

Heavy metals

Some of them activate enzymes other facilitate exchange and utilisation of oxygen and carbon dioxide, while most of these trace elements are required in adequate quantities through food etc.

Arsenic →

Arsenic is thought to occur throughout the universe. It is the ~~ma~~ twentieth most common element in the earth's crust, having concn of 1.8 ppm.

physical properties → Silver grey or tin-white, shiny, brittle, crystalline, metallic-looking element.

usual fatal dose →

① 200 to 300 mg for arsenic trioxide.

② 25 to 30 ppm can be lethal in 30 mins.

Clinical features →

Skin → Hair loss.

GI → Abdominal pain, dysphagia, vomiting.

eye → conjunctivitis lacrimation.

Air → Irritation.

Liver → Fatty degeneration.

Kidney → uraemia.

Neurological → Hyperpyrexia, convulsions, coma.

CVS → hypotension, tachycardia.

Diagnosis →

1) urine analysis.

2) Blood level.

3) Radiography

Investigation →

Monitor CBC, Serum electrolytes, urinalysis, Renal function test, ECG.

Management → ① Supportive care.
(gastric lavage, intravenous fluids,
cardiac monitoring etc).

② chelation therapy.

③ Haemodialysis or exchange transfusion.

② Mercury → (liquid silver)

physical properties → Heavy, silvery liquid which is per se non-toxic, but vapourise at room temp.

Uses → Antiseptic and disinfectant, Dental amalgam, Diuretic, purgative etc.

usual fatal dose →

Man is estimated at 100 gms.

Mercuric chloride 0.5 to 1 gm/70 kg.

Mercurous chloride 1.5 to 2 gm/70 kg.

Clinical features →

a) Acute poisoning →

① Inhalations

② Ingestion

③ Injection

b) chronic poisoning →

① Inhalation.

② Ingestion

- colitis

- melanosis coli

- Dementia

- Tremor

- Renal failure.

- Acrodynia (pink disease)

Diagnosis →

1. X-ray.

2. Blood mercury level.

3. Urine mercury level.

4. Hair analysis.

Treatment →

A. Acute poisoning → (metallic mercury and inorganic compounds)

Inhalation →

- Supportive measures.
- chelation.

Ingestion →

- Administer laxatives.
- Demulcents for corrosive compounds.
- Stomach wash.
- chelation.

Injection →

2. Organic mercurials →

- Supportive measures.
- chelation is not very effective.

B. Organic mercurials.

- Supportive measures.
- chelation is not very effective.

B. Chronic poisoning:

- chelation therapy.
- Supportive care.

Toxicokinetics (2 Marks)

1) Define and enlist the various parameters of toxicokinetics.

⇒ The study of 'how a substance gets into the body and what happens to it in the body.'

Parameters →

1. Area under the drug concⁿ curve.
2. Volume of Distribution V_d
3. Clearance.
4. Plasma clearance.
5. Renal clearance.
6. Plasma half life.
7. Single organ elimination rate.
8. Extraction Ratio.

Elimination →

Only types of drugs

The various methods of eliminating absorbed poisons from the body, including the following —

① Forced diuresis.

② Extracorporeal techniques.

① Haemodialysis.

② Haemoperfusion.

③ peritoneal dialysis

④ Haemo filtration.

⑤ plasma pheresis.

⑥ plasma perfusion.

⑦ cardio pulmonary bypass.

explore possible diagram

① Forced diuresis → Most drugs taken in overdose are extensively detoxified by the liver to produce inactive metabolites which are voided in the urine.

Sometimes — hepatic degradation produces active metabolites but secondary compounds are the converted to non-toxic derivatives, under these @

Forced diuresis is inappropriate.

The procedure should be undertaken only if the following condition are satisfied.

① A substantial proportion of drug is excreted unchanged.

② The drug is distributed mainly in the extracellular fluid.

③ The drug is minimally protein bound.

6) Explain the management cocaine detoxification →

⇒ Hypertension →

① Minimise physical activity and sedate with benzodiazepines.

② Ice baths packs, cool water with fans. etc.

Anxiety and agitation →

① Diazepam 5-10 mg IV

lorazepam 2-4 mg IV titrated to effect.

② physical restraints.

convulsions:

① Diazepam 5-10 mg IV / lorazepam 2-4 mg IV
titrated to effect

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Cerebrovascular Accidents → Neurosurgical consultation is mandatory.

Hypertension → It is usually short lived and often followed by significant hypotension.

Arrhythmias →

- ① Sinus tachycardia

- observation

- oxygen

Diazepam 5-10 mg IV.

- ② Supraventricular tachycardia.

- observation.

- oxygen

- Diltiazem 20 mg IV or verapamil 5 mg IV.

Myocardial infarction →

- ① IV line

- ② oxygen.

- ③ Aspirin to inhibit platelet aggregation.

Aortic dissection → The hypertension that precipitated aortic dissection must be controlled immediately with nitroprusside and calcium channel blockers.

Pulmonary oedema

~~Furo~~ Furosemide 20-40 mg IV.

Morphine sulfate 2 mg IV.

Rhabdomyolysis →

- ① cardiac monitoring

- ② serial potassium determinations.

Acidosis → correction of acidaemia through supportive care measures such as hyperventilation.

1) Define and classify antidotes →

Antidotes are agents that negate the effect of a poison or toxin. Antidotes mediate its effect either by preventing the absorption of the toxin, by binding and neutralizing the poison, antagonizing its end-organ effect.

Classify → ① Specific Antidotes. ^{give example} Atropine.
② Adjuvantal antidotes. magnesium.
③ Obsolete antidotes. copper sulfate.

2) Explain the role of antidote in poisoning.

- ⇒
1. Inert complex formation.
 2. Accelerated detoxification. ^{give eg}
 3. Reduced toxic conversion.
 4. Receptor site blockade.
 5. Toxic effect bypass.

3) Write a short note on antidotes and give examples with their clinical application.

⇒ All that is required is intensive supportive therapy with attention to all the details mentioned in the preceding pages of this ~~ch~~. Specific antidotes are rarely necessary, beside the fact that only a few genuine antidotes exist in actual practice.

Eg → Acetylcysteine ^{write the def of antidotes} (Paracetamol) → Amanitin.

Calcium Salts (oxalates) → calcium antagonists

4) Explain Accelerated detoxification and reduced toxic conversion antidote with examples.

⇒ Accelerated detoxification → Some antidotes accelerate the detoxification of a poison.

eg → Thiosulfate accelerates the conversion of cyanide to non-toxic thiocyanate.

Reduced toxic conversion →

The best example of this mode of action is provided by ethanol which inhibits the metabolism of methanol to toxic metabolites by competing for the same enzyme.

5) Write the composition of universal antidote.

⇒ Activated charcoal is a fine, black, odorless, tasteless powder made from burning wood, coconut shell, bone sucrose or rice starch followed by treatment with an activating agent → ? ? Cf.

6) Define Adjunctive antidotes with example.

⇒ Drugs such as atropine and magnesium are used to counteract the end-organ effects in organophosphorus poisoning.

Eg → Activated charcoal → For most poisons.

Benztropine → Dystonia.

✓ chlorpromazine → Psychotic states.

7) Define and mention the composition of obsolete antidote.

⇒ A poison that counteracts another poison.

composition →

copper sulfate → phosphorus

cysteamine → paracetamol

Diethyldithiocarbamate → Thallium

Fructose → Ethanol

Levallorphan → opiates

Nalorphine → opiates

Silibinin → Amanitin

✓ Tocopherol → Paraquat

universal antidote → Ingested poisons.

8) Explain toxic effect bypass antidote action with example.

⇒ An example of this type of antidotal action is provided by the use of 100% oxygen in cyanide poisoning.

1) other examples

4) What is the role of atropine in mushroom poisoning?

⇒ Atropine in large doses is used for treatment of anticholinesterase organophosphorus poisoning. Antidote for symptoms of mushroom poisoning by cholinomimetic alkaloid muscarine found in certain mushroom.

↳ Add a note on Mycotoxins poisoning.

⇒ Myco is the fungus and it produced naturally poison.

↳ Mycotoxins are Secondary metabolites of fungi that are recognized as toxic to other life forms.

↳ It can be heat stable, not destroyed by canning or other processes.

↳ It can cause Death, Respiratory problems, Reproductive problems, liver, kidney or other organ damage, cancer bleeding, birth defects.

2) Write the management for Arthropods bite.

→ topical or oral antihistamines, calamine lotion,
topical corticosteroids,
cold compresses
Systemic glucocorticoids.

6) Write the treatment of Bee bite.

⇒ ^{mustard} Applied topically and cold compress

Antihistamine → Reduces or stops an allergic reaction.

Steroid → Simulates hormone effects to reduce inflammation on for tissue growth and repair.

Analgesic → Relieves pain.

Treatment →

- 1) Stomach wash with normal saline performed gently may be of benefit in massive ~~ing~~ ingestions.
- 2) Activated charcoal is ineffective.
- 3) Magnesium hydroxide soln.
- 4) Obtain serum iron levels, creatine, electrolytes, blood haemoglobin concn.
- 5) Correction of hypovolaemia and metabolic acidosis.
- 6) Chelation therapy.

Conclusions

Primary goals of chelation therapy:

- To reduce metal retention
- To decrease morbidity and mortality
- To prevent complications

Many efficient chelators exist today

Administer less toxic chelator when possible

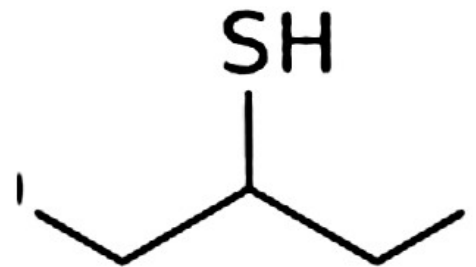
Unsolved issues:

- Chelation of cadmium, chromium, platinum...
- Chelation therapy in infants, children and during pregnancy
- Combined chelation therapy (chelators, vitamins, minerals...)

What is the use of BAL?



Dimercaprol, also called British anti-Lewisite (BAL), is a medication used **to treat acute poisoning by arsenic, mercury, gold, and lead.** It



may also be used for antimony, thallium, or bismuth poisoning, although the evidence for those uses is not very strong. It is given by injection into a muscle.

 DMSA in toxicology



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Meso-2,3-dimercaptosuccinic acid
(DMSA) is a **sulfhydryl-containing, water-soluble, non-toxic, orally-administered metal chelator** which has been in use as an antidote to heavy metal toxicity since the 1950s.