Toxicological emergencies

Acute Poisoning

Slightly less than 1 per 1000 exposed/intoxicated patients dies (this number is higher for intensive care patients, ~ 0.2-4%)

Acute poisoning

Circa 1 person per 1000 decease

Although, who will it be?

Under-estimation ↔ over-estimation of an intoxication

Under-estimation caused by symptoms not present at admission:

- absorption takes time e.g.; extended release medicines, such as theophylline, lithium, tricyclic antidepressants, calcium- or beta blockers
- distribution to target organ takes time
- metabolism to active metabolite takes time

acute clinical toxicology = emergency care

Recognition of primary effects in order to prevent or to reduce secondary effects

Initial evaluation of patient

- Short orientation on exposure and medical history
- Physical examination
- Laboratory analysis
- Additional diagnostic procedures

But first of all check vital signs

- Airway
- Circulation
- Neurological disability
- Temperature
**Assessment respiration**

- Is the airway at risk?
- Efficacy of breathing? (is the patient's blood being oxygenated?)
- Pattern of breathing?
  - Rate: increased / decreased?
  - Type: shallow, irregular

**Assessment circulation**

- Pulse?
- Rhythm?
- Blood pressure?
- Capillary refill?

**Neurological assessment**

- Ataxia, tremor, unable to stand
- Depression or stimulation CNS?
- Assess level of consciousness
  - Glasgow Coma Scale
- Seizures?
- Determine: pupil size
  - pupil reactivity on bright light

**Hyperthermia**

- Muscular hyperactivity or hyper-rigidity?
- Increased metabolic rate?
- Impaired thermoregulatory mechanisms?
  - Anticholinergic medicines
  - Antihistamines
  - Cyclic antidepressants
  - Salicylates
  - Hallucinogens
  - Sympathomimetic drugs
Hyperthermia

- Serotonin syndrome (tremor, restlessness, increased muscle tone)
- Monoamine oxidase (MAO) inhibitors in combination with serotonin re-uptake inhibitors
- Tricyclic antidepressants
- Amphetamines
- Neuroleptic malignant syndrome (rigidity, autonomic dysfunction
- Antipsychotic drugs or withdrawal dopaminergic agents

Laboratory analysis

Objective: to investigate whether or not vital functions are threatened

- Coma → hypoglycaemia, carbon monoxide, cyanide?
- Administer always glucose and oxygen
- Electrolyte disturbances?
- Liver / kidney damage?
- Acid-base disturbances?

Laboratory analysis

- Hb, Ht, leukocytes
- Blood gas, lactate
- Electrolytes
- Glucose
- Creatinine, urea (BUN)
- Creatine
- Liver enzymes (yGT, AF, ASAT, ALAT)
- Anion gap
- Osmol gap
- Take additional blood- and urine samples for specific analyses, such as toxicological analyses

Acute poisoning

After initial evaluation an extensive investigation of the patient is needed

- Exposure and medical history
- Extended physical examination
- Specific laboratory analysis
- Additional diagnostic procedure

Acute poisoning

- Start with supportive care
- Prevent absorption
  - Gastric lavage (ingestion < 1h)
  - Activated charcoal (ingestion < 1h)
- Whole bowel irrigation (especially relevant in extended release medicines)
- Increase elimination e.g.
  - Extracorporeal elimination?
  - Haemodialysis
  - Hemoperfusion
  - MARSH
- Antidotes?
- Pacemaker?
- Aortic Balloon Pump?
- Extracorporeal life support (to support circulation and/or respiration)?

Acute poisoning

- Exposure and medical history
- Patient’s age (some organ functions are less adequate, e.g. kidney function)
- Patient’s body weight
- Name of product/compound
- Concentration/dose (calculate dose/kg)
- Duration of exposure
- Time of ingestion/exposure
- Observed symptoms in chronological order
- Therapy instituted so far
Acute poisoning

Thorough physical examination
“From the head to the toes”
Confirm the suspected diagnosis
Detect the unsuspected

However, be aware of
- Ingestions of more than one compound at the same time
- Underlying medical problems
- Maintenance medications for chronic diseases
- Secondary organ failure (e.g. kidney and/or liver failure)

Acid-base disturbances

Basics:
- Arterial pH
  - Normal range: 7.35 to 7.45
  - Acidosis: < 7.35
  - Alkalosis: > 7.45

- Disturbances
  - Respiratory: change in pCO2
  - Metabolic: change in HCO3

Acid-base disturbances

Osmol gap (most frequently caused by)
- Acetone
- Ethanol
- Ether
- Ethylene glycol
- Glycerine
- Isopropyl alcohol
- Mannitol
- Methanol
- Severe hyperlipidaemia
- Severe proteinuria
- Ketoacidosis
- Lactate acidosis

Osmol gap (difference between the calculated and measured osmolality)

\[
\text{Calculated osmol} = 2 \times [Na^+] + \frac{[glucose]}{18} + \frac{[BUN]}{2.8}
\]

\[
\text{[Na^+] in mEq and [glucose] and [BUN] in mg/dL}
\]

Normal value: 275-300 mosm/kg

Anion gap = cations - anions
- \([Na^+ + K^+] - [Cl^- + HCO_3^-] \)

All concentrations in mEq

Normal value: 9 - 12 mEq/L

Anion gap (most frequently caused by)
- Lactate (seizures)
- Ketoacidosis
- Salicylates
  - Salicylates, ketones, lactic acid
- Ethanol
- Acetate
- Methanol, formaldehyde
- Formic acid
- Ethylene glycol
- Glycolate, oxalate
- Formaldehyde
- Toluene
- Ammonium chloride
Acid-base disturbances

Osmol Gap / Anion Gap
methanol poisoning

Toxicological analysis

Specific toxicological analyses are needed to evaluate the clinical situation:
- To confirm the diagnosis of poisoning when in doubt
- To determine the cause of the Osmol and/or Anion gap
- To plan therapeutic interventions
  - Antidotes
  - Extracorporeal removal methods (e.g., hemodialysis)
- To plan re-institution of maintenance therapy
- Declaration of brain death
- For forensic reasons

Toxicological analysis

Important for screening at emergency department to determine initial strategy:
- Amphetamines
- Barbiturates
- Cannabis
- Cocaine
- Tricyclic antidepressants
- Ecstasy (MDMA, MDA, etc.)
- Opiates

Additional diagnostic procedures

- X-ray

Additional diagnostic procedures

- Electrocardiogram (ECG)
- Electroencephalogram (EEG)
Perform always an ECG

Consider IC-admission

Seizures e.g.:
- amphetamine, anticholinergic medicines, buproprion, carbamazepine, cocaine, insulin, carbon monoxide, LSD, lithium, lead, parathion, propranolol, theophylline, INH, phenothiazine, quetiapine, strychnine, tricyclic antidepressants

Hyperthermia e.g.:
- amphetamine, amphetamine derivatives, anticholinergic medicines, cocaine, 2,4-dinitrophenol, LSD, pentachlorophenol, salicylates, serotonin syndrome, malign neuroleptic syndrome

Consider IC-admission

Realise, hypotension \(\rightarrow\) shock is frequent present in intoxicated patients
- Recognise hypotension
  - low blood and pulse pressure
  - capillary refill decreased
  - unrest
  - alertness decreased
  - diuresis decreased
  - acid-base disturbances
- Initial treatment
  - fluid resuscitation
  - dopamine/noradrenaline
  - ‘air goes in and out’, oxygen is O.K.
  - consider whether an antidote is available?

Consider IC-admission

Prominent ECG changes following some relevant intoxications

<table>
<thead>
<tr>
<th>Broadening QRS-complex</th>
<th>P-interval prolongation</th>
<th>QT-interval prolongation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Digitalis 1a and 1c</td>
<td>Beta-blockers</td>
<td>Classical 1a antiarrhythmic agents (e.g. quinidine, procainamide)</td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>Clozapine</td>
<td>Amiodarone</td>
</tr>
<tr>
<td>Cocaine</td>
<td>Haloperidol</td>
<td>Sotalol</td>
</tr>
<tr>
<td>Hydroxychloroquine</td>
<td>Metoprolol</td>
<td>Diltiazem</td>
</tr>
<tr>
<td>Antihypertensives</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tricyclic antidepressants</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


Consider IC-admission

Metabolic acidosis e.g.:
- cocaine, cyanide, ethanol, ethylene glycol, medicines inducing seizures, iron, isoniazid (INH), metformin, methanol, salicylates.
- Intoxication with these agents and if metabolic acidosis is present than it concerns a severe intoxication

Rhythm disturbances e.g.:
- amphetamines, amphetamine derivatives, ß-blockers, calcium blockers, clonidine, chloral hydrate, clonidine, chlorothiazide, cocaine, fluoride, phystostigmine, heart glycosides (digitalis), carbon monoxide, phenothiazines, lithium, quinidine, quetiapine, tricyclic antidepressants.

Consider IC-admission

Initial changes in digoxin, ß-blocker or calcium channel blocker poisoning

<table>
<thead>
<tr>
<th>Initial changes</th>
<th>ß-blocker</th>
<th>Calcium blocker</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mental changes</td>
<td>decreased</td>
<td></td>
</tr>
<tr>
<td>Respiratory</td>
<td>increased</td>
<td>decreased</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>decreased</td>
<td>decreased</td>
</tr>
<tr>
<td>Serum electrolytes</td>
<td>increased</td>
<td>decreased</td>
</tr>
<tr>
<td>Urine output</td>
<td>increased</td>
<td>decreased</td>
</tr>
<tr>
<td>Allergies</td>
<td>increased</td>
<td>decreased</td>
</tr>
<tr>
<td>ECG findings</td>
<td>increased</td>
<td>decreased</td>
</tr>
<tr>
<td>Seizure</td>
<td>no effect</td>
<td>decreased</td>
</tr>
<tr>
<td>Severe AV block</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Hypotension</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Temperature</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Respiratory</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Bradycardia</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Hypertension</td>
<td>x</td>
<td>x</td>
</tr>
</tbody>
</table>
Therapeutic interventions in digoxin, ß-blocker or calcium channel blocker poisoning

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Digoxin Fab</th>
<th>ß-blocker</th>
<th>Calcium blocker</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ascorbic acid</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Calcium ions</td>
<td>++</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Glucagon</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Catecholamines</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Intravenous glucose</td>
<td>++</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Phosphate ester solution</td>
<td>+</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Pacemaker</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Lipid emulsion</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Aorta balloon pump</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Extracorporeal life support (ECLS)</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

- not indicated; + advocated; ++ strongly advocated

Therapeutical interventions in cocaine or tricyclic antidepressants (tca’s) poisoning

<table>
<thead>
<tr>
<th>Therapy</th>
<th>cocaine</th>
<th>tricyclic antidepressants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium bicarbonate i.v.</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Magnesium i.v.</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Potassium i.v.</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Lidocaïne i.v.</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Benzodiazepine</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Pacemaker</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Lipid infusion (lipid recue therapy)</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Aorta balloon pump</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Extracorporeal life support (ECLS)</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

- not indicated; + advocated; ++ strongly advocated

Important to realise, the following steps are important:

- Exposure
- Absorption
- Bioavailability
- Target organ
- Changes in target organ
- Intoxication

Biokinetik and bidynamics

Casus:  
- Presentation of symptoms and diagnostic procedures  
- Diagnosis  
- Therapy  
- Take home messages

Casus 1:  
- 12 h before admission, ingested 96 tab of 500 mg acetylsalicylic acid
- Presentation ED ward  
  - unrest, aggressive to ED personnel  
  - transpiration  
  - respiratory rate 22/min  
  - heart rate 110/min, blood pressure 110/90 mmHg  
  - temp 36.9 ºC

Man 39 y
What is your strategy?
- You wait because the patient is stable and can be admitted to the general internal ward?
- Sedation for unrest?
- Observation at ICU, and interfere when the patient deteriorates?
- Other suggestions?

Casus 1
Man 39 y
- Activated charcoal was not administered
- Sedation was started for unrest
- Respiratory rate was slightly increased (26/min)
- Following respiratory alkalosis, arterial pH turned to normal values
- Bicarbonate was not administered
- Salicylic acid concentration gradually decreased
- Haemodialysis was not initiated because the patient was stable

Physician’s conclusion: the patient is improving

Salicylic acid poisoning:
- Early symptoms:
  - fever, dizziness, nausea, hyperventilation, vomiting, diarrhoea
- Severe intoxication:
  - high fever, mental disturbances, seizures, brain oedema, coma, non-cardiac long oedema, respiratory failure, kidney failure, heart failure, vasodilatation, shock, death

Casus 1
Man 39 y
- Following 32 h the patient was comatose
- His clinical condition deteriorated within a short period; high fever, long oedema, respiratory, kidney failure, metabolic acidosis
- Patient was intubated, and mechanical ventilation was initiated
- Preparation for acute haemodialysis was initiated
- Despite supportive therapy the patient suddenly died in a deep shock

What had happened?

Salicylic acid poisoning:
- When acidosis increases plasma concentration of unionised salicylic acid increases

Diffusion of unionised salicylic acid into the cells is facilitated; severity of intoxication increases, also in the brain

When unionised salicylic acid is elevated distribution volume increases, therefore salicylic acid plasma concentration can decrease while clearance is not increased
- distribution volume normally ca. 0.16 L/kg,
- in case of an intoxication increase to 0.34 L/kg

Lab results
<table>
<thead>
<tr>
<th>constituent</th>
<th>normal range</th>
<th>hours after hospitalisation</th>
</tr>
</thead>
<tbody>
<tr>
<td>creatinine</td>
<td>0.6-1.2 mg/dL</td>
<td>1.21 1.52 2.16</td>
</tr>
<tr>
<td>potassium (K)</td>
<td>3.8-4.8 mEq/L</td>
<td>4.4 4.0 3.5 3.4 2.9</td>
</tr>
<tr>
<td>glucose</td>
<td>60-140 mg/dL</td>
<td>132 123 119 104 110</td>
</tr>
<tr>
<td>pH art</td>
<td>7.36-7.44</td>
<td>7.54 7.47 7.46 7.41</td>
</tr>
<tr>
<td>pCO2</td>
<td>34.5-45.8 mm Hg</td>
<td>30.8 31.5 27.8 32.3 31.5</td>
</tr>
<tr>
<td>HCO3-</td>
<td>23-27 mEq/L</td>
<td>25.8 23.0 19.7 20.1</td>
</tr>
<tr>
<td>anion gap</td>
<td>9 -12 mEq/L</td>
<td>17 20 21 23 17 16</td>
</tr>
<tr>
<td>salicylic acid</td>
<td>0 mg/L</td>
<td>1040 810 590</td>
</tr>
<tr>
<td>pH urine</td>
<td>&gt;9</td>
<td>8.5 5.5</td>
</tr>
<tr>
<td>ketones in urine</td>
<td>none</td>
<td>4+ 4+ #</td>
</tr>
</tbody>
</table>

* The intoxication occured 12 h before
† Measured with test strip: 4+ = high level of ketones

Casus 1

Management of salicylic acid poisoning

- Increase plasma pH by sodium bicarbonate i.v. (pH > 7.5 and < 7.6)
  - Goal is to reduce unionised salicylic acid concentration
- i.v. infusion of fluids and vasopressors
- Administer glucose (e.g. adults 100 mL of 50 %) in case of mental disturbances to prevent brain hypoglycaemia
  - Even when plasma glucose concentration is adequate
  - Glucose metabolism in brain is intensively increased
- Haemodialysis

Casus 1

Salicylic acid poisoning

- Salicylic acid plasma conc. toxic > 250 mg/l
- Symptoms are generally present > 400 mg/L ( > 2.9 mmol/L)
- Patient’s plasma concentration: 1040 mg/L
- Nomogram is based on:
  - Ingestion of one dose
  - Blood sample is drawn at 6h after ingestion
  - Nomogram underestimates toxicity in severe acidosis or chronic exposure
  - Clinical symptoms moderately correlates with plasma concentration

Casus 1

Management of salicylic acid poisoning

- Alkalosis by respiratory alkalosis is not a contra-indication for the administration of sodium bicarbonate i.v.
- Increase urine to pH (7.5 to 8.0) to increase salicylic acid excretion
- Normal elimination halftime (T½) 2-4.5 h
- In poisoned patients T½ increases to 24 h or even more as in this patient

Casus 1

Perform always haemodialysis if:

- Salicylate excretion decreases due to kidney failure
- Neurotoxicity increases
- Lung or brain oedema arises
- When bicarbonate infusion causes fluid overload
- Plasma salicylate concentration >1000 mg/L (>7.2 mmol/L)
- When the patient deteriorates while aggressive and optimal supportive treatment is provided

Casus 1

Take home messages

Salicylic acid intoxication

- Evaluate frequently patient’s clinical condition
- Determine frequently blood gas and salicylic acid concentration
- Start early with bicarbonate infusion
- In case of acidosis, unionised salicylic acid concentration distribution volume ↑ toxicity ↑
- Toxicity moderately correlates with plasma concentration
- Don’t wait too long to start haemodialysis
- Starting up haemodialysis takes time
Casus 2

Male 41 y
- Medical history: epilepsy following temporal lobe resection for mesial-temporal sclerosis
- Maintenance medication:
  - carbamazepine 5 dd 400 mg orally
  - phenytoin 2 dd 200 mg orally
- Fell from bicycle
- no circulation
- reanimation started
- ECG: ventricle fibrillation
- Following defibrillation recovery of circulation
- Transported to hospital

Casus 2 Lab analyses
- Blood gas paCO2 38 mmHg, paO2 72 mmHg,
- pH 7.47
- bicarbonate 28 mmol/L = 28 mEq/L
- Na+ 141 mmol/L = 141 mEq/L
- K+ 4.0 mmol/L = 4.0 mEq/L
- Cl− 109 mmol/L = 109 mEq/L
- Mg2+ 0.97 mmol/L = 1.94 mEq/L
- Urea (BUN) 10.4 mmol/L = 29.1 mg/dL
- creatinine 87 µmol/L = 0.98 mg/dL
- Total Bilirubin 32 µmol/L = 12.6 µg/mL
- Bilirubin direct 18 µmol/L

Casus 2 Management
- ECG:
  - PQ-time 166 msec
  - QRS time 98 msec
  - QTc-time 461 msec
  - antero-lateral ST-segment elevation suggestive for myocardial infarction
- Percutaneous coronary intervention (PCI) → stenosis in LAD → stent in LAD
- No traumatic injuries on CT scan present

Casus 2 Management
- Therapeutic hypothermia for 36 h at 36°C
- Neurological recovery good
- 3 days after admission again ventricular fibrillation
  - bolus of amiodarone 300 mg i.v.
  - amiodarone 300 mg/day i.v. via continuous infusion

Casus 2 Management
- 5 Days after admission → coma: E1M1V1
  - Phenytoin concentration
    - 11.8 mg/L total (therapeutic: 8-18 mg/L)
    - 3.29 mg/L (28%) unbound (therapeutic: 0.9-2 mg/L)
  - Carbamazepine concentration:
    - 27.4 mg/L total (therapeutic: 4.5-9 mg/L)
    - 10.9 mg/L (40%) unbound
  - ECG:
    - PQ time 178 msec
    - QRS time 144 msec
    - QTc 449 msec

Casus 2 Management
- 5 Days after admission → coma: E1M1V1
  - Phenytoin concentration
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  - ECG:
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    - QRS time 144 msec
    - QTc 449 msec
Casus 2
Carbamazepine toxicokinetics
- Unbound fraction is increased at toxic levels
- \( T_{1/2} \) 5-20 h in therapeutic range
- In this patient:
  - \( T_{1/2} 81.3 \text{ h} \) without haemodialysis
  - endogenous clearing was decreased by amiodarone
  - Amiodarone and/or desethyl amiodarone inhibit CYP1A1, CYP1A2, CYP2D6, and also by CYP1A2, CYP2C9
  - \( T_{1/2} \) 6.5 h following haemodialysis in combination with activated charcoal treatment
  - \( T_{1/2} \) 10.3 h activated charcoal alone

Casus 2
Carbamazepine toxicity
- Neurologic:
  - CNS depression to coma
  - Paradoxal convulsions
- Respiration:
  - Depression of ventilation
- Heart:
  - Prolongation of ventricular conduction
  - Rhythm disturbances (ventricular tachycardia or fibrillation)
- Electrolyte disturbances

Casus 2
Management carbamazepine poisoning
- Activated charcoal
  - 100 g
  - 50 g every 4 h (interrupt entero-hepatic circuit)
  - Whole bowel irrigation (for extended release tablets)
  - No antidote available
  - Extracorporeal elimination enhancement?
  - Haemoperfusion versus haemodialysis?

Casus 2
Management carbamazepine poisoning
- Extraorporeal removal is useful if
  - It concerns a severe intoxication
  - Relative molecular mass <500 D
  - Compound is water soluble
  - Small volume of distribution (Vd <1 L/kg)
  - Poorly bound to plasma proteins
  - Preferable single compartment kinetics
  - Low endogenous clearance (<4 ml/kg/min)
  - Extracorporeal elimination is not to risky for the patient

Casus 2
Management carbamazepine poisoning
- Carbamazepine is lipophilic
- In therapeutic range protein binding (70-80%)
- In our patient protein binding < 60%
- Molecule weight 236
- Vd 0.8 tot 1.9 L/kg adults; Vd 1.2 tot 3.5 L/kg children
- \( T_{1/2} \) in therapeutic range is 5 to 36 h

Casus 2
Management carbamazepine poisoning
- High flux haemodialysis (HF-HD)
  - filter Fresenius Helsion FX1000,
  - blood flow 350 mL/min,
  - dialysate flow 500 mL/min,
  - ultrafiltration rate 120 mL/h,
  - ultrafiltration coefficient 75 mL/(h mmHg)
- Symptomatic treatment

Casus 2

Carbamazepine concentrations in this patient

- Few hours after haemodialysis patient was awake
- ECG:
  - PQ time: 168 msec
  - QRS time: 90 msec
  - QTc time: 441 msec
- Treatment for intercurrent pneumonia with antibiotics
- Difficult weaning from mechanical ventilator
- Discharge to general ward after 19 days

Casus 2

Take home messages

- Interaction with other medicines may cause a severe intoxication
- Following toxic oral doses absorption is delayed
- T1/2 at toxic concentrations is decreased
- At toxic concentration protein binding is decreased
  - high flux haemodialysis is a good alternative for haemoperfusion
  - CVH is a less good alternative
- Following extracorporeal elimination ‘rebound’ of plasma concentration may occur! CVH may prevent rebound
- Realise that carbamazepine in overdose can paradoxically cause seizures

Questions?

- As you can cover, my NNT
- "Patient" foofoofoo