

CLINICAL TOXICOLOGY.

Date

Arsenic poisoning:

- Arsenic is a metalloid which is silver-grey in color and crystalline/metallic looking element.
- It is usually found in its related elemental form.

⇒ Organic & Inorganic forms of Arsenic are:

(i) Elemental Arsenic

(ii) Arsine gas.

(iii) Arsenic trioxide

(iv) Dimethyl arsine

(v) Arsenic pentoxide

(vi) Sodium arsenite

⇒ Usual Fatal Dose:

(i) 200 to 300 mg of arsenic trioxide

(ii) 25 to 30 ppm of arsine gas can be the most toxic form.

⇒ Toxicokinetics:

- After absorption,

Arsenic

↓

Redistributed in

liver, lungs, spleen

& intestinal wall

↓

Binds to sulfhydryl

group

↓

Arsenic replaces Phosphorus in bones.

- Aseptic does not cause **BBB**
- But, exsolved placental membrane and can cause intrauterine death

⇒ Clinical Features:

(i) Dermal -

- Hairless
- Hyperkeratosis
- Melanosis (Neck, Eyelids, Nipples)
- Bowen's disease
- Homan's sign
- Facial edema

(ii) Ocular -

- Conjunctivitis
- Lacrimation
- Dimness of vision

(iii) Gastrointestinal -

- Metallic taste
- Abdominal pain
- Bloody or rice-water diarrhoea
- Anorexia
- Nausea / Vomiting

(iv) Airways -

- Irritation of upper airways
- Perforation of nasal septum
- Bronchitis

(v) Liver -

- Fatty degeneration

- Hepatomegaly
- Jaundice
- Cirrhosis

(vi) Kidney -

- Oliguria
- Proteinuria
- Uraemia
- Nephritic changes

(vii) Cardiovascular -

- HTN
- Haemycardia
- Myocarditis

⇒ Diagnosis:

(i) Urea level - $>100\text{mg}$ in 24hrs

- Urgection of seabod can mislead the interpretation as there are considerable concentrations of organic azurine present

(ii) Blood level - $>10\text{mg/L}$ ($>1\text{mg}/100\text{ml}$)

- Less reliable because of short half-life of azurine in blood

(iii) Radiography

(iv) Haem level

(v) CBC, s. electrolytes, Urinalysis, UFT & RFT

(vi) ECG

(vii) CXR for pulmonary effects.

⇒ Treatment:

(i) chelation therapy -

- It is done with BAL (Dimercaprol), Penicillamine, DMSA and DMPS.

- BAL - 3 to 5 mg/kg IM every 4 hours until urine level drop to $< 50 \text{ mcg/24 hrs}$ x 7 to 10 days.

- Penicillamine - 100 mg/kg/day PO 6 hourly x 5 days.

(ii) supportive measures -

- Gastric lavage

- Intravenous fluids

- Cardiac monitoring.

Lead Poisoning:

- Lead exists as a highly lustrous, heavy, silvery-grey metal. It is quite soft and malleable.

- The forms of lead that exist are:

- (i) Lead acetate
- (ii) Lead carbonate
- (iii) Lead oxide
- (iv) Tetraethyl lead

- Other non-occupational sources of lead are:

- (i) Ayurvedic medicines
- (ii) Paint
- (iii) Retained bullets
- (iv) Ink
- (v) Automobile storage battery
- (vi) Silver jewellery workers.

⇒ Usual fatal dose:

- (i) 10 gm/70 kg for most lead salts
- (ii) 100 mg/kg - Tetraethyl lead.

⇒ Toxicokinetics:

- (i) Tetraethyl lead can be absorbed easily through intact skin.
- (ii) Children - 70% of total body lead is skeletal. While, in adults, over 95%.

(iii) Excretion - Urine (65%)
Bile (35%)

⇒ Mode of Action:

(i) Lead combines with sulfhydryl enzymes leading to interference with their action.

(ii) Lead decreases Heme synthesis

↓

Inactivation of enzymes.

such as Ferrochelatase.

and Decarboxylase

↓

Anemia

(iii) Lead increases Hemolysis.

↓

Release of immature

Red cells into

circulation

(iv) CNS - Oedema.

↓ Nerve conduction.

↑ psychomotor activity

Lower IQ.

Behavioural / Learning disorders

(v) CVS - HTN and Myocarditis

(vi) Kidney - Nephritis

(vi) Reproductive organ - Infertility

(vii) Interstitial Nephritis, \downarrow GFR and Non-specific proximal tubular dysfunction are typical.

(viii) Decrease in acid renal excretion.

\downarrow

\uparrow Blood urate levels
(GOUT)

\Rightarrow Clinical Features:

- MILD TOXICITY - (40 to 60 mcg/100ml)

- Myalgia
- Paresthesia
- Fatigue
- Irritability
- Abdominal discomfort

- MODERATE TOXICITY - (60 to 100 mcg/100ml)

- Arthralgia
- Muscular exhaustion
- Anorexia
- Anorexia, Metallic taste, Vomiting
- Constipation
- Weight loss
- HTN

- SEVERE TOXICITY - (>100 mcg/100ml)

- Lead palsy (wrist or foot drop)
- Burton's line
- Lead colic
- Lead encephalopathy.

⇒ Diagnosis :

(i) Blood - Low Hct / Hb.

Normal differential count

(ii) FEP and ZnP levels ($>50 \text{ mcg/100ml}$)

⇒ Treatment :

(i) Severe acute poisoning with encephalopathy

(a) BAL 4 mg/kg

(b) If cerebral oedema

→ Continued hyperventilation

→ Arterial CO_2 (25 to 30 mmHg)

→ Diuretics

(Mannitol 0.5 to 1 gm/kg by IV infusion over 10 to 20 mins)

→ (Glycerol 0.3 to 1 gm/kg orally)

→ Corticosteroids

(Dexamethasone - 16 mg/day or 1 to 2 mg/kg/day)

(c) For seizures.

→ IV Diazepam (A: upto 10 mg slowly)
(C: 0.1 to 0.3 mg/kg)

(d) Foley catheterisation

(e) After initial dose of BAL, repeat the same dose at 4 hourly intervals until blood levels fall below 40 mcg/100ml .

Then reduce BAL to 12 mg/kg/day in 3 divided doses.

(f) CaNa_2EDTA 75mg/kg/day IV int and reduce to 50mg/kg/day if patient improves

(ii) severe acute poisoning without encephalopathy. ($>70\text{mcg}/100\text{ml}$)

(a) BAL 12mg/kg/day

(b) EDTA 50mg/kg/day

(c) Discontinue BAL when blood level falls below $40\text{mcg}/100\text{ml}$ but continue EDTA $\times 5$ days.

(iii) Moderate poisoning (BL: 45 to $70\text{mcg}/100\text{ml}$)

(a) EDTA 50mg/kg/day

(b) when BL $<40\text{mcg}/100\text{ml}$, start oral chelation

(iv) Mild poisoning (BL: 20 to $35\text{mcg}/100\text{ml}$)

(a) D-Penicillamine 30mg/kg/day in 3 divided doses.

* Thiamine 10 to 50mg/kg improves the neurological manifestations of lead poisoning

* IV calcium gluconate - Lead colic

⇒ Autopsy features:

The most typical features of a patient of lead poisoning manifested are -

(i) Pale skin.

(ii) Emaciation.

(iii) Burtonian lines

(iv) Lead lines on X-ray

(v) Pathological lesions

(Kidneys, Liver, Male gonads, Blood vessels).

⇒ Clinical features :
POISONING WITH ELEMENTAL MERCURY AND
INORGANIC SALTS

(i) Acute poisoning

(A) Inhalation -

- Dyspnoea

- Cough

- Fever

- Headache

- GI disturbance

- Stomatitis

- Swelling of salivary glands

- Gingivitis

- Manifestations similar to Kawasaki disease

(scarlet fever, conjunctivitis, Fever, Reddened palm and soles, strawberry tongue, skin rash).

(B) Ingestion -

- It leads to corrosion of GI tract

- Abdominal pain

- Vomiting

- Shock

- Diarrhoea

- Mucosa of GI tract appears greyish

- Haematemesis

- Onset of Renal failure

- Pulmonary oedema

- Coma

- Pinkish urine

develops
few days
later

severe
cases

cc) Injection -

- s/c or IM injections may cause abscess formation with ulceration, extending tiny droplets of mercury.
- Mercurialism
(Thrombophlebitis, Granulomas and pulmonary embolism.)
- Repeated Hemoptysis is a typical feature.
- Leakage of mercury into arterial blood results in peripheral embolism with ischemia and sometimes gangrene.

iii) Chronic poisoning

(A) Inhalation -

- Hetero - classical and most consistent manifestations of chronic mercury poisoning.
"Dahivuy tremor"

- Ataxia, reeling gait.

- Fasciculation of the tongue in pediatrics

- Metallic taste.

- Anorexia.

- Nausea

- Increased salivation.

- Gingivitis, halitosis.

- Erythematous maculae or papular rashes.

(B) Ingestion -

- Colitis
- Metabolism
- Dementia
- Memory
- Renal failure
- Amyotrophy (Pink disease)

⇒ Diagnosis :

- (i) X-ray
- (ii) Blood mercury level $> 3 \text{ mcg} / 100 \text{ ml}$.
- (iii) Urine mercury level $> 10 \text{ mcg} / 100 \text{ ml}$.
- (iv) Hair analysis.

⇒ Treatment :

(I) Acute poisoning -

(A) Inhalation

- Supportive measures.
- Chelation.

(B) Ingestion.

- Administer laxatives.
- Stomach wash : Egg white or 5% albumin or plain milk.
- Demulcents for corrosive comp.
- Chelation.

(C) Injection.

- If abscess formation \rightarrow penicillin.
- Repeated incision to remove the mercury.

- Monitor CNS & RFT for toxicity
- Activated charcoal.
- chelation.

(ii) Chronic poisoning -

(A) chelation therapy

- BAL

100mg by deep IM, every 4 hours
for 48 hrs

↓

100mg every 8 hours for 8 to 10 days.

OR

- DMPS

5mg/kg IV or 6 infusions of 250mg/day

↓

100mg orally BD for 24 days.

OR

- DMSA

30mg/kg/day orally for 5 days

↓

20mg/day for 14 days.

OR

- D-Penicillamine

250mg qid for adults (20mg/kg/day)
for 5 to 10 days.

(B) supportive measures.

Iron Poisoning :

- It is silvery white in color and occurs as Hematite and Magnetite.
- It is an essential element and its deficiency lead to Anemia.

⇒ Usual fatal dose :

- (i) As low as 60mg/kg (children)
- (ii) On average, 200 to 250mg/kg can be lethal.

⇒ Toxicokinetics :

Iron poisoning occurs when serum iron level exceeds the total iron-binding capacity (TIBC), resulting in free circulating iron in the bloodstream.

⇒ Clinical features :

(i) Stage I (0.5 to 2 hrs)

- Hematemesis
- Abdominal pain
- Diarrhoea.
- Hematochezia.
- Lethargy
- Shock
- Acidosis.

(ii) Stage II

It may contribute to false security of recovery.

(iii) Stage III (2 to 12 hrs after stage I)

- Profound fever
- Severe acidosis
- Cyanosis
- ↓ Plasma volume
- Hypotn
- CNS depression

(iv) Stage IV (2 to 4 days)

- Possible Hepatotoxicity
- Convulsions
- Coma
- Acute lung injury

Monitor LFT & Bilirubin.

(v) Stage V (days to weeks)

- GI scarring and strictures
- GI obstruction
- Evaluate with barium contrast studies.

⇒ Diagnosis :

(i) X-ray

(ii) Serum iron level - $> 150 \text{ mcg/100ml}$

* Severe toxicity - $> 500 \text{ to } 600 \text{ mcg/100ml}$

(iii) Total leucocyte count, electrolytes, glucose, blood gas, clotting studies, LFT & RFT

(iv) ~~Def~~ Desferrioxamine 25 mg/kg IM

↓

If (+)ve → pinkish urine.

⇒ Treatment :

- (i) stomach wash with normal saline
- (ii) Activated charcoal is ineffective
- (iii) Magnesium hydroxide soln (1%) reduces the absorption of iron

(iv) Correction of hypovolemia and metabolic acidosis

(v) Chelation therapy - Desferrioxamine

- IV dose : up to 15 mg/kg/hr.
- IM dose : 90 mg/kg up to 1 gm/dose every 8 hours.
- Total daily dose : < 6 gms.

* Adverse effects of chelation:

- Sepsis
- Visual toxicity
- Ototoxicity
- Pulmonary toxicity
- Hypotn
- Renal toxicity : (↑ Cr)

Copper Poisoning:

It is lustrous, golden-red, ductile and malleable solid.

- It is a catalyst for Hearn synthesis and iron dismutation.

⇒ Uses:

- (i) Electrical conductivity
- (ii) Corrosion resistance.
- (iii) Ceramic, glass, enamel & porcelain works - copper oxide.
- (iv) Paint pigment - copper acetate.

⇒ usual fatal dose:

About 10 to 20 gm of copper sulfate

⇒ Clinical features:

(i) Acute poisoning -

- Myalgia, Abdominal pain, diarrhoea, Acidosis, Methemoglobinemia, Hemolysis, Jaundice

- Hepatomegaly
liver tenderness
↑ transaminase
Jaundice

} 2 to 3 days of
congestion.

- Acute renal failure (20 to 40%)

- Anuria or Oliguria.

- Inhalation of copper dust cause cough, sore throat, conjunctivitis.

(ii) Chronic Poisoning -

- Green hair discoloration in swimming pool.
- Cooking in copper or brass vessel can cause toxicity due to mendigris.
- Wilson's disease
- Discoloration of peripheral part of cornea (Kayser-Fleischer ring)
- Metal fume fever.
- Wheezing
- Rales
- Severe irritation, itching, erythema, dermatitis & eczema

⇒ Diagnosis :

(i) Serum ceruloplasmin level -
 $< 35 \text{ mg\%}$ in 24 hrs indicates severe toxicity

(ii) Blood copper level - $> 1.5 \text{ mg/100ml}$
* For pregnant women - $> 2.39 \text{ mg/l}$

(iii) Urine level - $> 0.6 \text{ micromole/day}$.

⇒ Treatment :

(i) Hemodialysis in early stages.

(ii) Egg white or milk orally help in detoxifying copper.

(iii) Stomach wash with potassium ferriocyanide.

(iv) Induced emesis is contraindicated.

(v) chelation -

(a) D-Penicillamine:

- 1000 to 1500 mg/day every 6 to 12 hrs.
(Adult)

- 30 mg/kg/day \Rightarrow 30 mg/kg/day in 2 to 3 divided doses.

(Pediatric)

\downarrow

Up to 100 mg/kg/day
depending on the
severity of symptom

(b) Dimercaprol:

- 3 to 5 mg/kg/dose deep IM every 4 hrs
for 2 days

(c) Unithial -

- 5% solution IM.
- 5 mg/kg s/c 3 to 4 times during
first 24 hrs.

\downarrow

2 to 3 times on day 2.

\downarrow

1 to 2 times daily thereafter.

(d) CaNa₂ EDTA:

- 75 mg/kg IM.
- slow IV infusion in 3 to 6 doses.
up to 5 days.

(vi) symptomatic treatment

- Antacids and ranitidine for prevention of gastric erosion.

(vii) Discoloration of hair

- shampoos containing penicillamine (250mg in 5ml of water & 5ml of shampoo).

• EDTA