MJF COLLEGE OF VETERINARY AND ANIMAL SCIENCE, CHOMU, JAIPUR

DEPARTMENT OF VETERINARY PATHOLOGY

Metal

Physical properties of the element in the solid state

ARSENIC POISONING

- Toxic and carcinogenic metalloid.
- Divide in to organic and inorganic and both have trivalent and pentavalent forms
- Drinking water > 0.25% arsenic; potentially toxic, especially to large animals

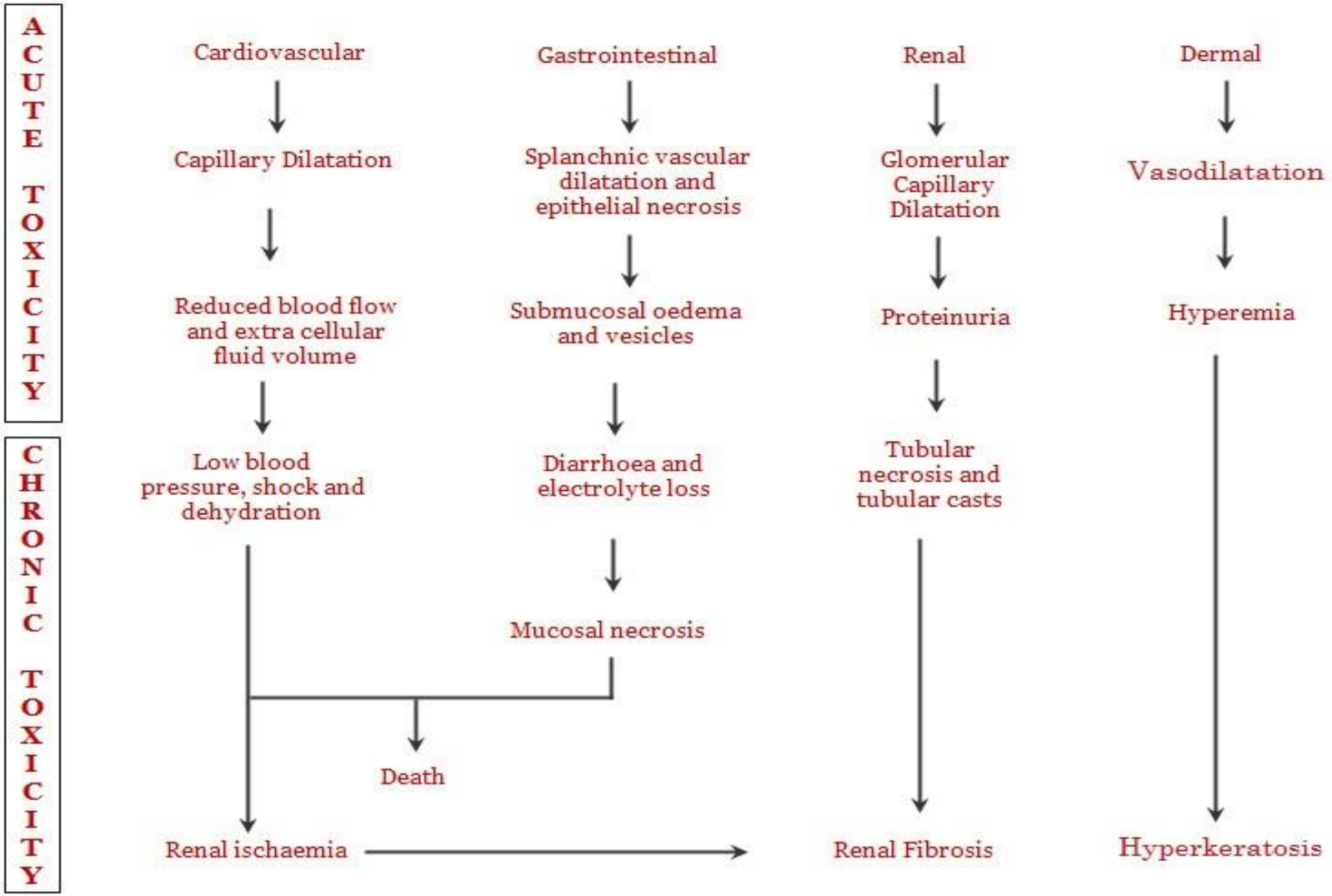
Source

- Organic As used in feed additive in poultry and swine
- Inorganic used in Pesticide, Herbicidal, Wood preservative
- Herbivores - eat contaminated forage.
- Sheep – dipping in arsenical baths
- Lead arsenate in baits intended for insects

Factors affecting toxicity

- Trivalent compound more toxic
- Pentavalent compounds - only after conversion to trivalent form
- Physical state – solid, coarse powder or fine powder or solution – finely divided soluble forms are more toxic
- The condition of the digestive tract
- Nature of ingesta

Mechanism of Toxicity



Clinical signs – Acute

- Peracute poisoning animals may simply be found dead
- Major effects on GIT & CVS
- Colic
- Profuse watery diarrhoea
- Dehydration
- Weakness, depression, weak pulse and cardiovascular collapse.
- The onset is rapid and signs are usually seen within few hours (or upto 24 hr).

Clinical signs – Subacute

- May live for several days
- Colic
- Anorexia
- Staggering
- Diarrohea with blood and/or mucosal shreds in faeces
- Polyuria and then anuria due to dehydration
- Partial paralysis of hind limbs, trembling, stupor
- Hypothermia

Clinical signs – Chronic

- Rare
- Wasting
- Poor condition
- Brick-red mucous membranes
- Normal temperature
- Weak and irregular pulse.

Clinical signs – Organic

- Affect Nerve
- Reduction in weight gain
- Incoordination, posterior paralysis and eventually quadriplegia.
- Blindness is characteristic of arsinilic acid intoxication

Post-mortem lesions

- Peracute toxicosis, no significant lesions
- Edema
- Rupture of blood vessels and necrosis of epithelial and subepithelial tissue.
- Perforation of gastric or intestinal wall
- Fluid, foul smelling and blood tinged GI contents
- Diffuse inflammation of liver, kidneys and other visceral organs.
- Liver may have fatty degeneration and necrosis
- kidneys have tubular damage.
- Lungs may be oedematous and congested.
- In cutaneous exposure the skin may exhibit necrosis and be dry or leathery.

Post-mortem lesions – Organic

- No Specific gross lesions
- Histopathologically Demyelination and gliosis of peripheral nerves, optic tract and optic nerves

Samples for confirmation of diagnosis

TOXICOLOGY

- 50 g liver, kidney; segment of stomach/intestine including content; sample of suspected poison (ASSAY(As))

HISTOLOGY

- - inorganic As: formalin-fixed stomach, intestine, cecum, large colon, liver, kidney, peripheral nerve;
- - organic As: formalin -fixed optic nerve and tract, peripheral nerve

Diagnosis

- History
- Clinical signs
- Post-mortem lesions
- Chemical examination of arsenic in tissues (liver or kidney) or stomach contents
- Normal concentration: > 1 ppm arsenic (wet weight basis)
- Toxicity concentration of >3 ppm
- Stomach contents – valuable within first 24-28 hrs
- Urine have high concentration for several days
- Speedy onset of GI damage compare to other metal

LEAD POISONING

- Most common causes of metallic poisoning in animals
- Fatal in cattle and sheep
- Occasionally observed in horses, dogs, and cats, and is rare in swine.
- Cattle - acute form
- Horses – chronic form
- Mainly neurologic sign but very small amount deposited in CNS

Sources of poisoning

- Lead paint and lead batteries
- Industrial lead - oil fields, Automotive and other mineral oils
- Lead parasiticide sprays - lead arsenate
- Lead in pastures near highways - exhaust fumes

- Toxicity by ingestion
- Only 1-2 % absorbed because of formation of insoluble complexes in the alimentary tract.
- Absorbed lead is slowly excreted in bile, milk, and urine
- Deposited in liver and kidneys in acute case
- Deposited in bones in chronic poisoning.

Mechanism of Toxicity

- Acute toxicity : Encephalopathy
- Subacute : Gastroenteritis
- Chronic case: Degeneration of peripheral nerves
- Lead localizes principally in the cytoplasm of capillary endothelial cells – leakage of plasma – edema
- Gastroenteritis associated with the caustic action
- Lead deposited in an inert form bone - liberated at a later date in sufficient quantities – cause chronic lead poisoning.

- The blue 'lead-line' at the gum-tooth junction, seen in man and the dog, not common ruminants because of failure to form tartar
- The 'leadline‘ - deposit of lead sulfide formed by the combination of lead with sulfide from the tartar
- The anemia in chronic lead poisoning associated with two basic defects: a shortened erythrocyte lifespan and impairment of heme synthesis
- Inhibiting heme synthetase, the enzyme which combines protoporphyrin and iron to form heme

Clinical signs - Acute

- GIT & CNS affected
- Signs appear within 24 hrs. of exposure
- Ataxia
- Blindness
- Salivation
- Spastic twitching of eyelids
- Jaw champing, bruxism (grinding the teeth)
- Muscle tremors and convulsions.

Clinical signs - Subacute

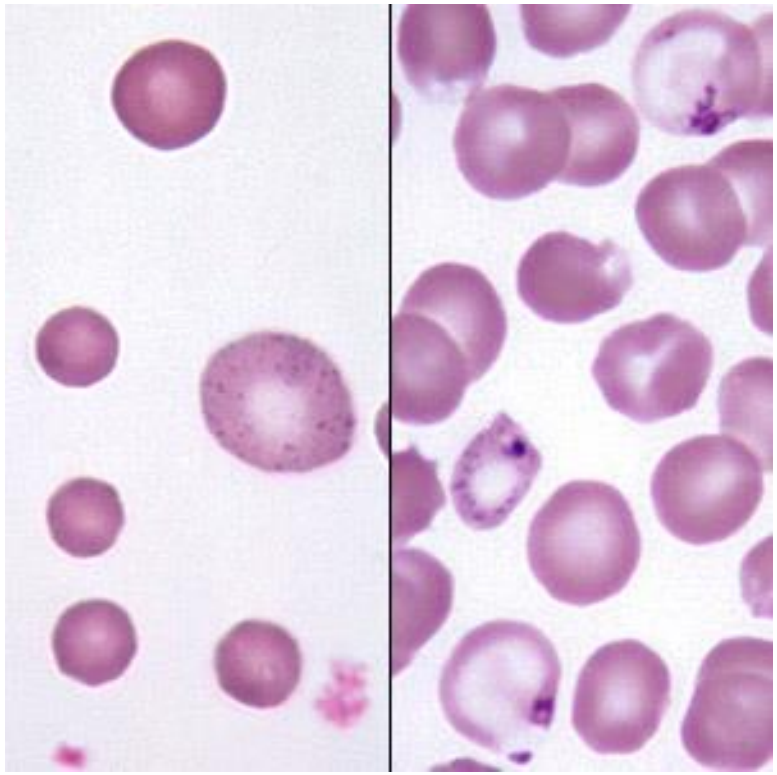
- Seen in sheep and older cattle
- Anorexia
- Rumen stasis
- Colic
- Dullness
- Transient constipation, frequently followed by diarrhoea
- Blindness
- Head pressing
- Bruxism
- Hyperesthesia
- In coordination.

Clinical signs – Chronic

- Similar to acute or subacute poisoning
- Common in horse
- Weight loss
- Depression
- Weakness
- Colic, diarrhoea
- Laryngeal or pharyngeal paralysis (roaring)
- Resulting in aspiration pneumonia.

Clinical Pathology

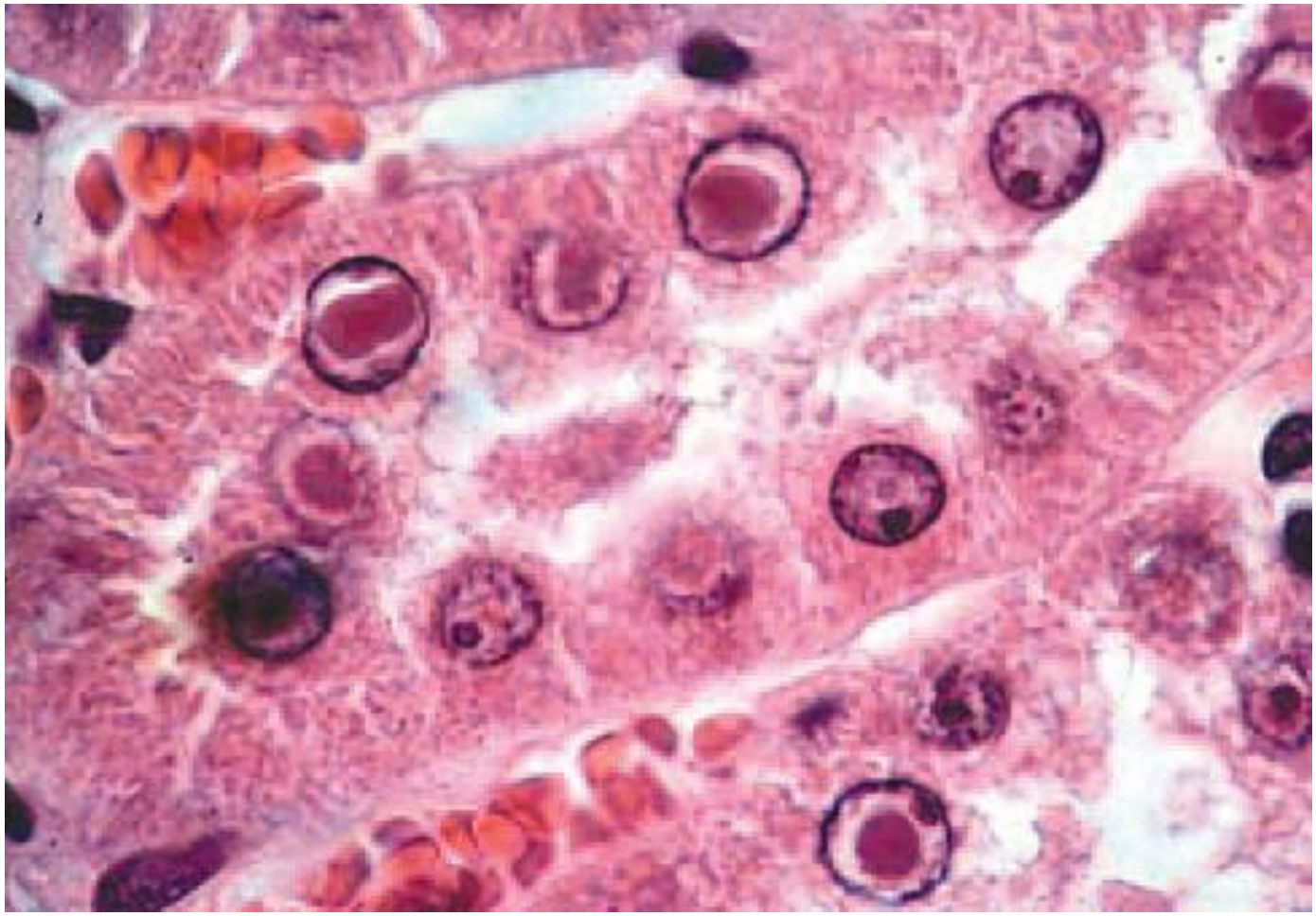
- Anaemia
- Basophilic stippling of RBCs
- Anisocytosis
- Poikilocytosis
- Polychromasia
- Hypochromasia



Left panel Regenerative anemia, macrocytes
Right panel: lead poisoning.

Post-mortem lesions

- Oil or flakes of paint or battery may be seen in the GI tract.
- Gastroenteritis.
- Congestion of cerebral cortex
- Flattening of cortical gyri
- Histologically, endothelial swelling, laminar cortical necrosis and oedema of white matter may be evident.
- Tubular necrosis and degeneration of "**intranuclear acid fast inclusion bodies**" may be seen in the kidneys.
- Osteoporosis in lambs.



lead toxicosis, kidney, cortex, rat.
Acid-fast intranuclear inclusion bodies present in the PCT are diagnostic of lead poisoning.

Samples for confirmation of diagnosis

Toxicology - 50 g liver, kidney, and reticulum content (ASSAY (Pb))

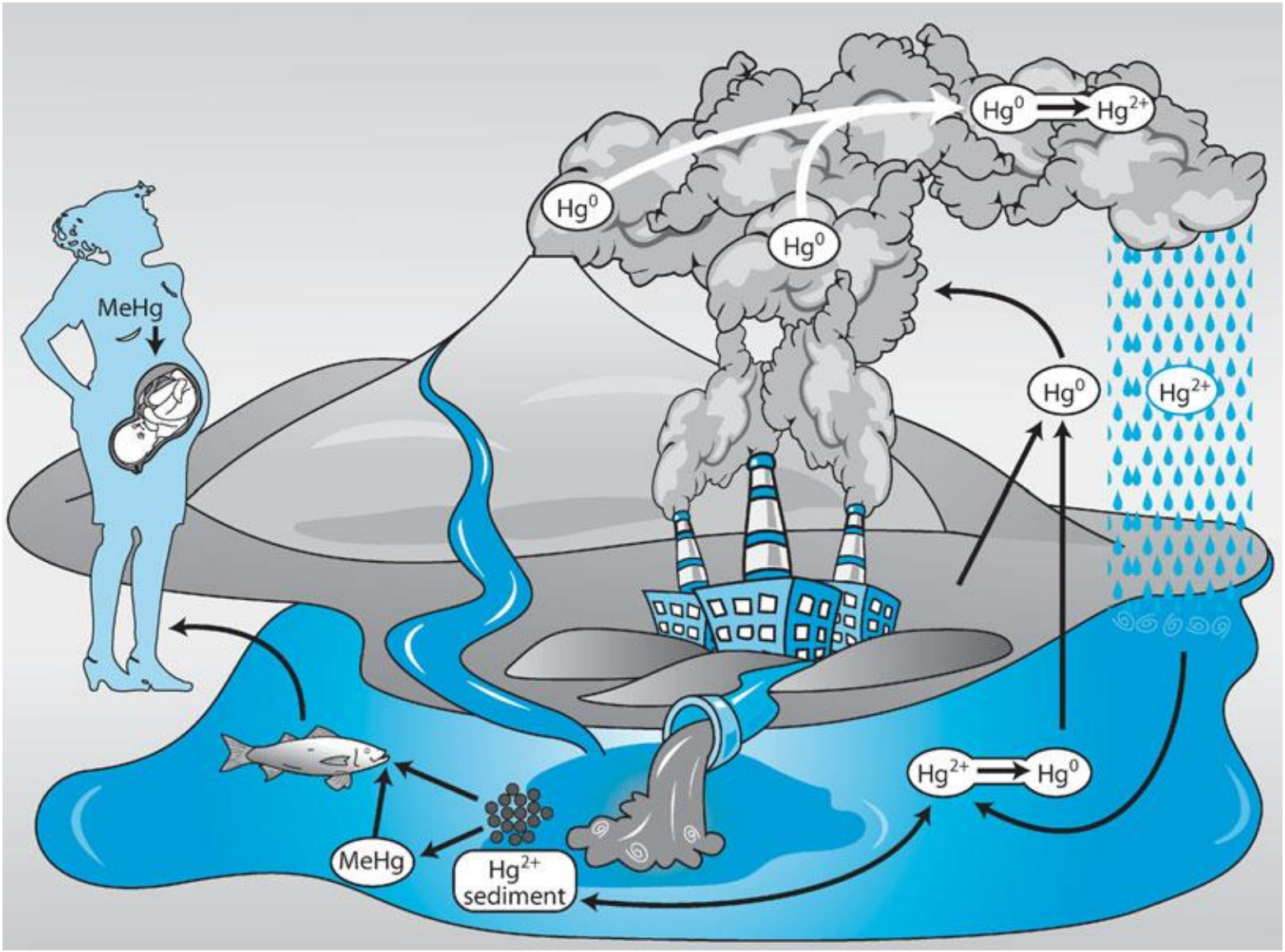
Histology - formalin-fixed cerebral cortex, kidney

Diagnosis

- History
- Clinical signs
- Post-mortem lesions
- Normal blood level of 0.05-0.25ppm
- Toxicity > 0.35 ppm in blood
- In liver or kidney cortex at > 10 ppm
- Amino levulinic acid (ALA) > 500mg / 100ml (normal level of 140mg / 100ml.)

MERCURY POISONING

- Organic and inorganic forms
- Both form have different toxicological sympotms
- Inorganic compounds more toxic – quite rare
- Organic compound less toxic than inorganic


Hg0
Hg2+
Hg0
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MeHg
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Hg2+
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MeHg
Hg2+
sediment

Sources of poisoning

INORGANIC

- Mercuric chloride, Mercurous chloride (calomel), yellow mercuric oxide, red mercuric iodide and mercuric nitrate.
- Mercurial ointments - direct absorption and licking
- Vapours - extremely toxic to sheep and cattle

ORGANIC

- fungicides - ethyl mercuric chloride and hydroxide)
- Seed dressing agents - methyl mercuric dicyandiamide and methoxy ethyl mercuric silicate
- Antiseptics - mercurochrome, thiomersal, phenylmercuric acetate and nitrate
- Diuretics – mersalyl
- Ingestion of flesh of animals which have been fed on mercurial fungicides.

Mechanism of Toxicity

- Inorganic – oral administration - coagulative effect of mercury in the lining of the gut – Colic & Diarrhea
- Organic - inhibition of protein synthesis, disturbance of neurotransmitter function, oxidative stress, and triggering of excitotoxicity mechanisms.

Clinical signs - Inorganic

- Vomiting
- Diarrhoea
- Colic
- Polydipsia
- Albuminuria and anuria (severe cases)
- Subnormal temperature (Only symptoms seen in cattle)
- Death in few hours
- If survives, death may occur several days later from nephrosis with uremia.

Inhalation of mercury vapours

- Dyspnoea
- Coughing, Nasal discharge
- Fever, Loss of appetite

Clinical signs - Organic

lengthy latent period of weeks

- CNS stimulation
- locomotor abnormalities
- Blindness
- Excitation
- Abnormal behaviour
- Chewing movements
- Incoordination
- Convulsions.
- “Neurological signs may be irreversible once they develop”

Post mortem lesions – Inorganic

ORAL

- Gastroenteritis
- Stomatitis
- Gingivitis
- Acute parenchymatous nephritis.

INHALATION

- Oedema of lungs
- Hydrothorax
- Hydropericardium
- Haemorrhages in epicardium and endocardium

Microscopic changes include necrosis of convoluted tubules of kidneys.

Post mortem lesions – Organic

- Degeneration of neurons
- Perivascular cuffing in the cerebrocortical grey matter
- Cerebellar atrophy of granular layer and damage to Purkinje cells.
- Coagulative necrosis of Purkinje network of heart

Samples for confirmation of diagnosis

Toxicology

- 50 g kidney, brain – half fresh and half in formalin
- 500 g of suspect feed
- Muscle tissue for potential residues in food animal edible tissues.

Histology

- formalin-fixed kidney, heart, oral and/or skin lesions;
- half of midsagittally sectioned brain (LM) .

Diagnosis

- History, clinical signs and post-mortem lesions
- Inorganic
  - Abnormaal amount in of mercury in the stomach contents, Kidneys (cortex) and liver.
- Organic
  - Normal < 1 ppm, Toxicity more concentartion

COPPER POISONING

- Necessary for haematopoiesis, myelin formation, connective tissue metabolism and enzyme systems.
- Sheep are affected most often , although other species are also susceptible.

Sources of poisoning

- Accidental ingestion during foot bath particularly in lamb
- Copper edentate use in the treatment of swayback disease- produce toxicity in lean animals
- Grazing of contaminated pasture over long period chronic toxicity.
- Ponds treated with copper sulphate for - sources chronic toxicity.
- Plants like **Heliotropium europium** or **Senecio sp. – liver toxic -** accumulation of copper - chronic copper poisoning.
- Plants like ***Trifolium subterraneum – high*** copper content.
- High copper molybdenum ratio within plants - chronic copper poisoning
- Low molybdenum intake enhances the storage of copper in liver.

Clinical signs - Acute

- Nausea
- Vomition
- Salivation
- Violent abdominal pain
- Dehydration
- Tachycardia
- Shock
- Collapse, ending in death.
- The faeces - deep green colour due to the presence of a copper-chlorophyll compound.

Clinical signs - Chronic

THREE STAGES

- **First stage** for 2 to 3 months (Stage of accumulation)
  No apparent clinical signs
  May decrease in ruminal fermentation and ruminal stasis.
- **Second stage** , for 14 -25 days (Stage of Hepatic affection)
  Impairment of liver function
  Anorexia, depression, weakness, thirst and diarrhoea.
- **Third stage**, 2-5 days (Stage of haemolytic crisis)
  Icterus, haemoglobinemia, haemoglobinuria and recumbency.
  Severe hepatic insufficiency is responsible for deaths.

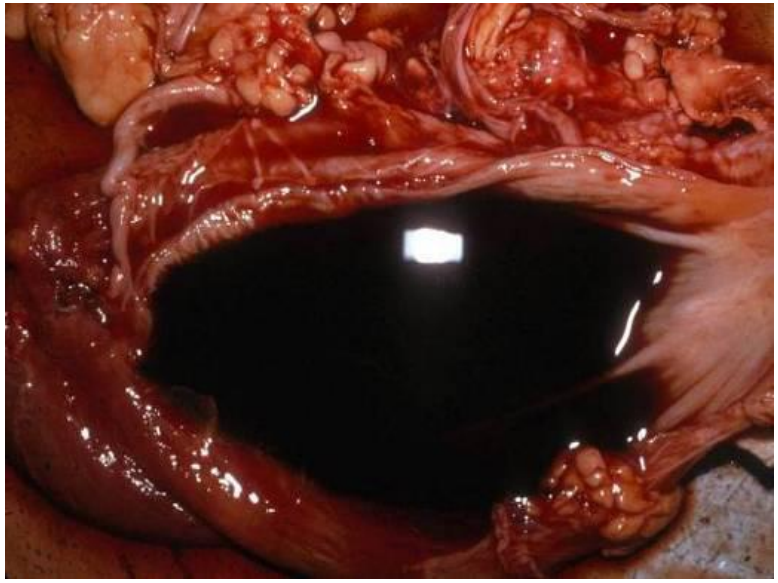
- Animals that survive acute episode may die of subsequent renal failure.
- Losses may continue for upto two months after dietary problem has been rectified.

Post mortem lesions - Acute

- Severe gastroenteritis
- Erosions and ulcerations in the abomasums
- Blood is found to have coagulated at the time of death.
- Icterus develops in animals that survive beyond 24hrs.

Post mortem lesions - Chronic

- Generalized icterus
- Liver - enlarged, yellow and friable.
- Gall bladder distended with thick greenish – brown bile.
- Swollen gunmetal coloured kidneys (showing haemorrhagic mottling when capsule is removed)
- Port wine-coloured urine
- Enlarged spleen with dark, brown-black (black berry jam) parenchyma
- Histologically, there is centrilobular hepatic and renal tubular necrosis and the brain may manifest spongy degeneration and astrocyte damage.



Samples for confirmation of diagnosis

Toxicology

- 5 mL blood
- 50 g liver and kidney
- 100 g stomach content
- 500 g suspect feed

Histology

- formalin-fixed liver, kidney, abomasum, spleen

Diagnosis

- History, clinical signs and lesions of copper toxicosis.
- Blood levels - Normal 1 µg/ml
- Blood levels - Toxicity 5-20 µg/ml
- Liver level - Toxicity > 150ppm
- Evidence of blue-green ingesta
- Deep green-coloured faeces
- Increased faecal (8000-10000 ppm) and kidney (> 15ppm, wet weight) - acute copper toxicosis.

NITRATES AND NITRITES POISONING

- Difficult to differentiate between these poisonings
- Nitrates can be converted into nitrities
- Both the forms toxic
- Ruminant convert nitrates to nitrate then to ammonia
- Ammonia - source of nitrogen by the rumen microflora for protein synthesis.
- However, if the rate of reduction of nitrate to nitrite exceeds that of nitrite to ammonia, then excessive nitrite accumulates in the rumen and gets absorbed into the blood stream and produces toxicity
- Pigs - most susceptible to nitrite poisoning
- Ruminants - most commonly affected
- Horses and dogs also affected

Source of poisoning

- Excessive ingestion of certain nitrates containing plants.
- Roots and stems usually contain more nitrate that leaves.
- High concentrations of Nitrates present in soil, ground after from deep wells
- Plants / crops grown on nitrate rich soil and / or water
- Ingestion of nitrate fertilizers (ammonium or potassium nitrate),
- Young animals are more susceptible to poisoning compared to adults.
- Hypovitaminosis A, pre-existing anaemia, methaemoglobinemia and fasting aggravate the toxicity of nitrates and nitrites.
- Monensin facilitates the conversion of nitrate to nitrite in the rumen and may result in poisoning in cattle or sheep on high nitrate fodder.

Mechanism of Toxicity

- Direct caustic action on alimentary mucosa
- Convert ferrous to ferric hemoglobin iron
- Convert Hemoglobin to methemoglobin in the blood (Brown color blood)
- Decreased Oxygen carrying capacity – Tissue hypoxia
- Vasodilation - dilate blood vessels - a drop in blood
- pressure
- Severe dilation of head, brain, meninges, and coronary vessels
- Visceral vessels being less sensitive
- Vasodilation causing shock

Clinical signs - Acute

- Severe dyspnoea with violent respiratory effects or gasping
- Rapid respiration
- Salivation
- Voiding of colorless urine
- Vomition, diarrhoea, colic
- Rapid and weak pulse
- Accelerated heart rate
- Progressive development of cyanosis of MM & unpigmented skin
- Ataxia, recumbence, terminal anoxic convulsions and death within 2-24hrs
- Chocolate brown colour of blood
- Abortion

Clinical signs - Chronic

- Rare, observed in poorly nourished animals drinking high nitrate content water
- Abortion
- Poor development of mammary tissue
- Infertility in adults
- Lower birth weight in newly born lambs
- Hypothyroidism and hypovitaminosis A in Ewe.
- Immunosuppression
- Increase in the incidence of mastitis, metritis and diarrhoea in calves and piglets

Post mortem lesions

- Dark chocolate brown or coffee brown colour of blood
- Clots poorly
- Brown stained tissues.
- Congestion and inflammation of intra-abdominal organs.
- Petechial and large haemorrhages on the serous surfaces.
- Generalized cyanosis
- Blood stained pericardial fluid

Samples for confirmation of diagnosis

Toxicology

- 1 cc aqueous humor (frozen)
- 1 cc urine (frozen)
- suspect forage material (dry) or other possible source of poison
- 100 g ingesta (with chloroform or formalin added) (ASSAY (nitrate/nitrite))
- 2 cc blood in 4 cc phosphate buffer (ASSAY (methemoglobin))

Diagnosis

- History
- Clinical signs
- PM findings
- Chocolate brown colour of blood and tissue
- Analysis of the stomach/ruminal and intestinal contents for nitrate/nitrite detection
- Estimation of meth-Hb and serum nitrite levels
- Serum positive diphenylamine spot test; 20 µg/ml nitrate
- In dead animals, positive diphenylamine spot test with ocular fluid indicating >50 µg/ml nitrate for confirmation of diagnosis.
- Response to methylene blue treatment.

FLUORINE POISONING

- Highly reactive
- Found in combination with many minerals/elements and rocks
- Fluorides emitted from industries
- Smoke dust coming out of volcanic eruptions
- Result in contamination of fields, pastures or water
- Expose low concentrations of fluorine for prolonged periods
- Accumulation of fluorides in body particularly bones and teeth without exhibiting any clinical signs
- Clinical sign seen after too much damage
- Acute fluorine poisoning - not commonly
- Chronic fluorine poisoning (fluorosis) very serious and important syndrome both in animals and human beings.

Acute fluorine poisoning

- Sodium fluoride, sodium fluoroacetate, sodium fluorosilicate
- Accidental ingesting of large quantities of fluorine containing salts
- Sodium fluoride kill worms in pigs and lice in poultry
- Sodium fluoroacetate is used as a rodenticide.
- Accidental ingestion of the baits
- Excessive licking of phosphate rocks Above 4-5 per cent sodium fluoride in feed is lethal for pigs.
- Lethal does of fluorosilicate is 100g for equines and 200g for bovines.

Clinical signs

- Vomition
- Anorexia
- Salivation
- Ruminal stasis
- Abdominal pain
- Gastroenteritis, diarrhoea
- Constant chewing
- Dyspnoea
- Excitability
- Nervous sysmtoms
- Death due to respiratory and cardiac collapse.

Post-mortem lesions

- Haemorrhagic gastroenteritis
- Congestion of viscera, particularly liver and kidneys.
- Bone and dental lesions are absent

Diagnosis

- It is very difficult, however, history and circumstantial evidences may be helpful

CHRONIC FLUORIDE POISONING (FLUROSIS)

- Prolonged ingestion of small but toxic amounts of fluorine in the diet/feed /water
- Non-fatal syndrome
- Productivity decarsed
- The fluorine gets deposited in bones and teeth (95-96%) without any apparent signs of toxicity.
- Very long latent period probably due to gradual saturation of bones and teeth with fluorine as these tissues act as sink for fluorine.
- Once these structures get saturated, fluorine ions start exerting general toxic effects

Ingestion of fluoride in fodder at levels less than

- 30ppm in young cattle and milking cows,
- 40ppm in beef cattle
- 50ppm in sheep
- 70ppm in pigs
- 90ppm in horses
- 150ppm in chickens

do not produce clinical signs of poisoning.

Sources of poisoning

- Feeds, fodder, water, mineral supplements rich in fluorine
- Top dressing of pastures with phosphate lime stone
- Fluorides emitted from industries
- Smoke dust coming out of volcanic eruptions
- Result in contamination of fields, pastures or water

Clinical signs

- First mottling, consists of light yellow, green, brown or black spots or bands arranged horizontally across the teeth.
- Mottling generally occurs on incisors, molars and premolars
- Dental lesions are painful.
- If continue exposure teeth become brittle and break
- Shedding of teeth
- Delayed incisors eruption in young
- Hypoplasia of teeth with wide gaps between the teeth.
- Due to uneven surface or shedding of teeth, mastication becomes difficult
- Other general signs are anorexia, dry and rough hair coat, ruffled fur or feathers, emaciation and reduced milk production.

OSTEOFLUROSIS

- Sudden onset of lameness, stiffness, painful gait
- It is moving and diagonal, observed first in one leg and then in other leg.
- Enlarged, thickened, painful bone
- Spurring and bridging of joints leading to rigidity of the spine.
- Other bone lesions are hyperostosis, osteoporosis
- More prone to fractures.
- Intermittent diarrhoea, polydipsia, polyuria, poorly concentrated urine
- Aplastic anaemia due to diminished bone marrow cavity
- Reduction in milk and wool production
- Anoestrous

Post mortem lesions

- Enlarged chalky white bones
- Rough bone surface
- Lateral exotoses of the long bones.
- Mottling of teeth
- Bone marrow cavity is diminished and shows gelatinous degeneration and aplastic anaemia
- Microscopically, bony trabeculae are thickened
- Degenerative changes are observed in kidneys, liver, adrenal glands, heart muscles and central nervous system.
- Irregular calcification of newly formed osseous tissue
- Hypoplasia of enamel and dentine.

Samples for confirmation of diagnosis

Toxicology

- Mandible / metacarpal / metatarsal , rib, vertebrae
- Urine

Histology

- Formalin-fixed metacarpal/ metatarsal/ mandible (LM)

Diagnosis

- History
- Clinical signs
- Post mortem findings.
- X-ray examination reveals sclerosis, perosis, hyperostosis or a combination of these.