1. G.I. decontaminatie
= actieve kool 1 gr/kg/lichaamsgewicht
2. Antidota
= Nabicarbonaat
3. Eliminatie
= repetitieve doses actieve kool

+ SUPPORTIEVE THERAPIE
(met hyperventilatie zo coma → respiratoire alkalose-inductie)

Intoxicatie met Methanol

Hyperpnee ; metabole acidose ; AG + OG

1. G.I. decontaminatie
= maagspoeling met 20 L
2. Antidota
= Ethanol i.v. tot bloedspiegel ethanol = 1 ‰
= Nabicarbonaat i.v.
= folinezuur
3. Eliminatie
= geforceerde diurese
= hemodialyse

+ SUPPORTIEVE THERAPIE

CO-intoxicatie

CO ontstaat door onvolledige verbranding van organische stoffen en is een geurloos en niet-irriterend gas

Bronnen van koolstofmonoxide zijn:

1. kachels met onvolledige ventilatie / slechte rookevacuatie
2. gaswaterverwarmers
3. industriële rook
4. onvolledige verbranding van wagenbrandstof
5. rook van alle soorten brand
6. tabaksrook
7. inhalatie van methyleenchloride (verfverwijders) die door de lever in CO worden gemetaboliseerd
8. gesloten anesthesiecircuit met desflurane of isoflurane

CO-intoxicatie

Registratie door de Belgian Poison Control Centre

- **1995 : 1036 gevallen - 1678 slachtoffers**
- **1996 : 948 gevallen - 1614 slachtoffers**
  54 overleden : 14 (20-29 jaar)
  8 (70-79 jaar)
  6 (10-19 jaar)
- **1999 : 634 gevallen - 1229 slachtoffers**

CO-intoxicatie

Factoren die het risico op CO intoxicatie beïnvloeden:

1. Socio-economische status

- **slechte behuizing:**

  slechte verluchting (indien aanwezig) - gebrek aan onderhoud - onvoldoende verluchting van de kamer - onjuist gebruik van de installatie

- **indicatoren:**

  1986: nationaliteit - status van de bewoner (eigenaar, huurder) - ouderdom van het huis

  1991: welzijn van een familie gecorreleerd met de beschikbare leefruimte per persoon

Project voor de toekomst:

- **incident "cartografie"**
- **incident "geografie" (selectieve voorkomingsmaatregelen)**

CO-intoxicatie

2. Meteorologische invloed

Gas boiler	Kolenkachel
cyclonale storing (regen)	hoge barometerdruk boven
lage barometerdruk	Midden-Europa
hoog barometerdrukverschil in de regio	klein barometerdrukverschil in de regio
hoge windsnelheden en	lage windsnelheden
bewolking	klein vertikaal/horizontaal luchtbeweging
lage visibiliteit	lage visibiliteit
hoge relatieve vochtigheid	hoge relatieve vochtigheid

Voertuiggerelateerde CO-intoxicatie:

- **gesloten garages / passagierscompartiment van de auto**
- **voornaamste oorzaken: slecht verluchtingssysteem - inademing van uitlaatgassen in verkeersopstopping - open ramen tijdens verkeersopstopping in een tunnel**

CO-intoxicatie

- **Diagnosestelling = moeilijk**
- **Symptomen = niet karakteristiek / niet specifiek**
- **Diagnose:**
  1. **ingegeven door de omstandigheden**
  2. **meerdere leden van eenzelfde familie / groep met identieke symptomen**
- **Systematische COHb screening van alle opnames in SPGD ?**
- **Sleutels voor snelle diagnose:**
  1. **zorgvuldige en volledige anamnese**
  2. **hoge achterdocht**
- **Anamnese moet gericht zijn op:**
  1. **symptoomgerichte screening**
  2. **screening van risicofactoren**
  3. **epidemiologische gegevens van de plaatselijke situatie**

CO-intoxicatie

- **neurologische symptomen**:

  hoofdpijn - slaperigheid - agitatie - prikkelbaarheid - verwardheid - duizeligheid - epilepsie - hyperreflexie - gezichtsstoornissen - ataxie - doofheid - paresthesie - hyporeflexie - coma - e.a.
- **cardiologische symptomen**:

  angor - hartkloppingen - aritmieën - infarct
- **andere symptomen**:

  nausea - braken - diarree - abdominale pijn - zweten - hyperventilatie - angst - koorts e causa ignota

Hyperbaric Oxygen Therapy:

HBO

if symptoms before or at the moment

of admission

Therapy:

1. removal from the source

2. 100 % of oxygen

3. 100 % of HBO until COHb < 5 %

Neurologic sequelae:

Triade: **- mental deterioration**
- urinary incontinence
- galt disturbance

Intervallum lucidum = 2 - 40 days

Psychiatric sequelae:

- affective incontinence syndrome
- intellectual deterioration with memory impairment

Special risk groups - HBO:

1. **known cardiovascular history**

2. **pregnant women**
   HBO 5 times longer with NBO intervals

[COHb] f = f ([COHb] m + fetal production CO)
steady state: [COHb] f = 10-20% x [COHb] m
fetal equilibration: 36-48 hours
mean [COHb] f >>> mean [COHb] m

t 1/2 [COHb] m = 2 hours
t 1/2 [COHb] f = 7 hours

R/ HBO time in pregnancy: x 5