CHAPTER 4

PATHOLOGICAL ALTERATIONS IN INDUCED ACUTE AND CHRONIC ARSENIC TOXICITY IN GOATS
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ABSTRACT
This chapter reports the gross and pathological effect of toxins in different parts of the body. Almost all tissues of animals, died due to arsenicosis, were collected and processed for the preparation of histopathological slides. Collected tissues should be immediately kept in 10% formal saline solution until the preparation of slides. It was found that all organs are affected by arsenic toxicity and the level of damage depends upon the duration of exposure and the affinity of arsenic binding. Various pathological changes in different tissue was observed due to acute and chronic arsenic toxicity. It was observed that there is severe damage in liver, kidney, which is mainly related with the detoxification and excretion of the xenobiotics.

INTRODUCTION
Histopathology is the branch of pathology, which concerns with the demonstration of minute structural alterations in tissues as a result of disease. However, the histopathological techniques are labour intensive, cumbersome and time consuming; their use in diagnosis of diseases is unequivocal. This study is useful in establishing the pathogenesis and pathology of any disease caused by bacteria, virus, chlamydeous, rickettsia, mycoplasma, parasite, toxin, poison etc.

Arsenic, as soluble arsenate or arsenite, is well absorbed (≥80%) in both humans and animals exposed by oral route. Absorption appears to occur by passive diffusion. Distribution occurs throughout the body (ATSDR, 2000a). Characteristic dermal lesions caused by long-term oral exposure to arsenic include hype keratinisation. A fraction of the hyperkeratinised coms may progress to squamous cell carcinoma of the skin. Signs of peripheral and/or central neuropathy are commonly seen in humans and animals exposed to arsenic orally. Some of the effects of arsenic seen in human are
supported by animal data, but animals do not develop dermal lesions and cancer as a result of oral arsenic exposure.

Disruption of oxidative phosphorylation and concomitant decrease in cellular levels of ATP in arsenic toxicity are thought to be important central events in the onset of cellular injury and cell death.

Chronic ingestion of inorganic arsenic has been related to increased incidence of cancer in the skin, urinary bladder, liver and kidney, while inhalation of arsenic causes lung cancer (Chain and Huff, 1997; Abermathy et al., 1999; Goering et al., 1999, Hughes, 2002) The results of long-term exposure due to elevated levels of inorganic arsenic in drinking water supplies include skin, lung, liver and bladder cancers (Kitchin and Ahned, 2003) as well as malignant neoplasms. Chronic arsenic exposure in the range of 0.01–0.04 mg/kg/day has been associated with skin cancer in Taiwan (Hsueh et al., 1995); respiratory cancers in Montana (Lubin et al., 1981); bladder cancer in Finland increased mortality from hypertensive heart disease, nephritis and nephrosis, and prostate cancer in Utah (Lewis et al., 1999); increased incidence of lung cancer, bladder cancer, and all cancers in Taiwan (Chiou et al., 1995)

Goats fed on low arsenic semi synthetic diets were reported to have died suddenly between 17th and 35th day of their lactation, and none of the low arsenic diet goats survived the second pregnancy. The low arsenic diet goats did not get pregnant survived to more than six years of age (Anke, 1991). Autopsies of the low arsenic diet goats revealed atrophy of cardiac and striated muscle fibres and distinct reduction of oxidative enzyme activity associated with the rupture of liver, heart and muscle mitochondrial membranes (Schmidt et al., 1984). Pathological alterations in induced chronic arsenic toxicity in goats were also observed by Biswas et al., (1998) and inflammatory changes in different organs were observed.

The cardiovascular system is a very sensitive target of arsenic toxicity. A number of effects have been observed including heart damage, vascular damage and hypertension (ASTDR, 2000). The series of studies by Tseng et al., 1995, provide suggestive evidence that hyperkeratosis and hyperpigmentation would occur in arsenic toxicity.

Evidences indicate that kidney is a target organ of arsenic toxicity. In fact acute renal failure has been reported in arsenite treated hamsters (Hirata et al., 1990), while chronic exposures of arsenate As V (Kirkvliet et al., 1980) and As III all have produced
significant renal pathology. Since kidney is the major organ for arsenic elimination and most of the arsenic is rapidly eliminated through the kidney (Goering et al., 1999), renal cells are, thus, exposed to a major portion of the absorbed arsenic dose. Chronic arsenic induced renal injury and subsequent proliferation repair could potentially progress to kidney neoplasia.

Renal involvement is often apparent in acute or subacute arsenic poisoning but usually only the more severe cases of chronic arsenic exposure show overt kidney effects. Varying degrees of renal tubular necrosis and degeneration result in toxic arsenic nephrosis. The neurological system may be affected by chronic exposure to inorganic arsenic compounds with the development of peripheral neuritis. So more or less there are involvement of all the tissues, which are very well studied in this chapter.

MATERIALS AND METHODS

Post mortem of animals was done which died due to acute and sacrificed in chronic arsenic toxicity. All the organs were examined very carefully for the presence of any lesion due to arsenic toxicity. Tissues like kidney, liver, brain, intestine, stomach, skin, spleen, heart, muscle were collected immediately in sufficient amount of 10% neutral buffered formalin this prevented further changes in tissues like autolysis by coagulating the tissue protein and preserve the constituents of the cells and tissues.

PROCESSING OF TISSUE

One square centimetre sized sections of different tissues were made for further processing. Tissues were first washed with running tap water for one hour. Paraffin wax does not infiltrate into the tissues in presence of alcohol or water, hence dehydration and clearing an essential process, was done by ethyl alcohol and Xylem.

Paraffin treatment was given at 60°C temperature. Higher temperature may cause charring of the tissue. Tissue blocks were prepared with the help of melted paraffin and metal moulds. Blocks are then kept in refrigerator until next process. Paraffin blocks were then trimmed to square shape and fixed to the cutting surface of metal block holder. By using sharp blade thin sections of about 3-5μ were cut down with the help of microtome. Glass slides were cleaned with 1% acid alcohol and then rinsed with distilled water and then soaked in 95% ethyl alcohol. Wipe it and dry with clean lint less cloth. Slides were then coated with glycerine and egg albumin of equal amount that affix the sections to the slide. Slides are then placed on hot plate to
remove the wax from the section. Staining was done using haematoxylin and eosin. Before staining tissue slides should be cleared and dehydrated.

**Fig 4.1** Processing of tissues for preparation of histopathological slides.
PROTOCOL FOR STAINING TISSUE SLIDES

FIG 4.2 FLOW CHART OF STAINING PROCESS OF HISTOPATHOLOGICAL SLIDES.
After staining the slides were ready to observe under microscope to see the histopathological changes. Haematoxylin is a basic stain for nucleus and eosin is acidic for cytoplasm.

RESULT AND DISCUSSION

All animals exposed to acute arsenic toxicity were died after 48 hours of the start of experimental trial and one subject was sacrificed after the period of six months. After the death of the subjects, post mortem was done and different organs were observed carefully for the development of any change as compared to the normal structure of the tissue.

**TABLE 4.1 RESULTS OF GROSS PATHOLOGICAL CHANGES IN ACUTE AND CHRONIC ARSENIC TOXICITY ARE PRESENTED IN THE GIVEN**

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>Organ affected</th>
<th>Gross lesions or other major observations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Acute</strong></td>
<td>Rumen</td>
<td>Congestion and Haemorrhages</td>
</tr>
<tr>
<td>Heart</td>
<td>Enlargement of heart, Echymotic and petechial haemorrhages</td>
<td></td>
</tr>
<tr>
<td>Abomasum</td>
<td>Congestion in the mucosal layer, Severe hemorrhagic abomasitis</td>
<td></td>
</tr>
<tr>
<td>Lung</td>
<td>Severely congested</td>
<td></td>
</tr>
<tr>
<td>Liver</td>
<td>Degenerative changes</td>
<td></td>
</tr>
<tr>
<td>Brain</td>
<td>Slight congestion</td>
<td></td>
</tr>
<tr>
<td>Kidney</td>
<td>Congested</td>
<td></td>
</tr>
<tr>
<td>Intestine</td>
<td>Hemorrhagic and congested</td>
<td></td>
</tr>
<tr>
<td><strong>Chronic</strong></td>
<td>Lungs</td>
<td>Petechial haemorrhages on the pleural surfaces</td>
</tr>
<tr>
<td>Liver</td>
<td>Yellowish and swollen</td>
<td></td>
</tr>
<tr>
<td>Brain</td>
<td>Congestion and edema</td>
<td></td>
</tr>
<tr>
<td>Muscle</td>
<td>Hyperemic</td>
<td></td>
</tr>
<tr>
<td>Kidney</td>
<td>Patches of haemorrhages at cortico-medullary junction, Pale yellow cortex.</td>
<td></td>
</tr>
<tr>
<td>Spleen</td>
<td>White necrotic foci</td>
<td></td>
</tr>
<tr>
<td>Gall bladder</td>
<td>Edema. Colour of the bile becomes watery</td>
<td></td>
</tr>
</tbody>
</table>
Grossly it was observed that more or less all organs were affected. There was slight change in tissues in acute arsenic toxicity but in chronic toxicity changes were more severe as arsenic remained in the body for longer period of time.
Fig 4.3 Petechial haemorrhages are seen on the pleural surface in chronic arsenic toxicity. On the lung surface certain reddish areas, showing severe congestion.

Fig 4.4 Yellowish swollen liver and edema of the gall bladder as a result of chronic arsenic toxicity.
Fig 4.5 Congestion and edema in the brain are the gross pathological findings in chronic arsenic toxicity.

Fig 4.6 Spleen of Goat shows white necrotic foci in chronic arsenic toxicity.
Fig 4.7 In chronic arsenic toxicity there are patches of haemorrhages at the corticomedullary junction along with the Pale yellow cortex.

Fig 4.8 Congestion of the ruminal surface in acute arsenic toxicity.
Fig 4.9 Echymotic haemorrhages on the pericardium in acute arsenic toxicity.

Fig 4.10 Carcas showing hyperemic condition in chronic arsenic toxicity in goats.
TABLE 4.2 HISTOPATHOLOGICAL ALTERATIONS IN TISSUES IN ACUTE AND CHRONIC ARSENIC TOXICITY.

<table>
<thead>
<tr>
<th>S.No</th>
<th>Organ affected</th>
<th>Histopathological changes</th>
</tr>
</thead>
</table>
<pre><code>  |                | Chronic: Increase number of mesenchymal cells. Coagulative necrosis of epithelium of proximal convoluted tubule in chronic arsenic toxicity |
</code></pre>
| 2    | Liver          | Acute: hydropic changes and coagulative necrosis in the hepatocytes.  
      |                | Chronic: hydropic changes and coagulative necrosis in the hepatocytes. |
| 3    | Skin           | Acute: No changes.  
      |                | Chronic: Hyperkeratotic skin. Arteriosclerosis on the arterioles of dermis and subcutis |
| 4    | Brain          | Acute: Necrosis of neuron. Satellitosis.  
      |                | Chronic: Central chromatolysis in neuron. Proliferation of glial cell. |
| 5    | Lung           | Acute: Hemorrhage in lung. Diffuse congestion in the lung along with haemorrhages in the alveolar septa. Edema in the interstitial tissue. Edema at some places in alveoli.  
      |                | Chronic: Interstitial pneumonitis and increased infiltration of the lymphocytes and macrophages in the wall of alveoli. |
| 6    | Muscle         | Acute: Swelling of skeletal muscle and loss of striation.  
      |                | Chronic: Muscle shows zenker’s degeneration and loss of striations |
Renal pathological alterations

In acute arsenic toxicity kidney parenchyma revealed extensive hemorrhage and vascular congestion. In addition, there were degenerative changes in the nature of both cloudy swelling and fatty degeneration and swelling of the epithelium of proximal convoluted tubule (Fig 4.11). There was coagulative necrosis (pyknosis) in the epithelium of Henle's loop and presence of albuminous exudates in the proximal convoluted tubules. Coagulative necrosis Characterization by conversion of the cell to an acidophilus opaque. The necrosed epithelial cells revealed chromatolysis which usually occurs with loss of the nucleus. This results most commonly from sudden severe ischemia. The pattern results from denaturation of not only structural proteins but also of enzymatic proteins, autolysis of the cells. Goodman et al., (1990) also reported the presence of albuminous exudates in the tubules, coagulative necrosis in the epithelial cells of loop of henle and hydropic degeneration of the epithelium of proximal convoluted tubule.

In the present study it was observed that in chronic toxicity of arsenic there was severe damage of the kidney tubules, which are initiated by many biochemical alterations (Fig 4.12). There was increased cellularity in the glomerulus possibly due
to increase in the number of mesenchymal cells. All the above changes indicated toxic nephrosis as a result of toxicant, arsenic.

Hydropic degeneration is due to hypoxic cell injury. The cause is failure of the sodium-potassium ion pump mechanism necessary to maintain appropriate osmotic pressure inside the cell. In case of hypoxia mitochondrial function is disrupted, curtailing the availability of ATP. Decrease in ATP also results in decreased protein synthesis becomes evident when swelling of intracellular organelles and detachment of ribosome lead to a loss of normal cytoplasmic basophilia and the cytoplasm assumes acidophilic stain. There is increase in water possibly in association with electrolytes or organic compounds with in the cytoplasm of cells.

With further damage there is marked disruption of organelles and the cytoplasm becomes waterlogged this is due to breakdown of structural protein.

Renal failure is caused by vasodilatation leading to increased glomerular filtration and capillary permeability. The resulting protein leak may cause acute tubular necrosis or diffuse interstitial fibrosis. Acute renal tubular necrosis and also cortical necrosis (Gerhardt et al., 1978) have been reported in severe acute poisoning (ATSDR, 1989). Tubular-interstitial nephritis has been reported in chronic poisoning (Parsed & Rossi, 1995).
Fig 4.11 Histopathological alterations in kidney in acute arsenic toxicity (H & E X 400)
A) Hydropic degeneration of the epithelium of proximal convoluted tubule.
B) Coagulative necrosis in the epithelium of loop of Henle. C) Presence of albuminous exudate.

Fig 4.12 Kidney showing (H & E X 400). A) Increase number of mesenchymal cells.
B) Coagulative necrosis of epithelium of proximal convoluted tubule in chronic arsenic toxicity.
Hepatic damage in arsenic toxicity

The great susceptibility of the liver to damage by an enormous array of pharmaceutical and environmental chemicals is a consequence of its primary role in the metabolism and detoxification of foreign compounds. The liver is vulnerable to a wide variety of substances and, as such, may exhibit any form of known hepatic lesions. The pathological effects of drugs and toxins on the liver can be broadly classified into acute and chronic.

The liver is the major organ of detoxification of arsenic, which accumulates in this organ after exposure. The basic functional unit of the liver is the liver lobule, which exists in two dimensions as a roughly hexagonal structure approximately 1-mm diameter. The lobule is constructed around a central vein with portal triads defining corners. Plates or cords of hepatocytes radiate centrifugally toward the portal areas from the central vein, like spokes in a wheel. Each hepatic plate is one cell thick in the adult, and bathed on either side by blood within the hepatic sinusoids, which maximizes contact of hepatocytes with blood flowing through the liver. Endothelial cells line the sinusoids and macrophages called Kupffer cells. Each portal track consists of a collagenous supporting stroma, which contains interlobular bile ducts and branches of the portal vein of the hepatic artery.

In acute arsenic toxicity there was hydropic change and coagulative necrosis in the hepatocytes (Fig 4.13). Farber, (1975) also reported the same changes in liver of arsenic toxicated animal. Fatty changes were due to the manifestation of sub lethal metabolic dearrangement with high-energy demand. It appears that the capacity of hepatocytes to metabolised fat got reduced and fat went on accumulating in liver leading to formation of vacuoles The variety of cells suggests the stages of inflammatory changes and exudative process in the organ. Necrosis in some areas was observed in chronic toxicity is simply a very severe manifestation of massive lobular necrosis, possibly resulted from transportation of toxins through portal vein. Necrosis usually occurs due to degeneration of structural proteins, which form compact homogenous mass. Nucleus of necrosed cell become pyknosed possibly due to reduced pH resulting from terminal anaerobic metabolism.

In chronic form of toxicity, liver parenchyma showed vascular congestion, massive haemorrhages and degenerative changes (Fig 4.14). Both the cloudy swelling and fatty degeneration of hepatic cells leads to coagulative necrosis (Gorden and Lough, 1972). The denaturation of cellular proteins and denaturation of hydrolytic enzymes as
well causing degeneration followed by coagulative necrosis. Kupffer cells present in the liver became swollen in chronic arsenic toxicity. They revealed brownish pigment hemosiderin in their cytoplasm. Hemosiderin is a shiny golden yellow or golden brown pigment derived from haemoglobin (Fig 4.15). The cause of formation of this pigment was the destruction or haemolysis of erythrocytes to an excessive degree. Our findings was supported by the finding of Cornelius et al., (1965).
Fig 4.13 Liver shows hydropic changes and coagulative necrosis in the hepatocytes. (H & E X 400)

Fig 4.14 Section of liver showing fatty changes in chronic arsenic toxicity. (H&E X 400) A) Fatty changes manifested by the accumulation of lipid in the form of large cytoplasmic vacuoles in hepatocytes. B) Displacement of nucleus to one side.

Fig 4.15 Liver shows swelling of kupffer cells and presence of haemosiderin pigment in the cytoplasm in chronic arsenic toxicity. (H & E X 400)
Effects on integumentry system

The skin is composed of three basic layers: the epidermis, dermis, and subcutaneous tissue. The epidermis is the outermost layer, followed by the dermis, and the inner most layers, the subcutaneous tissue. The epidermis protects the body from potential invading organisms or toxic substances and is further divided into five layers of strata. The outermost layer of cells is known as the stratum corneum, the stratum lucidum is directly under the stratum corneum, then the stratum granulosum, the stratum spinosum and the deepest layer of cells in the epithelium is the stratum germinativum, sometimes referred to as the basal layer. The skin is a dynamic organ with cells constantly dying and being replaced. The replacement process is normally an orderly movement of cells from the stratum granulosum upward to the stratum corneum. On the way through progression of the four upper layers, the cells leave their nutrient supply behind, produce keratin, and lose their nuclei and granules and die, forming scales in the outermost hard surface on the skin. This continuous process of epithelial proliferation and cell replacement is known as keratinisation.

The excessive and abnormal keratinisation of the epidermis was possibly due to the toxic effect of arsenic by combining with inactivating the sulphahydryl Groups in tissue enzymes (Fig 4.16). Thereby it interfered with the formation of disulphide bridge in 2 adjacent cysteine molecules to form cysteine required for keratin synthesis since its disulphide Group serves as covalent cross-link between the 2 polypeptide chains.

Arsenical keratosis in its fully developed form is a well established clinical syndrome, characterized by several specific pathological features, including hyperkeratosis, and defective pigmentation

In chronic arsenic toxicity there was arteriosclerosis in the arterioles of dermis and sub cutis (Fig 4.17). Arteriosclerosis was observed in which lesions begin with the infiltration of lipids into certain intimal cells. Further there is accumulation of intracellular and extra cellular lipids causing tissue degeneration and fibrosis, which involve tunica media. There is narrowing of vessel lumen producing partial or complete obstruction to blood flow leading to ischemia and infarction.
Fig 4.16 Image of hyperkeratotic skin in chronic arsenic toxicity. (H & E X 400)

Fig 4.17 Arteriosclerosis on the arterioles of dermis and subcutis in chronic arsenic toxicity. (H & E X 400)
Neurological effects in arsenic toxicity

An important question is the organ which govern the proper functioning of all organs of body get affected severely by arsenic toxicity? The result obtained by this study shows that in acute arsenic toxicity there was necrosis of neurons as well as satellitosis (Fig 4.18). Neurons were shrunken due to necrosis which indicates true degenerative process. Similar changes were in arsenic toxicity were also observed by Rahman, et al., 2001; Mukherjee, et al., 2003: Chawdhury, et al., 2000a, 2000b).

Oligodendroglial cells found in grey matter line up around neurons in some locations where they are called satellite cells. These cells provide nutrition particularly glucose to neuron, which is the sole source of energy. Under unfavourable conditions such as hypoxia they proliferate resulting in increased number of these cells near the neuron is called Satellitosis (Burkitt et al., 1991).

In chronic arsenic toxicity there was swelling of the endothelial cells of the capillaries along with central chromatolysis in the neuron. Proliferation of glial cells was also prominent finding in chronic arsenic toxicosis (Fig 4.19). In anoxia Nissi granules lose sharpness and undergo chromatolysis first centrally called central chromatolysis and then completely by general blackening of the cytoplasm.

Gliosis and satellitosis occurred around degenerating neurons and terminating in to necrophilia. But finally glial cells were found to be degenerated and this was probably due to non availability of energy as we know that arsenic anions can substitute for phosphate in many reactions, where ADP would normally phosphor late into ATP, in the presence of arsenic, ADP-arsenate is the end product and high-energy phosphate bonds are not formed. The unstable ADP-arsenate decomposes spontaneously and irreversibly, resulting in loss of energy by the cell. The energy depletion is also due to deficiency of phosphates ( Jones et al., 1997).
Fig 4.18 In acute arsenic toxicity there was (A) Necrosis of neuron. (B) Satellitosis. (H & E X 400)

Fig 4.19 In chronic arsenic toxicity brain shows. (A) Central chromatolysis in neuron. (B) Proliferation of glial cell. (H & E X 400)
Effect of arsenic on pulmonary tissue

Lungs receive the deoxygenated blood from different organs and this also contains different metabolites produced by the tissues. Therefore, the arsenic present in the impure blood also reaches to the lung and cause damage to the alveolar tissue.

In acute arsenic toxicity there was diffuse congestion in the lungs along with haemorrhages in the alveolar septa. There was edema in the interstitial tissues and also at some places in the alveoli because of increased permeability of vessel walls there is leakage of plasma into surrounding tissues producing localized swelling (Fig 4.20,4.21).

In chronic arsenic toxicity there was interstitial pneumonitis with increase infiltration of the lymphocytes and macrophages in the wall of alveoli. Interstitial pneumonia was characterized by exudation with in the alveolar septa (Fig 4.22). A few alveolar macrophages are also seen in the alveolar lumen. The septa become greatly thickened by infiltrating lymphocytes, macrophages and plasma cells. (Lay and Saloon, 1982)

The proliferation and hyper plastic changes in the bronchial wall and thickening of the alveoli indicated the enhanced metabolic and functional activity in an effort to make the oxygen demand which developed as a result of congestion and low concentration of haemoglobin which was observed from haematological values.
Fig 4.20 Haemorrhage in lung due to acute arsenic toxicity. (H & E X 400)

Fig 4.21 Lung in acute arsenic toxicity shows. (H & E X 400)
(A) Diffuse congestion in the lung along with haemorrhages in the alveolar septa. (B) Edema in the interstitial tissue. (C) Edema at some places in alvoli.

Fig 4.22 Interstitial pneumonitis and increased infiltration of the lymphocytes and macrophages in the wall of alveoli. (H & E X 400)
Muscle

In acute arsenic toxicity there was swelling of the skeletal muscle along with loss of striation. These changes are in patchy distribution. In Chronic changes muscle revealed Zenker's necrosis with or without loss of sarcolema nuclei. Zenker's degeneration occurs only in striated muscle. It is essentially a coagulation of proteins of the sarcoplasm. There is also evidence of loss of striations at some places (Fig 4.23,4.24).

Intestine

In acute arsenic toxicity there is vacuolar degeneration of the epithelium of deeper parts of crypts of liberkuhun. This was the cause of diarrhoea in animals.

In chronic toxicity there is atrophy of the cells of Crypts of Liberkuhn. Intestine shows infiltration of lymphocytes in the lamina propria as well as there is venous thrombosis partially occluding the lumen of blood vessel. Extensive inflammation and necrosis of the mucosa and sub mucosa of the stomach and intestine may occur and progress to perforation of the gut wall (Fig 4.25,4.26,4.27 & 4.28).
Fig 4.23 Swelling of skeletal muscle and loss of striation in acute arsenic toxicity. (H & E X 400)

Fig 4.24 Muscle shows zenker’s degeneration and loss of striations in chronic arsenic toxicity. (H & E X 400)
Fig 4.25 Intestine shows vascular degeneration of the deeper parts of crypts of Liberkuhn. (H & E X 400)

Fig 4.26 Intestine shows atrophied cells of crypt of Liberkuhn and the cells become cuboidal due to chronic arsenic toxicity. (H & E X 400)
**Fig 4.27** Section of intestine showing infiltration of lymphocytes in the lamina propria in chronic arsenic toxicity. (H & E X 400)

**Fig 4.28** Section of intestine showing venous thrombosis partially occluding the lumen of blood vessel in chronic arsenic toxicity. (H & E X 400)
ABOMASUM

In ruminants the stomach is divided into four parts that is rumen, reticulum, omasum and abomasum (true stomach). In acute arsenic toxicity there was severe congestion of abomasal mucosa. In chronic arsenicosis the deeper parts of the gland there is desquamation of glandular epithelium, which is lining of the fundus region of stomach (Fig 4.29, 4.30).

Spleen

The primary function of spleen is the filtration of blood to remove the foreign elements and destroy damaged erythrocytes. Spleen affected due to acute arsenic toxicity showed haemorrhages, congestion, necrosis of lymphoid cells and reduction in the size of lymphoid follicle. In chronic arsenic toxicity necrosis of lymphocytes of the malpighian corpuscles was observed this also effect the immune status of the animal which is expected to decrease (Fig 4.31,4.32).

Cotyledons

The cup like small structure (2 to 3 cm in diameter) of the uterus to which the foetus remained attached firmly with the mother are the cotyledons. In acute arsenic toxicity there was focal haemorrhages in the cotyledons which might be the probable cause of death of foetus in the womb of animals (Fig 4.33). Rudnai and Gulyas, (1998) reported an increase in spontaneous abortions, stillbirths, and prenatal mortality in Karcag, Hungary, due to arsenic in drinking water. In Bangladesh, Ahmad et al., (2001) reported a significant increase in spontaneous abortions, stillbirths, and preterm births. Increased arsenic in cord blood and the placenta was reported in Argentine women who drank water containing 200 [micro gram/L arsenic (Concha et al., 1998)
Fig 4.29 Abomasum shows severe congestion of mucosa in acute arsenic toxicity. (H & E X 400)

Fig 4.30 In Abomasum there is desquamation of granular epithelium in the deeper part of gland in chronic arsenic toxicity. (H & E X 400)
Fig 4.31 Spleen affected due to acute arsenic toxicity showed haemorrhage, congestion, necrosis of lymphoid cell and reduction of lymphoid follicle. (H & E X 400)

Fig 4.32 Spleen affected with chronic arsenic toxicity showing necrosis of the malpighian corpuscles. (H & E X 400)

Fig 4.33 Showing focal haemorrhages in the Cotyledons of uterus in animal suffering from acute arsenic toxicity. (H&E X 400)
CONCLUSION

This study proves that arsenic accumulates in all the organs of the body and is responsible for the development of toxic effects. Arsenic can cross all the barriers of the body and can reach to the brain and in the foetus through umbilical chord. Necrosis was observed in liver, an important organ responsible for the metabolic reactions. The denaturation of cellular proteins and denaturation of hydrolytic enzymes as well causing degeneration followed by coagulative necrosis. Kupffer cells present in the liver were found swollen in chronic arsenic toxicity. They revealed brownish pigment hemosiderin in their cytoplasm. Hemosiderin is a shiny golden yellow or golden brown pigment derived from haemoglobin. The cause of formation of this pigment was the destruction or haemolysis of erythrocytes to an excessive degree.

Therefore, in arsenicosis all chemical reaction gets altered leads to development of arsenicosis. In acute toxicity, also we observe pathological alterations though arsenic remains in body for very short period but this was enough for the development of changes in tissues. In spite of severe damage of tissues in chronic arsenicosis all subjects appeared to be healthy because tissue, which showed the significant damage, the liver, have the great power of regeneration. Skin helps to remove the arsenic by the replacement of old cells by new cells. Haemorrhages were observed in the cotyledons of uterus, which confirm the pathway of arsenic from mother to foetus. Further study is needed to determine the effect of arsenic toxicosis in foetus at different stages of gestation period.
REFERENCES


