Poisoning

• Acute or chronic damage caused by endogenous or exogenous substances
Causes

• Accidental
• Overdose
• Suicidal
• Violent
Statistical data

- Call for the ambulance: 15-20 %
- Female: male = 2:1
- Age: 20-40 years
- Toxins
  - 80-90 % drug
    - 85 % sedative (1/3), anxiolytic (2/3)
    - Alcohol + drug
- Reason
  - Suicidal: 80-90%
  - 10-15% accidental
  - 5% industrial
Contamination

- Gastrointestinal (oral)
- Inhalation
- Dermal
- Parenteral (iv narcotics, dope!)
Therapy I.

• Prehospital
  • General practitioner
  • Ambulance
    – Task:
      » Stabilizing of the vital parameters
      » Start the decontamination
      » Diagnosis
      » Decision about hospitalization

• LIMITATION: within the bounds of possibility
Therapy II.

• Hospital: **EMERGENCY UNIT**
  • Task:
    – Stabilizing of the vital functions
    – Reaching the diagnosis
      » toxicology tests: gastric lavage, vomitus, serum, urine
      » Laboratory tests: electrolyte, renal function, liver function, haemostasis, urine
    – Detoxication
    – Decision making
      » Transmit the patient (ICU, Psychiatry)
      » Home
  • Limitation: **TIME**
Intensive Care Unit

- Altered mental status
  - Intubation needed
  - Cerebral hypoperfusion, hypoxia (hypotension, arrhythmias)
  - Trauma (subdural haemorrhage)
- Cardio-respiratory system: unstable
  - Monitoring, DC, pacemaker, respiratory therapy
- Cardiopulmonary depressive substances
- Lethal dose
  - extracorporeal detoxication
Possibilities for detoxication

• Decontamination
  – Washing the surface with water
  – Gastric lavage
  – Activated charcoal
  – Forced diuresis

• Antidote

• Extracorporeal
Gastric lavage

- AMS_intubation
- 200 mls fluid
- Active charcoal (perforation, ileus, AMS!!!)

Contraindications!!!
- Acids or alkaline
## Poisons and antidotes

<table>
<thead>
<tr>
<th>Poison Type</th>
<th>Antidote</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzodiazepine</td>
<td>Flumazenil</td>
</tr>
<tr>
<td>Beta blocker</td>
<td>Glucagon</td>
</tr>
<tr>
<td>Digitalis</td>
<td>Digibind</td>
</tr>
<tr>
<td>CCB</td>
<td>Calcium-chlorid</td>
</tr>
<tr>
<td>Ethyleneglycol</td>
<td>Ethanol</td>
</tr>
<tr>
<td>Methanol</td>
<td>Ethanol</td>
</tr>
<tr>
<td>Opiates</td>
<td>Naloxone</td>
</tr>
</tbody>
</table>
Extracorporeal detoxication
Hemodialysis
(diffusion, osmosis)

Patient

Dialysate fluid

ultrafiltrate
Hemodialysis
Hemodialysis
Hemodiafiltration

Convective transport
Hemodialysis
osmosis, diffusion
HEMOPERFUSION

- Active charcoal capsule - absorption
Plasmapheresis

- Protein binding substances
Plasmapheresis
Examples for the management of a patient with acute intoxication in the Emergency Department

1. The patient with antihypertensive (ACEI) intoxication
2. Digitalis intoxication
3. Altered mental status-antidepressants
4. Intoxication with benzodiazepines
ACEI- mechanism

**VASOCONSTRICTION**
- ALDOSTERONE
- VASOPRESSIN
- SYMPATH. tone
- Angiotensinogen
- Angiotensin I
- Angiotensin II

**VASODILATATION**
- PROSTAGLANDIN
- tPA
- Kininogen
- Kallikrein

**A.C.E.**
- Inhibitor

**ANGIOTENSIN II**

**BRADYKININ**
- Kininase II
- Inactive Fragments
Symptomatic heart failure

Asymptomatic left ventricular dysfunction
- LVEF < 35 - 40 %

High cardiovascular risk

Hypertension

Cardiomyopathies (HCM, DCM)

ACEI indications

AHA / ACC HF guidelines 2001
ESC HF guidelines 2001
Decreasing mortality with ACEI

<table>
<thead>
<tr>
<th>Study</th>
<th>ACE-i</th>
<th>Disease</th>
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</thead>
<tbody>
<tr>
<td>CONSENSUS</td>
<td>Enalapril</td>
<td>CHF</td>
</tr>
<tr>
<td>SOLVD treatment</td>
<td>Enalapril</td>
<td>CHF</td>
</tr>
<tr>
<td>AIRE</td>
<td>Ramipril</td>
<td>CHF</td>
</tr>
<tr>
<td>Vheft-II</td>
<td>Enalapril</td>
<td>CHF</td>
</tr>
<tr>
<td>TRACE</td>
<td>Trandolapril</td>
<td>CHF / LVD</td>
</tr>
<tr>
<td>SAVE</td>
<td>Captopril</td>
<td>LVD</td>
</tr>
<tr>
<td>SMILE</td>
<td>Zofenopril</td>
<td>High risk</td>
</tr>
<tr>
<td>HOPE</td>
<td>Ramipril</td>
<td>High risk</td>
</tr>
</tbody>
</table>
ACE-i

Mortality %

n = 2006
St p AMI

Placebo

Ramipril

p = 0.002

months

Lancet 1993;342:821
Mortality\%  

Placebo  
n=1116  

Captopril  
n=1115  

\( p = 0.019 \)  

\( \% - 19\% \)  

n = 2231  
3 - 16 nap post AMI  
EF < 40  
12.5 --- 150 mg / day  


SAVE
ACEI

% Mortality

n = 2589
CHF
- NYHA II-III
- EF < 35


SOLVD (Treatment)

Enalapril
n=1285

Placebo
n=1284

p = 0.0036

months
<table>
<thead>
<tr>
<th>Drug</th>
<th>Bioavailability</th>
<th>Metabolism</th>
<th>Excretion</th>
<th>HD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benazepril</td>
<td>27 %</td>
<td>yes</td>
<td>urine</td>
<td>no</td>
</tr>
<tr>
<td>Captopril</td>
<td>70 %</td>
<td>yes</td>
<td>urine</td>
<td>35 %</td>
</tr>
<tr>
<td>Cilazapril</td>
<td>70 %</td>
<td>yes</td>
<td>urine</td>
<td>15 %</td>
</tr>
<tr>
<td>Enalapril</td>
<td>40 %</td>
<td>yes</td>
<td>Urine/stool</td>
<td>40 %</td>
</tr>
<tr>
<td>Fosinopril</td>
<td>35 %</td>
<td>yes</td>
<td>Urine/stool</td>
<td>no</td>
</tr>
<tr>
<td>Lisinopril</td>
<td>50 %</td>
<td>yes</td>
<td>urine</td>
<td>&lt;25 %</td>
</tr>
<tr>
<td>Perindopril</td>
<td>65 %</td>
<td>yes</td>
<td>urine</td>
<td>no</td>
</tr>
<tr>
<td>Quinapril</td>
<td>60 %</td>
<td>yes</td>
<td>Urine/stool</td>
<td>no</td>
</tr>
<tr>
<td>Ramipril</td>
<td>60 %</td>
<td>yes</td>
<td>urine</td>
<td>yes</td>
</tr>
<tr>
<td>Trandolapril</td>
<td>40 %</td>
<td>yes</td>
<td>Urine/stool</td>
<td>No data available</td>
</tr>
</tbody>
</table>
ACEI Toxicology

- rare
- Mostly mild symptoms

Management
- Lavage, charcoal
- In case of hypotension
  - iv. NaCl
  - Chatecholamines
  - Colloids
- Forced diuresis
- HD
Na\(^+\)\(+\) K\(^+\) K\(^+\) Na\(^+\) Na\(^+\) Ca\(^++\) Ca\(^++\) Na-K ATPase Na-Ca exchanger Myofilaments contractility Digitalis
N Engl J Med 1997;336:525

DIG study

Mortality %

Placebo
n=3403

Digoxin
n=3397

p = 0.8

N=6800
NYHA II-III

N Engl J Med 1997;336:525
Toxicology

• Symptoms
  – Gastrointestinal
    • Nausea, vomitus, diarrrhoea
  – Neurological
    • Vertigo, dizziness, blurred vision
  – Heart
    • Palpitation, arrhythmia (VT, VF, SVT), syncope
  – Laboratory findings
    • Serum digoxin, Potassium, Mg, GFR!
 – ECG
    ST-depression, bradycardicy, ventricular arrhythmias: bigeminy AV-block, VT,
 – atrial tachycardia + block
Management

- Hyperkalaemia Resonium
  - Glucose-inzulin
  - Calcium
  - Bicarbonate
- Avoid calcium
- Controlling of Ca, Mg
- AV block:
  - Atropin, pacemaker
- Arrhythmia (VT)
  - Phenytoin, lidocain
- Gastrointestinal decontamination
- Forced diuresis
- HD: no
- HP: yes
- Digibind
Tricyclic antidepressants

- 1959: imipramin (Melipramin)
- 1961: amitriptylin (Teperin)
- Michon et al: first case report in 1959
- 50 % of all suicidal cases
- Main problem: prescription
- Lehal outcome: 15 %
Mechanism of action of tricyclic antidepressants

- Presynaptic neuron
- Biogenic amines (NE + 5HT)
- Synaptic cleft
  - Release
  - Reuptake
- TCAs
- Postsynaptic neuron
- Receptor
Tricyclic antidepressants

- Effect (norepinephrine, serotonine, dopamine reuptake inhibitor)
  - Cardiovascular (within 24-48 hours)
    - Hypotension (alpha blockade)
    - Arrhythmias (cholinergic blockade-reentry, automaticity)
    - Myocardial toxicity
    - Pulse generation and conduction disorders
  - Neurological
    - Coma, AMS
    - Convulsion-generalized
    - Hyperthermia
  - Other
    - Urine retention
    - Ileus
    - ARDS
Asystole, paroxysmal AV block, Sinus arrest
Management

- Gastrointestinal decontamination
  - Total absorption is more than 8 hours
  - Active charcoal (50 g)
- Forced diuresis: no
  - HD
    - Ineffective, strong plasma protein binding
    - High distribution
  - HP
    - Ineffective: high distribution
- Na-bicarbonate
  - tissue acidosis – myocardium
- Antidote: cholinesterase inhibitor-physostigmin
  - May increase the onset of arrhythmias
- Monitoring!!!
Benzodiazepines

• Sedato-hypnotic effects, myorelaxant, anxiolytic, anticonvulsive
• 1955: chlordiazepoxide (Elenium, Librium)
• 1963: diazepam (Seduxen)
• 3000 types of benzodiazepines, 30 used as medicine
• 500 million tablets/year
Benzodiazepines

- Pharmacokinetics
  - Rapid absorption
  - Bioavailability: 70-100 %
  - >90% plasmaproteine binding, only the free is active
  - Renal excretion under 1%
  - postsynaptic neuron: increased GABA-erg activity
BZD-Toxicity

• **Symptoms**
  – Sedation, lethargy, headache, fatigue, sleepiness, sopor, coma

• **Therapy**
  – Gastrointestinal decontamination
  – Active charcoal
  – Forced diuresis no
  – Extracorporeal: no
  – **Antidote: flumazenil** (Anexate)
Altered mental status
GLASGOW COMA SCALE

Eye opening
4. Spontaneous
3. To speech
2. To pain
1. None

Verbal response
5. Oriented conversation
4. Confused speech
3. Inappropriate words
2. Incomprehensible sounds
1. None

Motor response
6. Obeys simple commands
5. Localized pain
4. Withdraws (normal flexion)
3. Stereotyped flexion
2. Stereotyped extension
1. None
## Organic brain syndrome

<table>
<thead>
<tr>
<th></th>
<th>Delirium</th>
<th>Dementia</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Onset</strong></td>
<td>Rapid</td>
<td>Slow</td>
</tr>
<tr>
<td><strong>Pattern</strong></td>
<td>Fluctuating</td>
<td>Fluctuating or stable</td>
</tr>
<tr>
<td><strong>Oriented</strong></td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Attention</strong></td>
<td>Disordered</td>
<td>Normal</td>
</tr>
<tr>
<td><strong>Cognition</strong></td>
<td>Disordered Impaired</td>
<td>Impaired</td>
</tr>
<tr>
<td><strong>Speech</strong></td>
<td>Incoherent</td>
<td>Perseveration</td>
</tr>
</tbody>
</table>
• ALZHEIMER’s DISEASE
• PICK’s DISEASE
• EXTRAMYRAMIDAL SYNDROMES WITH SUBCORTICAL DEMENTIA (M. Parkinson)
• MULTIPLE-INFANT DEMENTIA
• VIRUSES AND OTHER INFECTIOUS AGENTS (Creutzfeld, Syphilitic, HIV, TBC etc.)
• TOXIC AGENTS (heavy metal, dug abuse)
• METABOLIC DISORDERS (dialysis, hypothyreoidism, porphyria, uraemia, hepatic encephalopathia)
• VITAMIN DEFICIENCY (Vit. B12, Folate)
• CNS STRUCTURAL CHANGES (hydrocephalus)
• PSYCHIATRIC DISORDERS (SCH, MDS)
OBS – Common causes of delirium

- **DRUG INDUCED**: anticholinergics, narcotic analgesics, sedatives, hypnotics, corticosteroids, histamin blockers, antibiotics, etc.
- **INFECTION**: pneumonia, sepsis, meningitis
- **FLUID AND ELECTROLYTE IMBALANCE**: dehydratation, hypoglycaemia/hyperglycaemia, hyponatraemia
- **DRUG WITHDRAWAL**: alcohol, narcotics
- **CNS DISTURBANCES**: seizures, CVA,
- **PYCHIATRIC DISEASE**: sensory deprivation, depression, mania
- **OTHER CAUSES**: vasculitis, collagen vascular disease
OBS – ID management

1. Search and correct life-threatening causes
2. Discover and treat the underlying cause of delirium
3. Protect patient while diagnostic evaluation and therapy proceed
Thank you for your attention!