## Toxology

**Vital Functions**

- Bradycardia (PACED)
- Hypertension (CRASH)
- Tachycardia (FAST)
- Hypotension (C-SCAN)
- Hypothermia (COOLs)
- Seizures (OTS SCAMPELL)
- Tonicity of Cones

### Emesis

**Central stimulation:**

- Apomorphine

**Central & peripheral:**

- Syrup of ipecac.

**Plant alkaloids:**

- Emetine
- Cephaline

**Dosage:**

- Early vomiting: within (30 minutes)
- Late vomiting: after one additional 30 minutes

**Contraindicated with:**

- Organo phosphates
- Iron
- Corrosives

### Gastric lavage

- Insertion of tube into stomach and washing it with water & saline.

**Amount & composition of fluid:**

- 10 ml/kg (300 ml/kg) of 0.9% saline - up to 400 ml for adults.
- Continue lavage till clear (1000mL).

**Rationale:**

- Tachycardia

### Activated charcoal

**Indication:**

- Is combination of organic material & intended to increase surface area (1000 - 2000 cm<sup>2</sup>)

**Dosage:**

- 0.25 - 0.5 g/kg/1-2 hr (oral)
- 0.25 - 0.5 g/kg/hr (NGT)

**Procedure:**

- It is administered by nasogastric tube or orally.
- The solution is administered at a rate of:
  - 0.5 L/hr in children <5 years
  - 1.2 L/hr for adults.

**Contraindicated with:**

- Organo phosphates
- Iron
- Corrosives

### Whole bowel irrigation

**Indication:**

- Consists of using surgical bowel-cleansing solution polyethylene glycol (PEG), 60 g in a balanced isotonic electrolyte salt solution.

**Dosage:**

- Sodium bicarbonate
- Mg sulphate
- NaHCO<sub>3</sub>, Na sulphate

**Procedure:**

1. End point when the stools are clear

### MDAC (Gut dialysis)

**Indication:**

- 1. Drug remaining in the gut for long time:
  - Sustained release preparation: Theophylline,
  - Concretions: bile, cholesterol, calcium carbonate
  - Slow ing of thiocyanate: sodium thiosulphate
  - 2. Substances with EHC: Digitals, TCA, salicylates

**Dosage:**

- 0.25 - 0.5 g/kg/1-2 hr (oral)
- 0.25 - 0.5 g/kg/hr (NGT)

**Procedure:**

- It is achieved by alkalinisation of fluid in GIT with increase intraluminal bulk of fluids, activates GIT motility leading to propulsion of GIT contents.

**Contraindicated with:**

- Carbimazole
- Carbamazepine
- Dextrose
- Drugs not metabolized to more toxic drugs

### 2) KIDNEY

**PH alteration & forced diuretics**

**Procedure:**

- PO 1ml/kg loading dose then 0.5ml/kg/4hrs to maintain level at 100mg/dl
- 10 mg/kg for children & 0.1 mg/kg for infants (6 months & 2 y.)

**Indication:**

- Plasma exchange to remove large molecules & substance not indicated

- Acetaminophen (oral)

- 0.25 - 0.5 ml/kg/1-2 hr

**Contraindicated with:**

- If vomiting does not occur after 30 minutes, the dose is repeated.
- If no vomiting, gastric lavage should be carried out to remove secretes from the stomach (emetic is cardioactive component).

### 3) BLOOD

**Indication:**

- Use the same as hemodialysis but for toxins characterized by:
  - 1) Drug remaining in the gut for long time
  - 2) Peritoneal dialysis

**Contraindicated with:**

- Amphetamines
- Barbiturates & benzodiazepine

### Plasma Exchange & Phasmaphoresis

**Indication:**

- Replacement of plasma with protein solution
- Plasma exchange / Plasma phasmaphoresis

**Contraindicated with:**

- Methanol
- Ethanol
- Cyanide

### Chelation

**Contraindicated with:**

- Methanol
- Ethanol
- Cyanide

### Hemoperfusion

**Indication:**

- The same as hemodialysis but for toxins characterized by:
  - Hepatic compromise
  - Altered mental status

**Contraindicated with:**

- Methanol
- Ethanol
- Cyanide

### Antidotes

**Poison**

- Organophosphates
- Acetaminophen
- Opioids
- Alcohol
- Anticholinergics
- TCA, Cocaine, Salicylates

**Antidote**

- Atropine
- N-acetyl cysteine
- Digoxin
- Naloxone
- N-acetyl cysteine
- Sodium bicarbonate
- Flumazenil
- Flumazenil
- Oximetry
- Sodium bicarbonate

**Dose**

- Initial atropine dose (IV or IM) 2-3 mg (adult) 0.05mg/kg (child) Dose can repeated every 10 min. till Chvostek or Achilles response appears.
- Loading dose of 140 mg/kg followed by 70 mg/kg q4h for 17 additional dosages, giving a total of 72 hrs of therapy.
- If dose ingested in known No. of vials is ingested X 0.81
- 0.4 - 2 mg (max 10mg/min) / 0.01/kg (child) IV, IM
- 0.2 mg/kg/3-5 min. (max. dose: 5mg)
- 15 mg/kg/hr slow IV infusion (max. 60 min) or disappearance of rise in color of urine.
- Deep BHF city solution, 2.5 mg/kg/dose/4-6h for 2 days, then/12h for 7 days.

**Coma Coach**

1. Dextrose
2. Oxygen
3. Naloxone
4. Pure opioid antagonist, used for reversal of acute intoxication
5. Diagnostic and therapeutic
6. Deficiency: Wernicke’s encephalopathy

**Rational:**

- Heparinization common cause of LIOC
- DSW (50 % 100cc IV) or D5SW 2-4cc/kg in pedds

**Deficiency:**

- Oximetry: Toxins: insulin, oral hypoglycemic, ETOH, salicylates
- Non-tox: sepsis, hypothermia, hepatic failure, myocardial infarction

**Cautions:**

- Diabetic or hyperosmolar pts, cerebral infarct
- Toxicity of agent of delayed toxicity
- Hepatic compromise
- Altered mental status

**Substances poorly absorbed:**

- Acetaminophen
- Alcohol
- Methanol

**Dialyzable (LET ME SAV P)**

- Paracetamol
- Ethanol
- Oxygen

**Dialyzable drugs**

- Lithium
- Ethylene glycol
- Methanol

**Dialyzable drugs to metabolized to more toxic drugs**

- Methanol
- Ethylene glycol
- Paracetamol

**Caution & concomitant drugs**

- Sodium bicarbonate
- Sodium bicarbonate
- N-acetyl cysteine
- Sodium bicarbonate

**GIT decontamination**

- Not indicated in Ethanol because it’s absorbed rapidly

**References:**

- FOMSCU Lectures & Osama R. El Ghannam’s Book.
### Muscarinic "Cholinergic" actions (DUMBELLSS)

1. Diarrhea
2. Urination
3. Miosis
4. Bradycardia, Hypotension
5. Bronchospasm, Wheezes
6. Bronchorrhea
7. Pulm. edema
8. Ectropion
9. Lacrimation
10. Salivation
11. Skin sweating & subnormal temp.

**Examples:**
- Organophosphate
- Carbamate

### Adrenergic actions

1. Hypertension, Tachycardia
2. Hyperthermia, Tachypnea
3. Mydriasis
4. Diaphoresis
5. Excessive motor activity
6. Excessive speech
7. Tremors
8. Hyperactive bowel sounds.

### Toxidromes

**Muscarinic actions**

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### Anti-Cholinergics

**Peripheral manifestations:**
- Dry mucous membranes
- Hot, dry, flushed skin
- Hyperthermia
- Sinus tachycardia (early & most reliable sign of muscarinic receptor block)
- Markedly dilated pupils & blurred vision.
- Urinary retention (palpable urinary bladder).
- Bowel sounds are hypoactive or absent.

**Examples:**
- Belladonna alkaloids (Atropine, Scopolamine)
- Antipsychotics (Chlorpromazine)
- Cyclic antidepressants (Amitriptyline)
- Antihistamines (Chlorpheniramine)
- Local mydriatics (Cyclopentolate)
- Antispasmodics (Clidinium bromide)
- Antiparkinsonian medications (Biperiden)
- Plants & mushrooms (Atropa belladonna, Datura stramonium, Amanita muscaria)

### Nicotinic actions (MMAATCH)

1. Mydriasis
2. Muscle weakness & paralysis
3. Adrenal medulla activity is increased, leading to: T&H
4. Tachycardia
5. Cramps of skeletal muscles
6. Hypertension

**Examples:**
- Organophosphate

### Opioids

1. Mental status depression
2. Miosis (PPP)
3. Respiratory depression (slow rate & shallow resp.)
4. Decrease bowel sound
5. Bradycardia
6. Hypothermia

**Examples:**
- Opium
- Morphine
- Heroin

### Sedative Hypnotics

1. Mental status depression
2. Delirium, confusion, Hallucination & coma
3. Slurred speech, Blurred vision & diplopia
4. Ataxia, Nystagmus
5. Hypotension
6. Bradycardia

### CNS manifestation of cannabis

- Increased appetite
- Altered consciousness; perceptual distortions; memory impairment; occasional illusions and hallucinations
- Increased salivation
- Tachycardia, Hypertension
- Bradycardia
- Hypertension
- Bradycardia

### Withdrawal Symptoms of Opioids

- Constipation
- Nausea
- Vomiting
- Anorexia
- Insomnia
- Hypersomnia
- Hunger
- Thirst
- Increased appetite
- Sweating
- Crying
- Shivering
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- Shiving
### Toxic agent

#### Organophosphate

- **Supportive & Symptomatic treatment**
  - Prevention of further exposure
  - General management:
    - ABC & ComaCocktail if coma.
  - Monitoring of cardiac functions.
  - 2. Antidote: "Atropine"
  - 3. Symptomatic: TTT of seizures

- **Treatment**
  - 1. Activated charcoal.
  - - Emeris &
  - - Gastric lavage are contraindicated

- **GIT decontamination**

- **Enhancement of elimination**

#### Anticholinergics

- **Decontamination**: Treatment of symptoms, monitoring of cardiac function.
- **General management**: Decontamination, supportive measures.
- **Toxic agent**: Liver support, IV fluids.
- **Methanol**: Treatment of symptoms, monitoring of cardiac function.
- **Alcohol**: Treatment of symptoms, monitoring of cardiac function.

#### Alcohol

- **Methanol**: Treatment of symptoms, monitoring of cardiac function.
- **Ethanol**: Treatment of symptoms, monitoring of cardiac function.

#### Phenol

- **General measures**: Supportive care, cardiovascular support, control of seizures.
- **Toxic-specific measures**: For dermal exposure, wash with undiluted polyethylene glycol or copious amount of water.
- **Phenol**: Treatment of symptoms, monitoring of cardiac function.

#### Iron poisoning

- **TTT**: Decontamination, antidote, symptomatic.
- **Anti-dote**: Chelation Therapy: Dexasmine.
- **Mechanism of action**: Limits Fe entry into the cell.
- **Side effects**: Intracerebral Fe outside mitochondria.

#### Botulism

- **Supportive treatment**: IV fluids for hypotension, blood for bleeding and hemolysis, platelet concentrates, fresh frozen plasma to replenish coagulation factors.
- **Artificial ventilation** for the paralyzed patient.

#### Snake Bite

- **A. First aid measures**: Immobilization of the affected limb.
- **B. At hospital**
  - Stabilization of the patient
  - - Antidote (Polyvalent Antivenom)
  - - IV fluids for hypotension.
  - - Blood for bleeding and hemolysis.
  - - Platelet concentrates.
  - - Fresh frozen plasma to replenish coagulation factors.
  - - Artificial ventilation for the paralyzed syndrome of cobra or the pulmonary edema of vipers.
  - - Antibiotics and antitoxin serum.

#### Animal Poisoning

- **Care of the wound**:
  - - Cleaning, debridement of necrosed tissues and fasciectomy if peripheral vascular impairment follow limb edema and compartment syndrome.

#### Hemodialysis

- **Indications**: Blood methanol level is 25 mg/dl or severe acidosis.
- **Fluid replacement**: Dehydration.
- **Toxic agent**: Methanol poisoning.

#### Hemodilution Therapy

- **Indication**: Blood methanol level is 25 mg/dl or severe acidosis.
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#### Hemoperfusion

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**Therapeutic Drugs**

### Digitalis
- Assessment of the case
- Electrolyte disturbance:
  - Hyperkalemia (never use Calcium)
  - Hypokalemia
  - Hypomagnesemia: MgSO_4_
- Manage dysrhythmia:
  - Lidocaine and phenytoin are antiarrhythmic drugs of first choice
  - Severe bradycardias are treated with atropine, electrical pacing is used in unresponsive patients
  - Verapamil is useful for SVT’s
  - MgSO_4_
  - Cardioversion should be limited to patients with life-threatening arrhythmias and used at the lowest effective energy level
- Digoxin-specific antibody Fab fragments (Digibind®):
  - purified from sheep IgG, rapidly bind to circulating digoxin and are indicated in:
    - See lecture

### Salicylates
- ABCS: Pulmonary edema (intubate), tends to improve as serum salicylate level
- Symptomatic & Supportive Care:
  - Fluid/electrolyte management:
    - Rehydrate with 0.9% saline
    - Urinary output: 2-3 mL/kg/hr
    - Be careful with elderly/renal/cardiac patients
  - Coma: care of coma
  - Convulsions:
    - give succinylcholine with artificial respiration & oxygen
    - ( avoid the use of a CNS depressant)
  - Hypoprothrombinemia: vitamin K, Fresh blood or platelet transfusion.
  - Hypoglycemia: glucose 50%
  - Hyperthermia: Sponge bath, fans, cold water submersion
- Pulmonary edema: Oxygenation, Intubation (tends to improve as serum salicylate level - 4)

### Acetaminophen
- After 4 hrs: Antidote: N-Acetylcysteine (NAC)
- Mechanism of action:
  - It acts by increasing glutathione concentration to bind the toxic metabolite
  - It serves as a source of sulfate, so it increases conversion of paracetamol to its sulfate metabolite to decrease formation of other toxic metabolite.
- Oral NAC dose: loading dose of 140 mg/kg followed by 70 mg/kg q4h for 3 days.
- I.V. NAC dose:
  - Given if oral NAC failed: Increased risk of anaphylactic response.
    - 150mg/kg in 20 min. → then 50 mg/kg in 4 hr. → then 100 mg/kg in 16 hr.
  - Duration of I.V regime is 48 hrs.

### Psychotropic drugs
#### Antipsychotics
- A) General measures:
  - 1- ABC & ComaCocktail if coma (Intubation if severe R.D. / Assisted ventilation with PEEP)
  - 2- ABG, Cardiac monitoring, Serum electrolytes & toxicology screen.
  - 3- Venous access with a large bore IV line: to give IV fluid in hypotension.
- B) Management if complications:
  - 1- CNS depression & coma → Supportive care → Seizures → Diazepam
  - Hypotension: Respond to Ringer’s lactate or normal saline
    - If failed: a adrenergic agonist (Phenytoine).
  - 3- Cardiotoxicity:
    - Direct current cardioversion used in: SVT, VT, Torsade de points
    - Defibrillation followed by lidocaine used in: ventricular fibrillation.
    - Lidocaine is the 1st line agent, if fail we use phenytoin.
  - 4- Acute dystonia: Diphenhydramine (Benadryl) → Benzatropine (Cogentil)
  - 5- Parkinsonism: anti-parkinsonism drugs
    - NMS: Dr. Dantrolene → Bromocriptine → Diazepam → Cool the patient.
- A) General measures: As above
- B) Specific TTT:
  - a- Alkalization is the first line treatment for TCA induced conduction defects, arrhythmias & hypotension.
    - A bolus of NaHCO_3_ mEq/kg is given over several minutes.
  - b- Management of complicating factors:
    - 1- CNS depression & coma → Supportive care → Seizures → Diazepam
    - Hypotension: Respond to Ringer’s lactate or normal saline AND alkalization if failed: a adrenergic agonist (Phenytoine).
  - 3- Cardiotoxicity:
    - Alkalization is the most effective TTT for cardiac arrhythmias and for sinus tachycardia with widened QRS > 0.10 second.
    - Alkalization + Pacemaker for third degree heart block.
    - Drugs to be avoided → Physostigmine, Propranolol, Verapamil.
  - 4- Acidosis: treated by alkalization of urine
  - 5- Hyperthermia: cooling the patient.

### Antidepressants
- A) General measures: As above
- B) Specific treatment: main line of treatment is:
  - Sodium polystyrene sulfonate
  - Furosamide
- C) Symptomatic treatment:
  - 1- In mild to moderate cases with serum level ≤ 4 meq/L
    - Good hydration with IV infusion of normal saline.
    - After the patient is rehydrated fluid administration should be continued with half normal saline until toxicity is resolved.
    - Maintenance of electrolyte & fluid balance.
  - 2- Severe toxicity: TTT of Coma → Convulsions → Arrhythmias

### Lithium
- A) General measures: As above
- B) Specific TTT:
  - CNS depression.
  - Flumazenil (anestax) → 2 – 5 mg IV → Benzodiazepine antidote
  - Treating withdrawal

### Sedative & hypnotics
- A) General measures: As above
- B) Specific TTT:
  - CNS depression.
  - Diazepam 150mg/kg in 20 min.
  - Neuroleptics, h 1,2: As above
  - Physostigmine, Propranolol, Verapamil.
- A) General measures: As above
- B) Specific TTT:
  - CNS depression.
  - Flumazenil (anestax) → 2 – 5 mg IV → Benzodiazepine antidote
  - Treating withdrawal

### Hemodialysis
- 1- Gastric lavage:
  - Within 1 to 2h following ingestion, up to 12 hours (due to presence of concretions)
- 2- Activated charcoal & RDAC:
  - 1g AC absorbs 550 mg of ASA. Effective in 10:1 AC to salicylate
- 3- Whole bowel irrigation:
  - shown to be more effective for enteric coated or sustained release forms

### Hemodialysis
- 1- Gastric lavage:
  - Sodium bicarbonate: 1:2 meq/kg, followed by an IV infusion of 3 ampules in 1 L of 0.9%
  - Maintain urine pH at 7.5-8.0 & correct hypokalemia
  - Why hypokalemia???
  - (due to intracellular shift of potassium in exchange for hydrogen ions to compensate for the alkalosis).
- 2- Hemodialysis:
  - These are indicated due to the ability to remove salicylates, correct fluid, electrolyte, and acid-base disorders
  - Hemoperfusion.

### Hypokalemia
- 1- Gastric lavage: Should started as soon as possible, and may after several hours (if mortality decreased due to 1 blockage)
- 2- Activated charcoal (1g/kg) followed by
- 3- Cathartic:
  - (saline sulfate cathartic): enhances activity of the sulfate metabolic pathway → hepatic protection

### Lithium
- 1- Gastric lavage:
  - ( see lecture )
- 2- Emetics.
  - Usually not recommended because the patient is comatose, but used if securing airway.

### For BOTH Barbiturate & Benzo.
- 1- Gastric lavage:
  - With protected airway by cuffed Endotracheal tube.
  - Used as soon as possible in first 6 hours of greatest benefit.
  - but also delay used is possible (GIT motility decrease )
- 2- Activated Charcoal:
  - 1 gm / kg / BW

### For Barbbiturates only
- 1- Forced Alkaline Diuresis:
  - Help elimination of long-acting barbiturate.
  - Help ttt of Rhodamylomylsis
  - - Not useful in short or Intermediate acting
- 2- Hemodialysis (HD):
  - 4-6 time effective than FAD
  - - Used in associated ARF or compromised MI
  - - Not useful in short acting
  - 3- Hemoperfusion (HP).

### Dialysis
- 1- Dialysis:
  - if renal failure persists more than 48 hrs.
**Amphetamine**

1- **Stabilization:** - ABC, Oxygen, ECG monitoring, artificial ventilation.

2- **Symptomatic ttt:**
   - Agitation: Benzodiazepine (high therapeutic index & good anticonvulsant activity)
   - Seizures: Benzodiazepines
   - Hypertension & tachycardia: Alpha blocker or Na nitroprusside.

3- **Symptomatic ttt:**
   - Hypertension & tachycardia: Alpha blocker or Na nitroprusside.
   - Arrhythmia: antiarrhythmia measures.
   - Hyperthermia: cold compresses

4- **Rhabdomyolysis**: Na bicarbonate & hydration & maintain urine output of at least 3ml/kg/h.

**Cocaine**

1- **Stabilization:** - ABC, Oxygen, ECG monitoring, artificial ventilation.

2- **Symptomatic ttt:**
   - Agitation: Benzodiazepine (high therapeutic index & good anticoagulant activity)
   - Seizures: Benzodiazepines
   - Hypertension: immediate rapid cooling with ice water immersion
   - Hypertension & tachycardia: Alpha blocker (phenolamine) or Na nitroprusside.

3- **Dysrhythmias:**
   - Resolves following sedation, cooling, rehydration, and time to metabolize drug.
   - Additional pharmacological therapy for:
     - Supraventricular tachycardia: in stable patient (benzodiazepines & Ca channel antagonists) & in thermodynamically unstable patients (cardioversion).
     - Ventricular arrhythmia (lidocaine & Na bicarb.), unstable patients should be defibrillated.

4- **Rhabdomyolysis**: Na bicarbonate & hydration & maintain urine output of at least 3ml/kg/h.

**Opioids**

1- **General measure:**
   - If mild respiratory depression: Oxygen supplementation
   - If severe CNS depression and apnea: Endotracheal tube

2- **with altered consciousness**
   - I.V. thiamine (100 gm)
   - Glucose: Adult: 25g of 50% solution / Pediatric: 1 g/kg of 10-25% solution

3- **Opoid antagonists (Naloxone):**
   - It's short acting pure competitive opioid antagonists
   - Mechanism of action:
     - Competes with opioids for their receptors sites & rapidly reverses opioids actions.
   - Routes of administration: I.V., S.C., I.M., Intralingual, Endotracheal (rapid onset)
   - Dose:
     - With CNS depression or mild respiratory depression:
       - Initial dose should be low 0.1 mg i.v.
     - With severe respiratory depression:
       - Initial dose 2 mg i.v.
       - with no response after 2-3 minute, this dose can be doubled until there is a response or a total dose of 10 mg.

**Cannabis**

1- **ABC:**
2- **Clinical assessment for evidence of co-ingestions:**
3- **Decontamination:**
4- **Patients with acute paranoia or toxic psychosis:**
   - The drug should be stopped
   - The progress of symptoms observed
   - Support & gentle sedation with a benzodiazepine
   - Heavy user may need antidepressant medication

**Corrosives**

1- **Stabilization:**
   - Secure the patient’s airway, ageal and gastric tissue.
   - Establish an I.V. line.
   - Monitor vital signs closely.
   - Perforation: Preparation of the patient for surgery
   - Serologic testing.
   - Monitor fluid & electrolyte status and pH.
   - Patient is to keep fasting until endoscopy is performed.
   - Serial evaluation is performed.

2- **Supportive care:**
   - Pain killers as morphine
   - Anti-Shock measures: IV fluids, Blood transfusion and crystalloids.
   - Anti-biotics, to guard against infection
   - H2 blockers or proton pump inhibitors to minimize acid secretion
   - Steroids to prevent fibrosis.
   - Total Parenteral Nutrition (TPN) for at least three weeks.

3- **Surgical:**
   - Emergency surgery → in severe hemorrhage & in perforation
   - Elective surgery:
     - Esophageal bypass surgery
     - Dilatation of esophageal strictures
     - Repair of bronchoesophageal fistula
     - Gastroscopy for feeding purposes.

   - In ocular corrosive burn → Irrigate with running tap water for 2 min.
   - In corrosive inhalation → Oxygen, aerosol therapy with B2 stimulant & steroids.

**Drug dependence & drug abuse**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Stabilization</th>
<th>Symptomatic ttt</th>
<th>If ingested</th>
<th>If the nare contain residual white powder presumed to be cocaine:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amphetamine</td>
<td>- ABC, Oxygen, ECG monitoring, artificial ventilation.</td>
<td>- Agitation: Benzodiazepine (high therapeutic index &amp; good anticoagulant activity)</td>
<td>- Activated charcoal</td>
<td>- Rhabdomyolysis</td>
</tr>
<tr>
<td>Cocaine</td>
<td>- ABC, Oxygen, ECG monitoring, artificial ventilation.</td>
<td>- Seizures: Benzodiazepines</td>
<td>- Body stuffing or body packing: (intense decontamination)</td>
<td></td>
</tr>
<tr>
<td>Opioids</td>
<td>- ABC, Oxygen, ECG monitoring, artificial ventilation.</td>
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<td></td>
</tr>
<tr>
<td>Cannabis</td>
<td>No specific antidotes for cannabis</td>
<td>- Arrhythmia (lidocaine &amp; Na bicarb.), unstable patients should be defibrillated</td>
<td>- Whole bowel irrigation,</td>
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<td>- ABC, Oxygen, ECG monitoring, artificial ventilation.</td>
<td>- Hypertension &amp; tachycardia: Alpha blocker (phenolamine) or Na nitroprusside.</td>
<td>- Surgical removal in case of intestinal obstruction</td>
<td></td>
</tr>
</tbody>
</table>

**Others**

- Emesis
- Gastric lavage
- Cathartics
- Charcoal
- Are all Contraindicated

- Demulcents:
  - It minimizes damage to oral, esophageal and gastric tissue.
  - One to two glasses of milk maybe administered within 30 minute.
**Toxic agent & Doses**

**Iron poisoning**

- **Toxicity Levels**:
  - Severe toxicity: Normal = 50-159 μg/dL; 350-500 μg/dL =Moderate; > 500 μg/dL = Severe

- **Dose-Related Toxicity**:
  - < 20 mg/dL = Non-toxic
  - 20-60 mg/dL = Moderately toxic
  - > 60 mg/dL = Severely toxic

- **Lethal**:
  - 180-300 mg/dL = Lethal

- **Risk of Coma by Peak Serum Iron Level**:
  - < 500 μg/dL = 10%
  - > 60 mg/kg = Severely toxic
  - < 20 mg/kg = Non toxic
  - 350-500 μg/dl = Moderately toxic

**Psychotropic drugs**

1. Neuroleptics or antipsychotics e.g. (Phenothiazines)
2. Analytic e.g. (Benzodiazepines)
3. Mood stabilizing drugs (Lithium)
4. Antidepressants (e.g. TCA, MAO)

**Antipsychotics**

- **Mechanism of action**
  - Receptor blockade

- **1- Neurological manifestaion**
  - CNS depression: altered mental status = ataxia, stupor, coma
  - Sedation, weight gain (H1 blockade)
  - Extrapyramidal manifestations (D2)
    - Acute dystonia
    - Parkinsonism
    - Akathisia
    - Tardive dyskinesia
  - Convolutions
  - Gait problems
  - Insomnia
  - Anxiety
  - Low libido

- **2- Cardiovascular manifestations**
  - Serum lithium level:
    - 0.4-1.3 meq/L: Normal
    - > 1.3 meq/L: Lethal

- **Lithium Symptoms with Acute toxicity**
  - I- CNS
    - Mild toxicity: mental confusion, ataxia, tremors and exaggerated reflexes
    - Severe toxicity: convulsions and coma
  - II- Renal
    - Polyuria, polydipsia, DI and renal failure
  - III- CVS
    - Arrhythmias, if severe cardiac arrest.
  - IV- GIT
    - Nausea, vomiting and diarrhea

- **Symptoms with chronic toxicity**
  - MMOL/L effects
    - 0.5: None
    - 1.0: Mild tremor
    - 1.5: Coarse tremor
    - 2.0: Hyperreflexia, dysarthria
    - 2.5: Myoclonia, ataxia, confusion
    - > 3.0: Delirium, coma, seizures

**Clinical Features**

- **Stage I / 0-6 hour**
  - Direct corrosive insult to the intestinal mucosa
    - GIT upsets:
      - Nausea, vomiting, diarrhea
    - GIT bleeding:
      - Upper or lower GIT bleeding
    - If severe, GIT perforation:
      - Abdominal pain, perforation, peritonitis
    - Hypertension, shock, tachycardia
      - Vasodilatation
      - Hypovolemia in bleeding.
    - Hyperglycemia:
      - Impaired glucose tolerance
    - Metabolic acidosis:
      - Hydrogen is released in the conversion of ferrous iron to ferric iron
      - In blood: acidosis or interfere with Krebs cycle, disruption of mitochondria forcing anaerobic respiare.
    - Leucocytosis:
      - Due to invasion of damaged mucosa by bacteria

- **Stage II / 2-48 hours**
  - Quiescent phase:
    - Apparent (false) improvement of most of victims
    - Initial correction of hypovolemia and stabilizing measures: no overt clinical signs
    - Apparent recovery
    - GI symptoms subside
    - Little changes in mental status.
    - Hyperglycemia, leucocytosis, acidosis persist
    - Careful observation is necessary.

- **Stage III / 12-48 hours**
  - Worsening of hemorrhage, sev. lethargy and coma
    - (Multiple organ dysfunction)
    - Coma: CNS depression
    - Cardiovascular collapse:
      - Direct massive post arteriolar vasodilatation.
      - Hypovolemia in hemorrhage.
    - Cerebral edema
    - Pulmonary edema
      - VD and permeability:
    - Liver cell failure:
      - Jaundice, hyperglicemia, coagulation defect.
    - Renal failure:
      - Deposition of excess iron exceeding TIBC in soft tissues
      - Poor renal perfusion.
    - Severe metabolic acidosis
    - Leucocytosis, elevated PT

- **Stage IV / 2-6 weeks**
  - Healing of GI insult:
    - Liver: Hepatic damage & cirrhosis
    - Intestines:
      - Intestinal scarring (intestinal fibrosis):
        - Strictures
      - Gastric scarring

**Antipsychotics**

- **Mechanism of action**
  - Alpha adrenergic receptors
  - Dopamine receptors
  - Serotonin receptors
  - Histamine (H1 & H2)
  - Muscarinic receptors
  - Histamine (H1) receptors
  - Inhibition of C T-antimatic effect.

- **Mechanism of action**
  - Blockade of neurotransmitter receptors:
    - Cocaine: CNS depression
    - Antidepressant: Depressed mental status
    - Lithium: depolarization of CNS
    - Sedation & hypnosis
    - Antipsychotic: At theraputic level:
      - QT prolongation
      - Hypothyroidism
      - Disability 10%
    - At toxic level:
      - QT prolongation
      - Hypothyroidism
      - Disability 10%

- **Triyclic Anti-Depressants (TCA)**

- **Mechanism of action**
  - 1- Inhibition of neurotransmitter reuptake:
    - Blockade of neurotransmitter receptors:
      - TCA: Inhibition of neurotransmitter reuptake
      - TCA: Inhibition of neurotransmitter reuptake

- **Lethality**
  - Cardiac arrhythmias, severe hypotension

- **Symptoms with Acute toxicity**
  - Barbiturate
  - Sedative & hypnotics
  - Benzodiazepines

- **Mechanism of action**
  - Barbiturate
  - Sedation
  - Drowsiness
  - Ataxia
  - Cognitive impairment
  - Anterograde amnesia
  - Lack of concentration, hallucinations, excitability
  - Coma
  - Respiratory depression
  - Dysarthria
  - Ataxia
  - Cognitive impairment
  - Anterograde amnesia
  - Lack of concentration, hallucinations, excitability
  - Coma
  - Respiratory depression

- **Indications/users include**
  - Sedation
  - Drowsiness
  - Ataxia
  - Cognitive impairment
  - Anterograde amnesia
  - Lack of concentration, hallucinations, excitability
  - Coma
  - Respiratory depression
  - Dysarthria
  - Partial palsy
  - Diplopia
  - Nystagmus
  - Hypothermia
  - Hypotension
  - Hypotonia & hyporeflexia
  - Depression & abuse
  - Tolerance
  - Withdrawal symptoms

- **Toxicity**
  - 1- CNS:
    - Characterized by:
      - Dilated reactive pupil
      - Skeletal muscle relaxation
      - Cyanosis
      - Signs of shock
      - Rapid weak pulse, low BP, cold skin & hypothermia

- **2- Respiratory depression**
  - Resulting in hypoxia and apnea (short acting)
  - It's of rapid onset (half hour)
  - Pulmonary edema:
    - Hypoxia
    - Tachycardia
    - Bradycardia
    - Hypotension
    - Lethal

- **3- Hypotension**
  - It’s due to vasoplastic mechanism
  - Shock may occur due to vasoplastic & cardiac mechanisms.

- **4- Hypothyroidism**
  - It's frequent with appearance of J wave in EKG if temp falls beyond 35 C.

- **5- Skin**
  - Bullous skin erosion (barbiturate burn), in 7% of case between toes & fingers.

- **Lethality**
  - Asphyxia due to respiratory failure, circulatory failure, renal failure, pulmonary edema, brain edema.

- **Fatal Dose**
  - Long acting: 6 – 10 gm
  - Short acting: 2-3 gm

- **Fatal Period**
  - 1-4 days, sometimes more prolonged.
Amphetamines
symptomatic & CNS stimulants.

Alpha-methyl phenyl ethylamine

Amphetamine-type stimulants
(MAS), consists of:

1. Amphetamines
2. Ecstasy
3. Number of other synthetic stimulants such as:

- methcathinone,
- phenylpentamine
- fenetline

3. Physiological manifestations such as:

- hyperthermia,
- dysrythmias,
- intracerebral hemorrhage

2. release

- Catatolamines (Norepinephrine, dopamine) 
- Increased release of dopamine & serotonin

Inhibition by:

- Metabolic acids,
- Rhodonomaly,
- Acute tubular necrosis (acute renal failure).

Death from amphetamine toxicity results from:

- Hyperthermia,
- Dysrythmias,
- Intracerebral hemorrhage

Mechanism of action:

- Low dose:
- euphoria, alertness, hypersexuality
- Tachycardia, Tachypnea,Hyperpiria
- As the dose increases,:
- Anxious,
- Aggressive,
- Agitation.
- Seizures (Direct CNS effects)
- Psychotic (Hallucinations):
- Chronic effect give rise to:
- Manic syndrome.
- Movement disorders (depletion or dysregulation of dopamine):
- Psychosis or
- Cerebrovascular accidents:
- Hyperthermia, vasospasm,
- Lethargy, want to sleep, trouble

Mechanism of pulmonary mani.

- Tachypnea,
- Tachycardia,
- Mydriasis
- Hyperthermia occur (is the most critical)
- Mydriasis,
- Dilated pupils,
- Mydriasis

- Headache, due to:
- Hyperthermia, vasospasm, dysregulated neurotransmitters.
- A cocaine washed-out syndrome:
- yoga up to 4 hrs. (dopamine depletion):
- Lethargy, want to sleep, trouble

Mechanisms:

- Increased activation of dopaminergic
- neurons in the:
- nucleus accumbens, dopamine
- receptor sites in the:
- prefrontal cortex, amygdala, striatum, pallidum,
- caudate, accumbens.

CNs:

- Pituitary
- Hypothalamic
- Adrenal
- Spleen
- Gastric

CNs: potent (usually of cause of emergency)

1. Anxuas,
2. Aggressive,
3. Agitation.

CVS: F P:

- Hypertension, tachycardia, vasospasm
- Head to:
- Brain
- Head;
- Cerebral infarction,
- Intraparenchymal & subarachnoid hemorrhage.

Heart
- Myocardial ischemia or infarction.
- Angina
- Dyrhythmias
- Aortic dissection

Lung
- Noncardiogenic pulmonary edema might occur due to pulmonary vessels severe
- Vasospasm, acidosis, hypoxia.

Intestine
- Ileal colitis

Withdrawal symptoms:

- Anxiety, Abdominal cramps, Appetite stimulation, Headache, Lethargy, Depression.

Cocaine

Symptomatic, CNS stimulants & local anesthetic

A natural alkaloid contained in the leaves of Erythroxylum coca

- Causes seizures, dysthyrhythmias, & myocardial ischemia

This may be related to:

- COX2, sodium blocking effects
- Thrombin effect of cocaine.

Amphetamines more likely to cause psychosis than cocaine.

This related to the more prominent dopaminergic effects of amphetamines.

Read from lecture:

- Mechanism of pulmonary manifestations:
- Mucosal skeletole manifestations
- Obstetric manifestations
- Cocaine Dependency

Opioids

Opioids, 1 Are a broad class of alkaloid compounds that have opium-like effects. They are divided into:

- Naturally: Morphine & Codeine
- Semisynthetic: Heroin, Hydro-morphine, Oxy-morphine
- Synthetic:

- Meperidine, Methadone & Fentanyl

- Methadone & Oxymorphone:

- Paracetamol

Opiates:

Drugs derived from opium include:

(usually opiate & semi-synthetic)

Cannabis

Cannabis is a collective term referring to the bioactive substances from Cannabis sativa.

C. sativa contains a group of more than 60 chemicals called cannabinoids.

The major cannabinoids are:

- cannabinol, cannabinol, & tetrahydrocannabinol.

The principal psychoactive cannabinoid

1. delta-9-tetrahydrocannabinol (THC)

The common form of cannabis

Marijuana (dried parts of plants)

- 1.5 % of THC
- Hashish (from flowering tops of plant)

- 1-3.5 % of THC
- Hash Oil: 30 - 60 % of THC
- Pharmaceutical grade form of THC:

- Dronabinol, Marinol

In Acute Toxicity:

Low-Moderate Dose

Heart

- 11. Increased heart rate
- 12. Palpitations,
- 13. Pulmonary hypertension
- 14. Increased breath

Pulmonary

- 15. Dry mouth,
- 16. Decrease airway resistance & increase airway conductance
- 17. Conjunctival injection & IOP

CVS

- 1. Headache & blood pressure (+ sympathetic)
- 2. Risk of a heart attack

Endocannabinoid System

- Noncardiogenic pulmonary edema.
- Cellulitis & abscesses.
- Pulmonary emboli & peripheral emboli.
- Endocarditis & aspiration pneumonia.
- Prolonged or unusual seizures.
- Rhabdomyolysis with or without compartmental syndrome.
- Active metabolites of meperidine has convulsant activity.
- Metabolites of propoxyphene has cardiotoxic activity.

Absence:

- Local ischemia of the gastrointestinal tract
- May take longer to appear.

- Ischemic colitis

- Intestinal infarction

- Bowel obstruction such as vomiting or distension might suggest body packing.

Complications

- Opioid withdrawal

See the picture in the general scheme.

In the chronic toxicity:

- Reduced ADH,
- Abnormal hypothalamic-pituitary adrenal axis.
- Abnormal hypothalamic-pituitary gonadal axis.

- Decreased libido, irregular menses

- Thrombosis

- Decrease body weight

- Increased appetite

- Psychosis

- Anxiety

- Depression

- Sleep disturbances

Mechanism of action:

- Opioids: Evert their effects by interacting with specific receptor sites in the CNS (Mu, Kappa & Delta) resulting in inhibition of synaptic neurotransmission in central & peripheral nervous system.

The classical triad of opioid include:

- CNS depression
- Respiratory depression
- Miosis

CNs Range from euphoria to dysphoria & from sedation to coma.

Anxiety, mental powers.

Respiratory:

- Respiratory depression
- Non-cardiogenic pulmonary edema

Mechanism of action:

- Orthostatic hypotension, sinus bradycardia ventricular arrhythmias
- Reduced mobility
- Reduced bowel sound
- Anorexia, malnutrition & weight loss

Dermatology

- Flushing & urticaria
- Skin boils, cellulitis & needle tracks are lve users.

Endothelins

- Noncardiogenic pulmonary edema.
- Cellulitis & abscesses.
- Pulmonary emboli & peripheral emboli.
- Endocarditis & aspiration pneumonia.
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Anxiety, mental powers.
**Alcohol**
- Ethanol is CNS depressant from 0.5% - 1.5%.
- Concentration of ethyl alcohol:
  - Beer: 4% - 5%
  - Wine: 10-14%
  - Whisky & Vodka: 30-50%

**Route of admin.**
- Oral: drinking.
- Ethanol can also be admin. IV when used as an antidote for methanol or ethylene glycol.

**In chronic alcohols,**
- The pathway increases the NA/D ratio, changes the redox potential of the hepatocyte and contributes to the development of:
  - lactic acidosis
  - alcoholic ketoacidosis.

**Ethanol**
- Ethanol is the alcohol constituent of "alcoholic" beverages (beer, wines & spirits) and is a solvent commonly used in medicinal preparation.

**Mechanism of action:**
- Ethanol has toxic effects on almost every organ system.
- This toxicity is related to the effect of metabolite acetdehyde.
- At very high concentration:
  - Ethanol interact with and become integrated into the lipid bilayer of cell membrane
  - Increased membrane fluidity, and thereby interfered normal cellular function where ethanol act as an anesthetic
- At lower intoxicating concentration:
  - Almost every neurotransmitter system is affected by ethanol, but do not appear to be specific receptors for ethanol.
  - GABA is an inhibitory neurotransmitter that ethanol potentiates its activity.
  - Glycine, another inhibitory neurotransmitter is also influenced by ethanol.
  - Glutamate is an excitatory neurotransmitter that ethanol inhibit its function.
  - Ethanol influences the activity of adenylate cyclase which regulates synthesis of cAMP, which regulates many intracellular functions.

**Pathophysiology**

**Metabolic acidosis:**
- 1. Metabolic degradation of aspirin (sалициловой кислоты).
- 2. Renal dysfunction – retention of acidic metabolites.
- 5. Unbalance oxidative phosphorylation – accumulation of pyruvic & lactic acid.

**Respiratory alkalosis:**
- 1. Due to respiratory depression following respiratory stimulation.
- 2. Respiratory Alkalosis – due to 8 times more toxic than methanol.
- 3. Formic acid – is an inhibitory neurotransmitter.

**Respiratory Alkalosis**
- Alveolar ventilation increases.
- Lactic acidosis.
- Respiratory Acidosis.

**Pathophysiology:**

**Ethanol**
- CNS – Depression.
- Hypotension.
- flushing & sweating.
- Allergy – Rhinitis, Edema, Urticaria.
- Bronchial edema, shock.

**D. Alcohol ketoacidosis**

**Mechanism of action:**
- Methanol metabolism involves the formation of formaldehyde by an oxidation catalyzed by alcohol dehydrogenase.
- Formaldehyde is rapidly converted to formic acid, which is 6 times more toxic than methanol.
- Formic acid:
  - Responsible for ocular toxicity.
  - It inhibits cytochrome oxidase in the optic nerve.
  - Disturbing the flow of axoplasm.
- Both formic acid & lactic acid are responsible for:
  - Metabolic acidosis &
  - Decrease in plasma bicarbonate.

**Renal**
- Renal tubular damage – proteinuria with Na & water retention.
- Inappropriate secretion of ADH.
- Inhibition of prostaglandins necessary to maintain renal blood flow.
- Reversible acute renal failure.

**GIFT effects**
- Direct irritative effects – nausea & vomiting.
- GI bleeding to gastritis & exacerbation of ulcer.
- Mild liver necrosis, may occur.

**Salicylates**
- Toxic Dose:
  - Higher than 30 mg/dl – Symptomatic.
  - Acute single ingestion:
    - >100 mg/kg – Milder toxicity.
    - >500 mg/kg – moderate.
    - >1000 mg/kg – severe.
  - Chronic ingestion:
    - >180 mg/kg/day for 2 days.

**Pathophysiology:**

**ENT (Sialicoy) & CNS**
- First stimulate and then depress the CNS.
  - Confusion.
  - Dizziness.
  - Psychosis.
  - Convulsions & coma in severe cases.

**Respiration & acid-base balance**
- Hyperglycemia
- Hyperthermia
- Due to uncoupling of oxidative phosphorylation.

**Skin**
- Due to sweating & vasodilatation.

**Allergy**
- Rhinitis, edema, urticaria.
- Bronchial edema, shock.

**Blood**
- It affects both platelets & prothrombin.
- Small doses – Bleeding time.
- Whole blood ADG – Shows characteristic acid-base disturbance of salicylate toxicity.

**Salicylate level**
- Ferric chloride test to urine. (Qualitative test). Purple color change indicates presence of salicylates (false negative is rare).
- Monitoring serum salicylate level, every 2 hrs for the first 4 hrs, to reach peak level. Then every 4-6 hrs until it is less than 30 mg/dl.
- Arterial blood ptt.

**Ethyl Alcohol**
- CNS – Depression.
- Hypotension.
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  - Increased membrane fluidity, and thereby interfered normal cellular function where ethanol act as an anesthetic
- At lower intoxicating concentration:
  - Almost every neurotransmitter system is affected by ethanol, but do not appear to be specific receptors for ethanol.
  - GABA is an inhibitory neurotransmitter that ethanol potentiates its activity.
  - Glycine, another inhibitory neurotransmitter is also influenced by ethanol.
  - Glutamate is an excitatory neurotransmitter that ethanol inhibit its function.
  - Ethanol influences the activity of adenylate cyclase which regulates synthesis of cAMP, which regulates many intracellular functions.

**GIT**

In acute intoxication:
- Nausea, vomiting & abdominal pain.

In chronic intoxication:
- Abdominal pain is related to esophagitis, gastritis, pancreatitis, hepatitis or cirrhosis.

**CNS**
- Acute intoxication/ altered mental status (AMS).
  - Low BAGS occur associated with euphoric feelings.
  - At higher serum levels there is increasing CNS depression with:
    - Altered speech – Altered perception of the environment
    - Ataxia – Nystagmus
  - At very high serum levels coma & respiratory depression.

**Hypoglycemia** is another manifestation of acute intoxication, and may be associated with malnutrition in the chronic alcoholic.

**Wernicke-Korsakoff syndrome:**
- Ethanol interferes with thiamine (vitamin B1) absorption, ethanol induce hepatic disease leads to:
  - decreased thiamin storage &
  - decreased activation to coenzyme thiamine pyrophosphate.
  - Manifested by:
    - response to thiamin therapy
    - Ocular disturbance (diplopia, blurred vision, bidirectional nystagmus),
    - Ataxic gait & confusion.
  - Also, Thiamine deficiency may lead to wet beriberi cardiomyopathy.

**Korsakoff psychosis:**
- Permanent state of cognitive dysfunction characterized by the inability to remember recent events or learn new information.
- Nutritional:
  - Alcoholic hyponatremia
  - Hypoglycemia
  - Hypocalcemia, hyperglycemia, hyperthermia
  - Nutritional: Pellagra, beriberi.

**Psychiatric:**
- Depression, personality disorder, suicide.

**Alcohol withdrawal:**
- 1- Minor:
  - Symptoms begin 6 to 8 h after reduced alcohol intake may last for several days.
  - Minimal sympathetic symptoms (tremor, anxiety, nausea, vomiting, flushed skin, sweating, tachycardia or hypotension).
- 2- Moderate:
  - 24-36 h after reduced ethanol intake.
  - Increased sympathetic symptoms with:
    - Hallucination (visual, auditory, tactile, olfactory).
- 3- Severe:
  - Increased sympathetic symptoms with:
    - Fever, altered mental status or convulsion.
    - Seizures
    - Tonic-clonic convulsions
    - 7-8 h after cessation of alcohol intake.
- D- Delirium tremens (DTs):
  - Autonomic hyperactivity with fever, tachycardia tachypnea, hypertension.
**Botulism**

- Gram +ve anaerobic bacillus that release neurotoxin “Botulin”.

**Toxin types:**
- [B, C1, C2, C3] / C beta
- [D, E, F, G]
- Food contaminated with C. botulinum toxin type A and B often does not look or smell normal and appears putrefied because of the action of proteolytic enzymes.

**Pathophysiology:**
- The human oral lethal dose is 1 μg/kg from the toxin.
- Botulin toxin binds to specific receptors on the mucosal surfaces of gastric and small intestinal epithelial cells where endocytosis followed by transcytosis permits release of the toxin on the senosal cell surface.
- Release into the systemic circulation allows uptake into presynaptic acetylcholine containing neurons.
- As a result, cholinergic transmission at all acetylcholine-dependent synapses in the peripheral nervous system is impaired.
- However, there is no effect on central nervous system or axonal conduction.
- Tonsils are distributed to target sites via hematogenous dissemination.
- Tonsils act on the presynaptic par of neuromuscular junctions leading to decreasing the amount of ACH release

**Clinical picture**
- **Acute complications:**
  - a. Upper airway obstruction and injury.
  - b. GI hemorrhage.
  - c. Esophageal & gastric perforation.
  - d. Sepsis.
  - e. Tracho-bronchial necrosis, atelectasis.

**Electrocardiogram:**
- a. Mediastinal.
- b. Precordial.
- c. Pleuritis.
- d. Trachobronchial-oesophageal fistula.
- e. Esphago-aortic fistula.

**Comprehensive complications:-**
- a. Esophageal obstruction.
- b. Pyloric stenosis.
- c. Squamous cell carcinoma of the esophagus.
- d. Vocal cord paralysis.

**Clinical manifestation of toxicity**
- **Acute**
  - Brady-dysrhythmias
  - GIT manifestations
  - Lethal, confusion, and weakness

- **Chronic**
  - arrhythmia
  - GIT manifestations
  - Visual (yellow vision)
  - Confusion, Delirium, hallucination

**Diagnosis**
- Clinical picture
  - 4 to 18 days later > cranial nerve palsy AND the other neurologic findings typical of botulism may appear.

**Anticholinergic manifestations**
- See the scheme

**Pathology**
- They are cardiac glycosides
- Most come from the Loxoglossum plant.
- The drugs have a low therapeutic index.

**Factors affecting distribution:***
- Hypokalemia, acid or alkalies and help to prevent stomach induce buffering effect on
- Hypokalemia +ve anaerobic bacillus that remain localized.
- Areas of contact time in these areas.
- Crystal result in penetrating injury that remain localized.
- Liquid formation increases the contact time of the stomach.

**Corrosives**
- Factor contributing to injury :
  - 1. pH and concentration.
    - Esophagus begins to ulcerate at pH 12. Acids with pH 2 or less cause significant injury.
  - 2. Volume of caustic ingested:
    - Large volume result in greater direct injury and potential for perforation & injury to other system. High volumes enhance the risk of emesis, causing further damage.
  - 3. Contact time :
    - Acid & alkalies with high viscosity have prolonged tissue contact and amplification of injury.
  - The passage of caustic through areas of normal anatomic narrowing increase contact time in these areas.
  - Crystal result in penetrating injury that remain localized.
  - Liquid formation increases the contact time of the stomach.

**Oxidant**
- Presence of fluid in the stomach affords immediate dilution effect on the ingested caustic.
- The presence of solid food in the stomach induce buffering effect on acid or alkalies and help to prevent damage.
  - 1) Ingestion of acid on an empty stomach damage of the lower two-third of the stomach, sparing only the fundus.
  - 2) Ingestion of acid on a full stomach harm only the pylorus and lesser curvatures

**Organophosphates**
- It’s potent cholinesterase inhibitors high toxic & nontoxic 
- Organophosphorous compounds bind to or inhibits acetylcholinesterase of acetylcholine in the synapse.
- By time the compound undergoes a conformational change (aging) renders the enzyme irreversibly resistant to reactivation.
- Carbamate compounds unlike organophosphates, are transient cholinesterase inhibitors.

**Mechanism of action**
- Acids with pH 2 or less cause large volume result in greater direct injury and potential for perforation & injury to other system. High volumes enhance the risk of emesis, causing further damage.

**Clinical manifestation of toxicity**
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**Gastrointestinal effects**
- Headache, fatigue, confusion, blurred vision, alteration of color perception, and halos on dark objects.

**Mechanism of action**
- Aortic fistula.
- Gastric perforation.
- Dissecting aneurysm.
- Mediastinitis.
- Tracheobronchial-oesophageal fistula.

**Pathology**
- The human oral lethal dose is 1 μg/kg from the toxin.
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**Clinical manifestation of toxicity**
- **Acute**
  - Brady-dysrhythmias
  - GIT manifestations
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- **Chronic**
  - arrhythmia
  - GIT manifestations
  - Visual (yellow vision)
  - Confusion, Delirium, hallucination
  - Hypokalemia, why?

**Mechanism of action**
- When the prescription of fluid in the stomach affords immediate dilution effect on the ingested caustic.
- The presence of solid food in the stomach induce buffering effect on acid or alkalies and help to prevent damage.
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