Arsenic: metallic arsenic = black colour

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Poisonous Compounds:

→ Arsenic oxide / Arsenic trioxide / Sankhya / Somalkhar / White arsenic
- no taste or smell
- sparingly soluble in water

→ Copper arsenite / Sheele's green / Paris green / Emerald green

→ Arsenic acid

→ Sodium & potassium arsenate

→ Arsenic trichloride / Butter of arsenic

Action:

Arsenic combines with SH groups of mitochondrial enzymes → (Pyruvate oxidase, phosphatases)

Interference with cellular respiration

→ uncoupling of mitochondrial oxidative phosphorylation

→ targets vascular endothelium → increased permeability → oedema, hemorrhage

→ irritation of mucous membrane

→ remote depression of CNS

Signs & Symptoms:

I] Fulminant Type: caused by massive doses (3-5g) of arsenic ⇒ rapidly absorbed

→ death within 1-3 hours from shock & peripheral vascular failure

→ capillaries are markedly dilated ∴ marked fall of BP

→ no GI symptoms

II] Gastroenteric Type: common form of acute poisoning (resembles bacterial food poisoning)

→ symptoms appear ½ - 1 hour after ingestion

→ sweetish metallic taste

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(1) GIT: constriction in the throat & difficulty in swallowing
→ burning & colicky pain in oesophagus, stomach & bowel
→ intense thirst, projectile vomiting
→ tenesmus & irritation about the anus
→ expelling of stools frequently & involuntarily
→ stools: dark-coloured, stinking, bloody
⇒ later becomes colourless, odourless & watery resembling rice-water stools of cholera
→ garlic odour of breath & faeces

(2) Hepatic: fatty infiltration

(3) Renal: • Oliguria • Uraemia • Urine contains albumin, red cell casts
• pain during micturition

(4) CVS: • Vasodilation & acute circulatory collapse • Ventricular tachycardia
• Ventricular fibrillation

(5) CNS: • Headache • Hyperthermia • Convulsions • General paralysis
• Vertigo • Tremors • Coma

(6) Skin: • Loss of hair (delayed) • Skin eruptions

(7) Death: due to circulatory failure

III] Narcotic form: GI symptoms are very slight
• Giddiness • Formication & tenderness of muscles
• Delirium • Coma, Death

→ Late sequelae: • Haematuria • Anaemia • Thrombocytopenia
• Acute tubular necrosis • Leucopenia

Fatal Dose: 0·1 - 0·2 g As_2O_3

Fatal Period: 1 - 2 days.

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Treatment:

(1) Stomach emptied → wash thoroughly & repeatedly with large amount of warm water & milk

(2) Freshly prepared, hydrated ferric oxide p.o. in small doses (converts toxic arsenic to non-toxic ferric arsenite)

(3) B.A.L. ⇒ 400-800 mg on Day 1
⇒ 200-400 mg on Days 2 & 3 in divided doses every 4 hours
⇒ 100-200 mg in 2 divided doses for 7-10 days
→ Penicillamine may be used with B.A.L [100mg/kg daily upto 1-2g in 4 divided doses for 5 day]

(4) DMSA or DMPA (instead of B.A.L) may be used.

(5) Demulcents

(6) Castor oil / $MgSO_4$ (prevent intestinal absorption of arsenic)

(7) Glucose-saline with sodium bicarbonate

(8) Haemodialysis or exchange transfusion (in renal failure)

Toxicokinetics:

→ well absorbed from GIT, RS & skin
→ upon absorption ⇒ bound to protein portion of Hb & α-globulins
→ distributed in all organs & tissues
→ does not cross BBB
→ inorganic arsenic can cross placenta
→ found in muscles for several days & in keratin-containing tissues for years.
→ eliminated by kidneys as methylated As (found in urine within 30 min of ingestion)
→ has an enterohepatic circulation

PM Appearance:

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External:

→ Signs of dehydration: – sunken eyeballs
– shrunken body

→ cyanosed skin

Internal:

(1) Mouth, pharynx, esophagus: generally unaffected (may be inflamed / ulcerated)

(2) Stomach:

→ Mucosa: • swollen, edematous, bright red
• shows erosions & ulcerations
• mass of sticky mucus covers mucosa

→ Congestion – most marked along greater curvature, posterior part & cardiac end
– most prominent at crests of rugae

→ submucous haemorrhages in curved lines

→ red velvety appearance of stomach wall

→ petechiae scattered over mucosa

→ If putrefaction has occurred: yellow streaks in subperitoneal layer of stomach

(3) Small Intestine: appears flaccid [Arsenic converts to yellow sulphide due to H_2S gas]

→ mucosa: inflamed, pale violet, shows submucous hemorrhages

→ large flakes of mucus

(4) Liver, Spleen, Kidneys: • congested, enlarged, cloudy swelling, fatty change (after few days)
• glomerular nephritis

(5) Haemorrhages: in all abdominal organs

(6) Lungs: congested with subpleural ecchymoses

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(7) Heart: sebendocardial petechial haemorrhages (SEPH) of ventricles

(8) Brain:
- Edema
- Patchy necrosis
- Haemorrhagic encephalitis
- Congested meninges

Tests for Arsenic:

(1) Marsh test: Hydrogen passed through suspected material (ex: vomit) → Arsenic combines with H_2 to form AsH_3 → AsH_3 passed through a jet & burnt → thin film of arsenic is formed over porcelain

(2) Gutzeit Test

(3) Reinsch test

(4) Neuron Activation Analysis (NAA) & Atomic Absorption Spectroscopy [AAS]

(5) Excretion of > 100 µg in 24 hours urine

MLI:

→ Arsenic used to be the most favourite homicidal poison
- cheap
- tasteless
- easily available
- odourless

(1) Arsenophagists: people who take arsenic daily in the mistaken belief that it is an aphrodisiac.
→ development of tolerance
→ signs of chronic toxicity ✓

(2) Safe levels in drinking water: 10 parts per billion (PPB)

(3) Postmortem of Imbibition: In exhumation, possibility of:
- imbibition of arsenic from stomach into neighbouring viscera
- contamination from surrounding soil (Arsenic in soil is usually found as insoluble salt, but is required to be in soluble form for its imbibition into the body).

	Arsenic poisoning	Cholera
Pain in throat	Before vomiting	After vomiting
Purging	After vomiting	Before vomiting
Stools	Dark-coloured & bloody, later rice-watery	Rice-watery, not bloody & passed continuously involuntarily.
Tenesmus & anal irritation	Present	Absent
Vomited matter	Contains mucus, bile, blood	Watery without mucus, bile, blood
Voice	Not affected	Rough & whistling
Conjunctiva	Inflamed	Not inflamed
Analysis of excreta	Arsenic present	Cholera vibrio present
Circumstantial evidence	Of arsenic poisoning may be present	Other cases of cholera in locality.

Mercury (Quick Silver):

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→ Liquid metal, bright silvery appearance, volatile at room temperature.

→ poisonous: mercuric compounds > mercurous compounds

→ metallic mercury is not poisonous if swallowed ∵ it is not absorbed

Action:

→ Mercuric ion binds to -SH group of enzymes & cellular proteins, nucleic acids & mitotic apparatus.

→ acts on cerebellum, temporal lobe, basal ganglia & corpus callosum in CNS.

Poisonous Compounds:

→ Mercuric chloride ($HgCl_2$)

→ Mercuric oxide (brick-red crystalline powder)

→ Mercuric iodide (scarlet-red powder)

→ Mercuric cyanide (white prismatic crystals)

→ Mercuric sulphide / cinnabar / sindoor

→ Mercurous chloride (calomel)

Symptoms:

I] First Phase:

→ acid metallic taste

→ feeling of constriction in the throat

→ mouth & tongue ⇒ corroded, swollen, greyish-white coating

→ hot burning pain in the mouth, stomach

→ diarrhoea, blood-stained stools

→ circulatory collapse

→ hoarse voice

→ difficulty in breathing

→ vomit contains greyish, slimy mucoid material with blood & shreds of mucus membrane.

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II] Second phase: (If person survives, 2nd phase begins in 1-3 days)

- Glossitis
- Ulcerative gingivitis
- loosening of teeth
- necrosis of jaw
- Renal tubular necrosis ⟹ transient polyuria, albuminuria, uraemia, acidosis.
- Recovery within 10-14 days
- After many days ⟹ membranous colitis leading to dysentery, ulceration of colonic mucosa & haemorrhage

Fatal Dose: 1-2 g of mercuric chloride

Fatal Period: 3-5 days

Treatment:

(1) Gastric lavage: Milk / egg-white / 5% salt-poor albumin / 2-5% sodium bicarbonate

(2) Whole bowel irrigation (may be useful)

(3) Penicillamine: for less severe mercury vapour & inorganic mercury poisoning.

⟹ P.O 100 mg/kg every 6 hours (max: 1 g/day) for 5 days in children
250 mg QID for 5 days in adults

(4) BAL ⟹ chelating agent of choice

⟹ dose regimen is same as for arsenic

[BAL & penicillamine should not be used in combination]

(5) Urine alkalinization

(6) High colonic lavage with 1:1000 solution of sulphoxylate BD

(7) Haemodialysis (in case of significant kidney damage)

PM Appearance: GIT mucosa ⟹ inflammation, congestion, coagulation, corrosion

→ If patient survives for a few days ⟹ large intestine shows necrosis (due to re-excretion of mercury into large bowel)

→ acute tubular & glomerular degeneration or haemorrhagic glomerular nephritis

→ liver: congested, cloudy swelling or fatty change.

Chronic Mercury Poisoning (Hydrargyrism):

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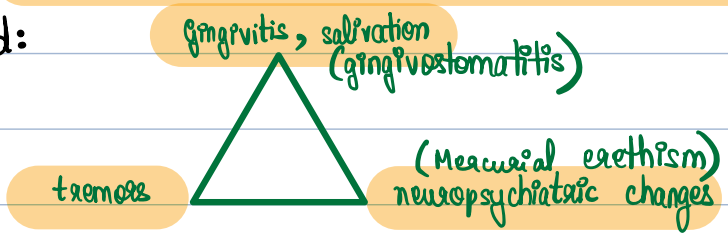
→ may result from:
- continuous accidental absorption by workers
- excessive therapeutic use
- if ointment (as external application) is used for a long time.

→ Chronic exposure triad:



Symptoms:
- Salivation
- Inflammation of gums, blue line at junction of teeth & gums
- GI disturbances
- Anaemia
- Anorexia
- Weight loss
- Chronic inflammation of kidneys with uraemia
- Danbury tremors (moderately coarse & interspersed by jerky movements)

→ progresses to

Hatter's shakes / Glass-blower's shakes

[Patient is unable to dress himself, write legibly or walk properly]

→ progresses to

Concussio mercurialis

(no activity is possible)

→ **Mercurial erethism:** seen in persons working with mercury in mirror manufacturing units.
- anxiety, depression
- shyness, timidity
- irritability
- loss of confidence
- delusions, hallucinations
- suicidal melancholia
- loss of memory
- insomnia

→ **Mercurialentis:** eye change due to exposure to
- vapour of mercury
- brownish deposit of mercury through cornea on anterior lens capsule

→ generalised body rash

Acrodynia / Pink disease: idiosyncratic hypersensitivity reaction, particularly in children
- → caused by chronic mercury exposure
- → insidious onset
- → anorexia, insomnia, sweating, skin rash, photophobia
- → hands & feet become puffy, pinkish, painful, paraesthetic, peeling of skin

Minamata Disease: organic mercurial poisoning
→ due to eating of fish poisoned by mercury
→ disaster in Japan in 1956

Excretion of Mercury: by liver, kidneys, & colonic mucous membrane
→ normal blood mercury level: 4 µg / 100 ml.

Test: Suspected solution + piece of copper wire + few drops of HCl
→ silvery coating of mercury on copper wire

MLI:

(1) Stains of red sulphide of mercury resemble blood stains
(2) Criminal abortion: mercury salts introduced in vagina
(3) Accidental poisoning: — thermometers breaking in the mouth
— Complication of Hg-sealed syringes for arterial blood drawing
— disk battery ingestion
(4) Homicidal / Suicidal poisoning: rare

Lead: heavy, steel-grey metal

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→ Lead acetate (sugar of lead) ⇒ white crystals
→ Lead carbonate (safeda) ⇒ white crystalline powder
→ Lead chromate ⇒ bright yellow powder
→ Lead monoxide (litharge)
→ Lead tetroxide (red lead, vermillion sindur)

Action:

→ interacts with –SH groups & interferes with enzymes necessary for haem synthesis, haemoglobin & cytochrome production.
→ interferes with mitochondrial oxidative phosphorylation
→ causes haemolysis

Toxicokinetics:

Absorption: absorption of inorganic lead compounds from GIT is slow
→ rapid absorption by inhalation
→ absorption from skin is poor
→ crosses the placenta
→ typical cumulative poison
→ gradually stored in bones

Excretion: largely excreted in faeces
→ absorbed lead is excreted mostly in urine

Acute Poisoning:

- astringent metallic taste
- dry throat, thirst
- burning abdominal pain
- nausea, vomiting
- headache, insomnia
- peripheral circulatory collapse
- paraesthesias
- coma, death

cerebellar ataxia is common in children.

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Fatal Dose: 20 g lead acetate / 40 g lead carbonate

Fatal Period: 1 - 2 days

Treatment:

(1) Gastric lavage: 1% Na_2SO_4 or $MgSO_4$

(2) Demulcents

(3) BAL + DMSA

(4) Penicillamine

(5) $CaCl_2$ (10% solution) 5 mg i.v.

(6) Peritoneal dialysis or haemodialysis

Chronic Lead Poisoning / Plumbism / Saturnism:

Causes:

- Inhalation of lead dust & fumes by makers of white lead, smelters, plumbers, painters, etc.
- continuous absorption of minute amounts from drinking water stored in lead cisterns
- absorption through raw or intact skin
- Use of ghee stored in brass or copper vessels lined with tin in which oleate of lead is formed.
- Absorption of vermillion from scalp
- Children: chewing or licking toys / walls / furniture

Signs & Symptoms:

1] Facial pallor: particularly around the mouth (due to vasospasm)

2] Anemia: polychromasia, punctate basophilia, reticulocytosis, nucleated RBCs (sideroblasts)

→ ↓ in PMN cells & platelets.

→ Punctate basophilia / Basophilic Stippling: presence of many dark blue coloured pinhead-sized spots in cytoplasm of RBCs (due to toxic action of lead on porphyrin metabolism)

- due to inhibition of 5-pyrimidine nucleotidase ⟹ impaired ability to rid the cell of RNA degradation products
  → eosinophilia
  → porphyrinuria (~ 500 µg/day)

3] Lead line / Burtonian line: stippled blue line seen on gums
→ appears due to subepithelial deposit of granules at junction of gums & teeth only near dirty or carious teeth
→ due to formation of lead sulphide

4] Colic & Constipation: colic of intestines, ureters, uterus & blood vessels
→ colic occurs at night

5] Lead Palsy: occurs late
- tremors
- numbness
- hyperaesthesia
- cramps
- muscle fatigue (wrist drop, foot drop)

6] Encephalopathy: present in almost every case of plumbism
- vomiting
- headache
- insomnia
- visual disturbances
- irritability
- delirium, hallucinations
- convulsions, coma, death

7] CVS & Kidneys: • vasoconstriction ⟹ hypertension, permanent arteriolar degeneration
- chronic arteriosclerotic & interstitial nephritis.

8] Reproductive System: • Menstrual derangements ⟹ amenorrhea, dysmenorrhea, menorrhagia
- sterility, abortions

9] Other Systems: • Dyspepsia • Anorexia • Emaciation • General weakness
- headache • loss of hair

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Treatment:

I] Severe Acute Poisoning with Encephalopathy:

→ BAL 4 mg/kg immediately
- Repeat 4 hourly until blood lead levels fall below 40 µg/dL.
- 12 mg/kg/day in 3 divided doses

→ $CaNa_2EDTA$ 75 mg/kg/day I.V. infusion
- Reduce 50 mg/kg/day as condition improves

→ Oral chelation with D-penicillamine 10 mg/kg/day TID for 20 days.

II] Severe poisoning without encephalopathy: (BL > 70 µg/dL)

→ BAL 12 mg/kg/day [Discontinue when blood lead level < 40 µg/dL]

→ EDTA 50 mg/kg/day [continue for 5 days after stopping BAL]

→ continue oral chelation until blood lead (BL) < 15 µg/dL.

III] Moderate poisoning: [BL: 45-75 µg/dL]

→ EDTA 50 mg/kg/day

→ Begin oral chelation when BL falls < 40 µg/dL.

IV] Mild poisoning: [BL: 20-35 µg/dL]

→ D-penicillamine 30 mg/kg/day in 3 divided doses

PM Appearance: (not constant)

→ blue line on the gums at the junction of gums & teeth

→ fatty degeneration of paralyzed muscles.

→ stomach & intestine:
- ulcerative / haemorrhagic changes
- contracted & thickened.

→ brain: pale & swollen.
- PAS positive, pink-staining, homogenous material may be seen in perivascular space

→ Heart: hypertrophy, atheroma of aorta

→ Bone marrow : ↑ cellularity , ↓ fat.

→ segmental demyelination of peripheral nerves.

Cause of Death:

→ Acute poisoning : gastroenteritis & subsequent shock

→ Chronic poisoning : malnutrition , respiratory failure , renal failure , encephalopathy.

MLI:

→ acute poisoning is rare.

→ homicidal poisoning is rare.

→ Accidental chronic poisoning is seen in metal workers.

→ not used for suicide.

→ Diachylon paste (lead oleate) ⟹ used for criminal abortion.

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Copper:

not poisonous as a metal alone; Copper compounds are strong inhibitors of enzymes.

→ Copper sulphate (blue vitriol)

→ Copper subacetate (verdigris)

Toxicokinetics: copper is a normal constituent of the body

→ Copper content of the body: 150 mg

→ safe daily dietary intake of copper: 2-3 mg.

→ absorbed through lungs, mucous membranes

→ excretion: bowel > kidney.

Signs & Symptoms:

- symptoms appear within 15-30 minutes
- metallic taste
- increased salivation
- burning pain in stomach with colicky abdominal pain.
- thirst
- nausea
- eructations
- vomitus = blue/green
- diarrhoea
- acidosis, uraemia
- faeces ⟹ liquid, brown (not bloody)
- oliguria, hematuria, albuminuria
- severe cases ⟹ haemolysis, haemoglobinuria, methemoglobinaemia, jaundice, pancreatitis, cold perspiration, severe headache, paralysis of limbs, death due to hepatic or renal failure or both.

→ Acute inhalation of large dose of copper dust / fumes ⟹ upper respiratory irritation (sore throat, cough), conjunctivitis, palpebral oedema, sinus irritation.

Fatal Dose: 30g $CuSO_4$; 15g copper subacetate

Fatal Period: 1-3 days

Treatment:

1] Stomach wash with 1% potassium ferrocyanide (forms insoluble cupric ferrocyanide)

2] Emetics are c/I.

3] Demulcents (form insoluble albuminate of copper)
4] Haemodialysis (useful in early stage of poisoning)
5] Castor oil
6] Chelation with penicillamine / EDTA / BAL.

PM Appearance:

→ skin may be yellow
→ Greenish-blue froth at mouth & nostrils
→ Gastric mucosa & stomach contents ⟹ greenish / bluish
→ Gastric mucosa ⟹ congested, swollen, inflamed, may be eroded
→ Liver: soft & fatty
→ degenerative changes in PCT of kidney.

Chronic Poisoning:

may occur in metal workers due to inhalation of dust or from food being contaminated with verdigris.

→ Chronic inhalation of $CuSO_4$ spray ⟹ Vineyard Sprayer's lung ⟹ histiocytic granulomatous lung.

→ Chronic poisoning of Copper ⟹ Wilson's disease

- green line on gums
- peripheral neuritis
- degeneration & atrophy of muscles
- nausea, vomiting
- malaise
- gradual anaemia
- colic, diarrhoea

→ presence of copper deposits in tissues ⟹ Chalcosis

Test: suspected solution + NH_4OH → greenish-blue precipitate soluble in excess & forms a green solution

MLI:

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→ rarely used for homicide due to its colour & taste

→ suicide cases are rare

→ Accidental poisoning: ● eating food contaminated with verdigris (formed by action of vegetable acids on copper cooking vessels which are not properly tinned)

● swallowing of $CuSO_4$ by children due its attractive colour

→ consumption of copper salts for criminal abortion

→ used as a cattle poison rarely.