Arsenic

What is Arsenic?

- Arsenic is a naturally occurring element widely distributed in the earth's crust. In the environment, arsenic is combined with oxygen, chlorine, and sulfur to form inorganic arsenic compounds. Arsenic in animals and plants combines with carbon and hydrogen to form organic arsenic compounds.
- Pure Arsenic is black in color, non-toxic and not absorbed from the GIT.
- Salts and compounds of As are poisonous

Forms of Arsenic

Elemental -- Non toxic
Organic -- Low toxicity
Inorganic -- Toxic
Gaseous -- Highly toxic

What are the uses of Arsenic?

Compounds of As	Uses
As_2O_3 (White Arsenic)	•Rat poison, fly papers, etc •Anti-termite agent
Sulfides of As (Arsenic disulfide, Arsenic trisulfide)	Sometimes used as depilatories
Cu compds of As (Copper arsenite – Scheele's green, Copper acetoarsenite – Paris Green)	•Coloring agent for wall papers, toys, etc. •Insecticides
As compounds of Pb, Na, K	Weed killer, Insecticide, Fungicide, etc.
Organic Arsenicals (Carbarsone, Tryparsamide, Glycobiarsol, Melarsoprol, etc.)	Treatment of Trypanosomiasis, amoebiasis, etc.

What happens to As when it enters the environment?

- Arsenic may enter the air, water, and land from wind-blown dust and may get into water from runoff and leaching.
- Arsenic cannot be destroyed in the environment. It can only change its form.
- Rain and snow remove arsenic dust particles from the air.
- Many common arsenic compounds can dissolve in water. Most of the arsenic in water will ultimately end up in soil or sediment.
- Fish and shellfish can accumulate arsenic; most of this arsenic is in an organic form called arsenobetaine that is much less harmful.

Routes of absorption

- Arsenic is well absorbed by all routes ; Oral, Inhalational , parenteral .

  GI absorption depends on solubility
  Greatest absorption occurs in the small intestines and colon

  RS: Large particles deposit in the upper RT.
  Smaller particles travel to the alveoli where they are 80% absorbed.

  Skin: minimal absorption through intact skin
  prolonged topical application causes irritation which increases absorption.

How might one be exposed to As?

- Ingesting small amounts present in your food and water or breathing air containing arsenic.
- Breathing sawdust or burning smoke from wood treated with arsenic.
- Living in areas with unusually high natural levels of arsenic in rock.
- Working in a job that involves arsenic production or use, such as copper or lead smelting, wood treating, or pesticide application.

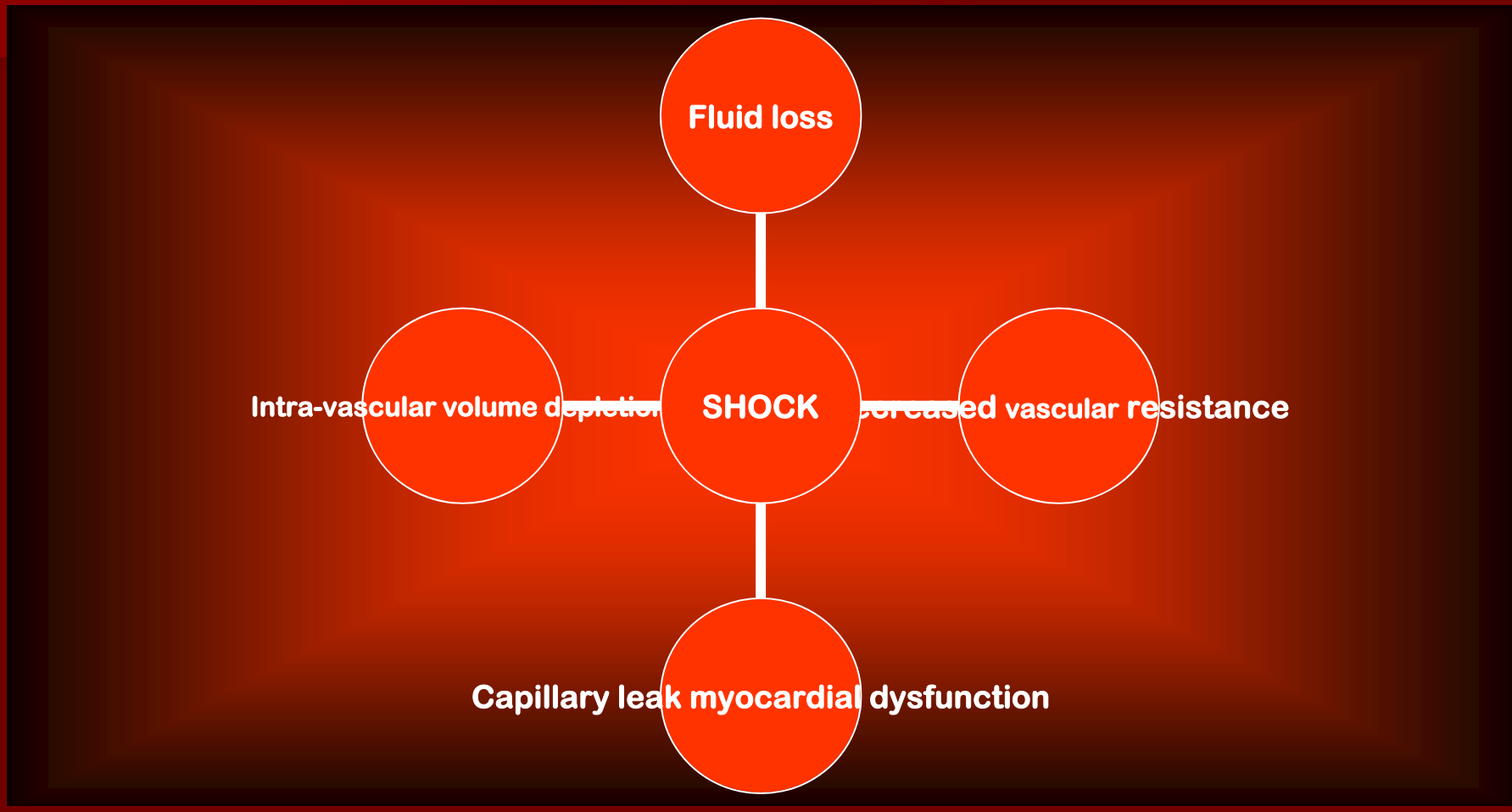
Some other scenarios

- Consumption of contaminated Alcohol – ”moon shine” alcohol
  Contra-band Opium
    - Ground water
    - Sea food
    - Sewage Gas

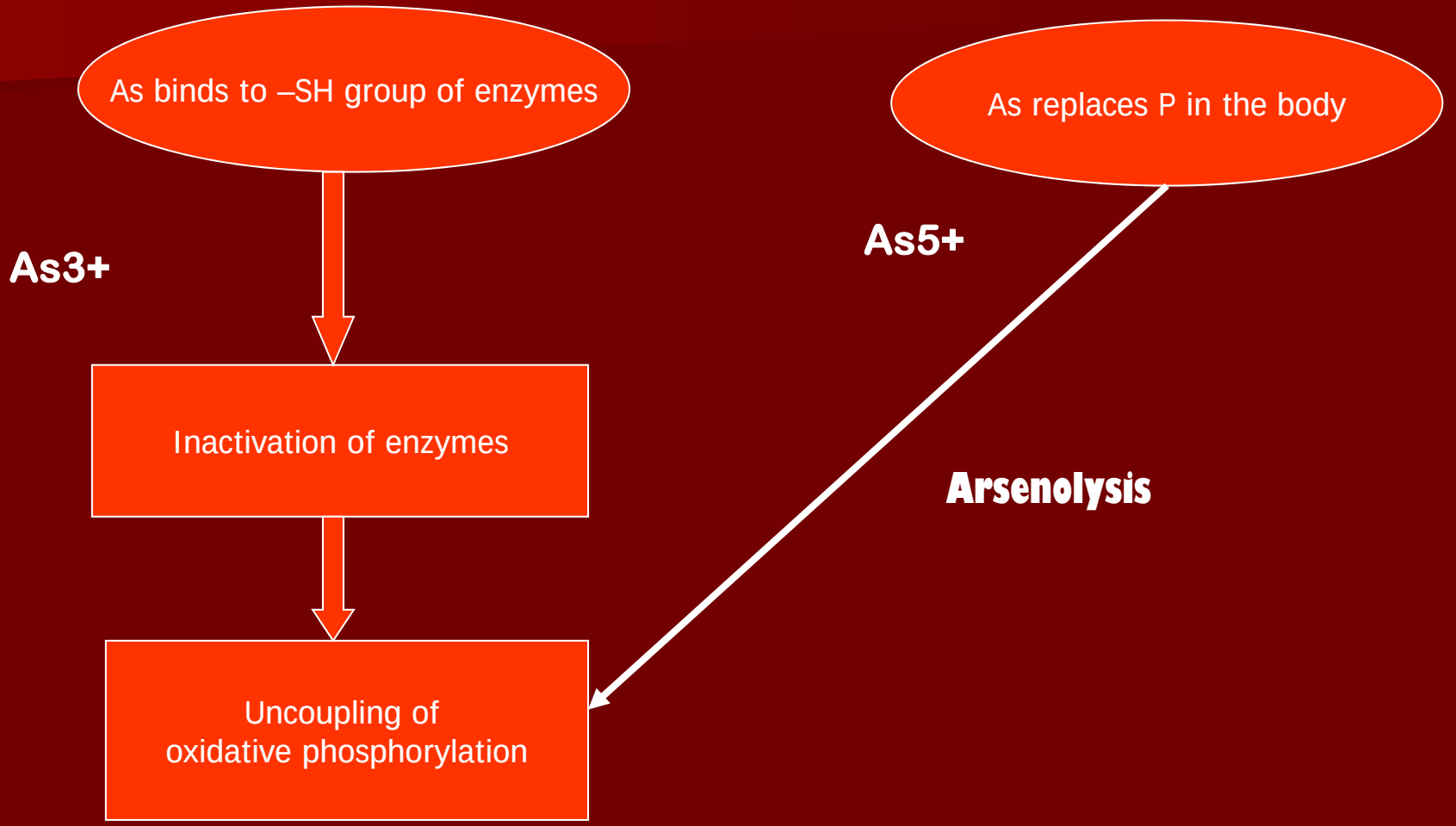
Mechanism of Action-Macro level

- Inflammation and necrosis of GI mucosa. Dilatation of blood vessels and Endothelial damage .

Patho-physiology of Shock



Mechanism of action-Micro level



Mechanism of action

Induces production of Growth promoting Cytokines and Growth factors in keratinocytes→

Dermal toxicity

Induces inhibition of DNA synthesis in Bone marrow →

Blood disorders

Toxicokinetics

- Well absorbed through Inhalation, Ingestion and through skin
- Once absorbed it binds to the Globin of Hb and is redistributed within 24 hours to the tissues, esp., liver, spleen, lungs, intestines, skin, bone

- As does not cross Blood-Brain-Barrier
- Inorganic As can cross placenta – fetus is affected
- Breast milk does not contain significant amounts of As

Metabolism and Elimination

- As is metabolised by Methylation to Methyl arsonic acid and Di-methyl arsonic acid which are predominantly excreted by kidneys.
- Fecal elimination – about 5% of oral dose
- Biliary excretion also occurs
- Sweat and Skin desquamation- very small amounts. (alternate deposits)
- Excreted in stomach and intestine after absorption, even when given by routes other than mouth

How can arsenic affect health?

- Breathing high levels of inorganic arsenic can give one a sore throat or irritated lungs.

- Ingesting very high levels of arsenic can result in death.
- Exposure to lower levels can cause nausea and vomiting, decreased production of red and white blood cells, abnormal heart rhythm, damage to blood vessels, and a sensation of "pins and needles" in hands and feet.

How does arsenic affect health?

- Ingesting or breathing low levels of inorganic arsenic for a long time can cause a darkening of the skin and the appearance of small "corns" or "warts" on the palms, soles, and torso.
- Skin contact with inorganic arsenic may cause redness and swelling.
- Organic arsenic compounds are less toxic than inorganic arsenic compounds. Exposure to high levels of some organic arsenic compounds may cause similar effects as inorganic arsenic.

Carcinogenicity

- Ingestion of inorganic arsenic can increase the risk of skin cancer and cancer in the lungs, bladder, liver, kidney and prostate.
- Inhalation of inorganic arsenic can cause increase risk of lung cancer.

How does arsenic affect children?

- Children may be less efficient at converting inorganic arsenic to the less harmful organic forms. For this reason, children may be more susceptible to health effects from inorganic arsenic than adults.
- Long-term exposure to arsenic in children may result in lower IQ scores.
- Inhaled or ingested arsenic can injure pregnant women or their unborn babies(?) Studies in animals show that large doses of arsenic in pregnant females can cause low birth weight, fetal malformations, and even fetal death.
- Arsenic can cross the placenta and has been found in fetal tissues. Arsenic is found at low levels in breast milk.

Clinical features

- Clinical features depend on- form of Arsenic, rate of absorption, time course of ingestion: acute, sub-acute, chronic

Clinical features of acute As toxicity

- Fulminant type:
  - Occurs on ingestion of a massive dose (>3 – 5 g)
  - Shock and peripheral vascular collapse result in rapid death
  - No findings on autopsy other than presence of As in stomach

Clinical features of acute As poisoning

- Gastroenteric type:
  - Vomiting, Abdominal pain – increase on pressure
  - Diarhoea – (d/d cholera) due to production of vesicles in submucosa of intestines
  - Dehydration and collapse leads to death in 24 – 48 hours
  - Dysphagia
  - Tenesmus and muscle cramps

Differences between As toxicity & Cholera

	Arsenic	Cholera
Pain in throat	Before vomiting	After vomiting
Purging	Follows vomiting	Precedes vomiting
Stools	• Rice watery in early stages, later bloody • Shows Arsenic	• Rice watery • Shows Vibrio cholerae
Tenesmus	Present	Absent
Vomited matter	Contains mucus, bile & blood	No mucus, bile or blood
Voice	Not affected	Rough and whistling
Conjunctiva	Inflamed	Not inflamed

Clinical features of acute As toxicity
CNS Manifestations

Acute Encephalopathy

Cerebral edema **Focal micro-hemorrhages**

Direct CNS toxicity->

Cerebral edema -> Seizures

Cardiac dysrythmias ->

Coma

Delerium

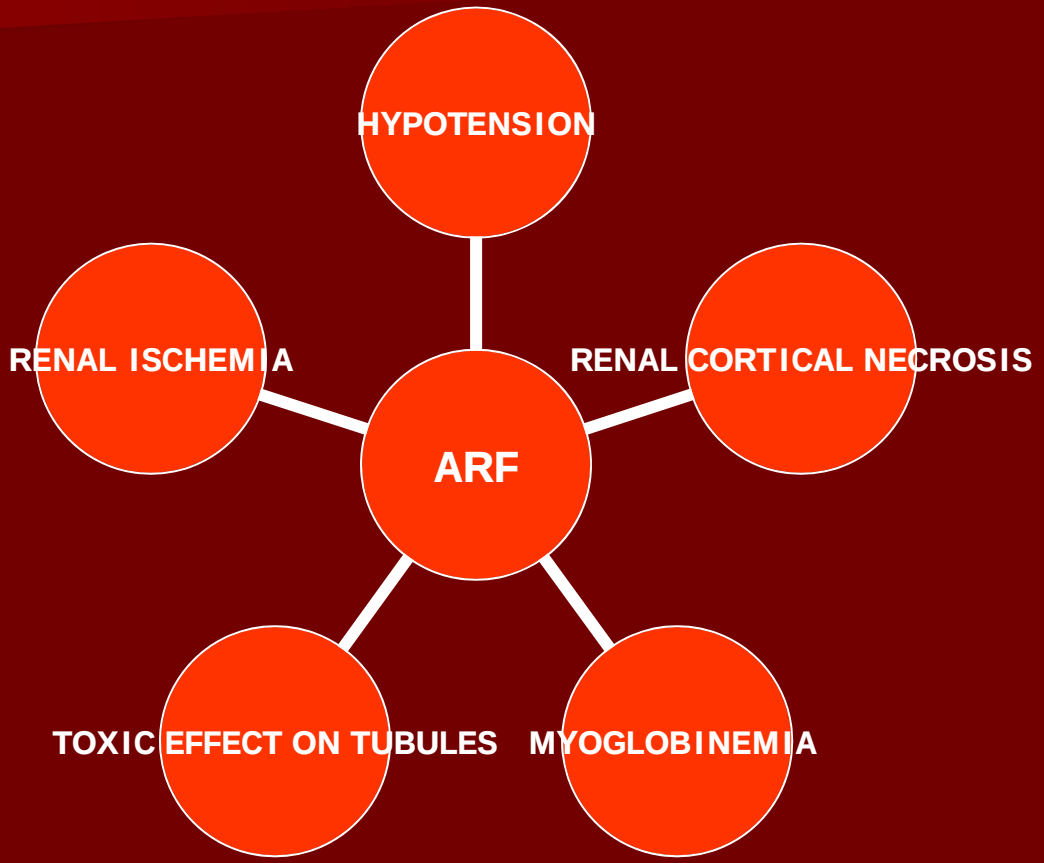
Clinical features of Acute As toxicity CVS Manifestations

- Sinus Tachycadia
- Orthostatic hypotension
- Frank Shock
- Dysrythmias

Clinical features of acute As toxicity

- Respiratory system: Pulmonary edema, ARDS Respiratory failure
- Hepatitis
- Rabhdomyolysis
- Hemolytic Anemia
- Acute Renal failure
- Nerve palsies

Patho-physiology of Renal failure



In less severe cases

- Persistent Gastro-enteritis
- Mild hypo tension
- Mucosal irritation- like pharyngitis
- Metallic taste, Garlicky odor
- GI ulcerative lesions with hemorrhages
- Toxic Erythroderma & exfoliative dermatitis

Sub-acute Toxicity

Symptoms develop sub-acutely days to weeks after acute toxic episode.

Sub-acute Toxicity

- Peripheral Neuropathy – due to Axonal degeneration
  "pins & needles", numbness, reduced sensations

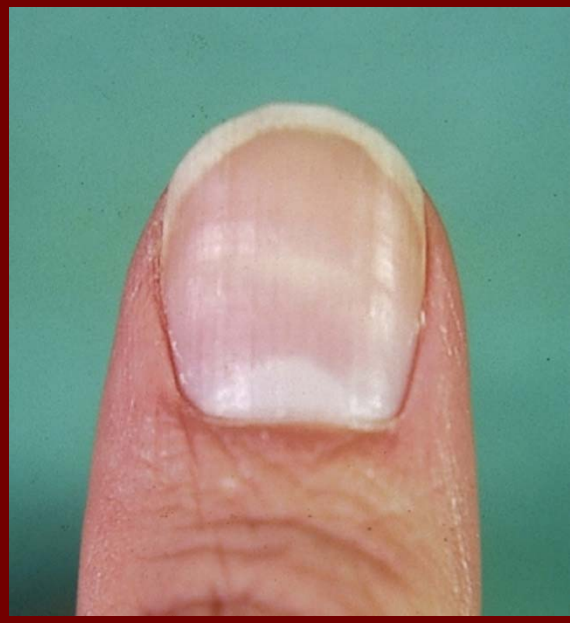
- Motor weakness – Ascending flaccid paralysis ; Gullian-Barre
- Encephalopathic syndrome – headache, confusion, delirium, seizures
- Nerve palsies– 6th Nerve palsy

Sub-acute Toxicity

- Skin – Diffuse pruritic macular rash

  Desquamation, Alopecia, Oral herpetic lesions

Aldrich Mees lines - **Horizontal 1-2mm thick white lines in nails**



Sub-acute toxicity

- RS :Dry cough , Hemoptysis,
  Patchy Interstitial infiltrate
- Nephropathy
- Persistent GI symptoms
- Pancytopenia
- Weight loss
- CVS : Dysrythmias
- Facial & Peripheral edema

Chronic As toxicity

General – Weakness, Anorexia, nausea, vomiting, garlicky odour in breath

Catarrhal signs – Rhinorrhoea, conjunctivitis, cough

Skin, hair & nails – Pigmentation of skin (Rain drop pattern) esp. on face and neck

Faint rash

Palmo-plantar keratosis of skin

Thickening of nails

Aldrich-Mees lines

Alopecia, ulcerative lesions

Chronic As toxicity

Nervous system – Peripheral neuritis,

Encephalopathy

Muscle wasting of extremities

Ataxia

Mental changes

Chronic toxicity

- Lung cancer
- Renal & bladder cell cancer
- Hepatic angiosarcoma
- Epidermal & basal cell carcinoma
- Cirrhotic and Non-cirrhotic portal HT
- Aplastic anemia & agranulocytosis
- Black foot Disease- Gangrene of the feet

Diagnostic Tests

- Abdominal Radiography
- Urinanalysis – Urine As level >50micro gm/L, >100micro gm/24h
- Complete blood counts- Megaloblastic anemia, leucopenia, thrombocytopenia, basophilic stipling of RBC'
- Renal & Liver function tests
- Chemical tests: Reinsch test, Marsh test
- Neutron activation analysis: especially useful to diagnose chronic poisoning. Helps in estimating the concentration of As in hairs, nail, bone, etc.

Treatment of As poisoning

Acute As poisoning is life threatening and should be treated agressively

Specific antidote – BAL as deep intramuscular injection

General/Supportive

1. Advanced life support monitoring
2. I.V fluids , dopamine for B.P, Blood products in case of GI h'mg
3. Gastric lavage then activated charcoal
4. Butter and greasy subs prevent absorption
5. Alkalies not to be given as they increase solubility of As
6. Freshly precipated, hydrated ferric oxide orally in small doses converts toxic As to non toxic ferric oxide

Treatment of As poisoning

7. Whole bowel irrigation with PEG
8. Alkalization of urine – $NaHCO_3$ in I.V fluids
9. Treat convulsions, ventricular tachycardia
10. If HOMICIDAL poisoning suspected-outside food to be forbidden, visitors to be monitored

Chronic poisoning:

- BAL
- Supportive measures

DIMERCAPROL

- Chemical name: 2-3-dimercaptopropanol
- Common name: British Anti Lewisite (BAL)
- BAL has 2 unsaturated –SH groups which combine with the metal in circulation and tissue enzymes are spared
- The compound so formed is stable (when BAL is given in sufficient dose) and excreted through urine
- Useful against many metallic poisons like Arsenic, Mercury, Mercury, Bismuth, Gold, etc.

DIMERCAPROL

- Preparation: Available in India as 2 ml ampoules containing 50 mg/ml of BAL rachis oil and benzyl benzoate
- Dose: 3 – 5 mg/kg on Day 1 & 2 — 4 hourly
  Day 3 — 6 hourly
  Day 4 – 13 — 12 hourly
- Route of administration: Deep intramuscular injection

DIMERCAPROL

- Should not be used when liver is damaged
- Side effects:
  - Nausea
  - Vomiting
  - Tingling of extremities
  - Tachycardia
  - Raised BP
  - Burning sensation in the mouth
  - May induce hemolytic in G-6-PD deficient individuals

Postmortem appearances of Arsenic poisoning

- All of the above clinical features +
- Stomach – velvety red congestion
- Heart – subendocardial hemorrhages
- Liver – fatty degeneration

Viscera to be dispatched

- Routine viscera
- Bone
- Scalp hairs (plucked)
- Finger and toe nails
- Skin from the back

Tolerance

- Some people take As daily as a tonic or as an aphrodisiac, and they acquire tolerance upto 0.3gm or more in a single dose
- Such people are called ARSENOPHAGISTS

MLI of Poisoning

- Homicide: Cheap, easily available, colorless, tasteless, odourless, highly toxic, S/S resembles natural diseases, No antidote, capable of being administered with food or drink. But the disadv are delays putrifaction, can be detected in complete decomposed bodies, found in nails, hairs, bones for several yrs, can be detected in charred bodies or ashes
- Suicide rare
- Accidental
- Abortifacient
- Animal poison

Post Mortem imbibition of As

- In exhumation, the possibility of imbibition of As from the stomach into neighbouring viscera and also contamination from the surrounding earth should be remembered
- Keratin tissue absorbs As by contamination from outside
- Therefore the conc of As in nail and hairs is much more greater then the conc of As in the contaminating fluid
- If As introduced in stomach after death transudation of As occur in organs of Lt side earlier then Rt side

THANK YOU