CHAPTER 2
REVIEW OF LITERATURE

The term ‘metal’ designates an element which is a good conductor of electricity and whose electrical resistance is directly proportional to the absolute temperature. Metals whose atomic weights are greater than that of sodium or whose density is greater than 5 g/cm³ are commonly called ‘heavy metals’ and the term is used synonymously with ‘trace metals’, ‘trace-inorganics’, ‘micronutrients’ and ‘microelements’. The heavy metals/trace elements are known to exert a positive/negative influence on plants, animals and human beings.

The positive aspect or essentiality of the metal is recognized when it is determined consistently in healthy living tissues. Further, the depletion/removal of such metals results in deficiency symptoms which disappear when they are returned to the tissues. Iron (Fe), copper (Cu), cobalt (Co) and zinc (Zn) are the true metals which are indispensable to the living cells in low levels. Venugopal and Luckey (1975) identified Mn, Fe, Co, Cu, Zn and Mb as trace metals which are toxic when their concentration levels exceed the limit required for correct nutritional response. With reference to dose response and availability, the metals are classified into 1) non-critical metals, 2) toxic but very insoluble or very rare metals, 3) very toxic and relatively accessible metals (Gupta and Salunkhe, 1985).
Among the heavy metals, cadmium has raised the most concern because of its high toxicity coupled with a long biological half life, low rate of excretion and exceptional tendency of accumulation in various organs of man and animals, especially in the kidneys and liver (Van Bruwaene et al., 1984; Bernard and Lauwerys, 1984; Jones and Cherian, 1990).

2.1 SOURCES OF CADMIUM POLLUTION

Rapid industrialization and urbanization as well as man’s misuse and abuse of the environment have generally increased the concentration of heavy metals in the environment. The literature available on the sources of cadmium is briefly reviewed in the following paragraphs.

2.1.1 Cadmium in the Atmosphere

The recorded cadmium content in nature was 0.15 mg/kg in the earth crust; 0.15 μg/ml in marine water and 0.01 μg/m³ in air. Cadmium is principally obtained as a secondary product in the refining of other metals such as zinc and lead which contain cadmium as an impurity. The United States of America (USA), Union of Soviet Socialist Republic (USSR), Canada, Japan and Western Europe are the most important countries producing cadmium. The yearly world production of cadmium amounts to a few thousand tonnes of which 5.2 per cent of cadmium is released into the environment annually (Lauwerys, 1978). The disposals of metal rich wastes from secondary metal refining activities, waste incineration, tyre and oil residues from vehicles and tobacco smoke are some of the sources which dissipate cadmium into the environment.

Industrial fumes contain mainly cadmium oxide, cadmium chloride and cadmium sulphide which elevates the cadmium concentration in the
In the industrial areas, cadmium emission varied from 0.05 to 25 μg/m³ and the highest level of 25 μg/m³ was found in the vicinity of an operation such as smelters. Cigarette smoke contributes cadmium in the air. Twenty cigarettes can contain 30 μg of cadmium of which 2 to 4 μg can be inhaled. In the general environment 13 to 19 per cent of the cadmium inhaled is absorbed (Hallenbeck, 1984).

2.1.2 Cadmium in Soil and Water

Agricultural soils are mainly contaminated by phosphatic fertilizers and sludge disposal. The cadmium content of rock phosphate is variable and depends on its geographical origin (Williams and Davids, 1973). In a Belgian survey of thirty-one common phosphatic fertilizers, the cadmium concentrations ranged from 0.1 to 80.8 mg/kg. Intensive cultivation of vegetables, especially the leafy vegetables like lettuce and spinach increased the cadmium content in the soil due to the addition of phosphatic fertilizers (Van Bruwaene et al., 1984).

The flooded irrigation water is the most important source of heavy metals (Cd, Cu and Cr). Epstein and Chaney (1978) reported that sewage sludge used as a plant nutrient, has contaminated the cultivated soil. Forstner and Wittman (1981) estimated Cu and Cd in sewage sludge as 700 μg/kg and 10 mg/kg, respectively. Flowing waters (brooks and river) contained 0.0001 to 0.003 mg/l of cadmium (Bartik and Piskac, 1981). The rain waters, storm waters run off and the wastewaters received from different sources through natural and anthropogenic activities, contributed significantly to the heavy metal content, mainly cadmium and zinc (Yeats and Bewers, 1983). Cadmium compounds like cadmium oxide, sulphide, carbonate and hydroxide are insoluble in water and cadmium fluoride, bromide, iodide, chloride, nitrate and sulphate are soluble in water (Gupta and Salunkhe, 1985).
2.1.3 Cadmium in Plants

Concentration of cadmium in the edible roots, tubers and grains are usually lower than the leaves of the same plants. All plants contained cadmium in detectable concentrations ranging from 0.01 to 1.0 mg/kg (dry weight) and severely contaminated plants may contain more than 400 mg/kg of cadmium (Bartik and Piskac, 1981). Page et al. (1981) reported that cadmium concentrations in various parts of the plants in decreasing order were roots > leaves > fruits > seeds/ storage organs. Gupta and Salunkhe (1985) reported that tobacco leaves accumulated higher cadmium levels. The concentration of cadmium in the plants depends on the level of cadmium in the soil, fertilizers and water.

2.1.4 Cadmium in Feeds of Farm Animals

Cocchier and Fiore (1987) analysed feed and water of farm animals in Campania for cadmium and found that the cadmium concentrations ranged from 0.180 to 0.498 mg/kg in feed stuff. Commercially prepared feeds of cattle, poultry and pigs contained a wide spectrum of ingredients from products and by-products of plants and animals. Mumma et al. (1986) reported that considering various constituents of feeds, there is possibility of contamination by agricultural and industrial pollutants, especially heavy metals, during processing. The fish meal made up of many trash fishes and marine organisms like crab, squilla, scallops, clams, gastropods and small fishes contained very high level of cadmium (Zoological Survey of India, 1987, 1991).

The cadmium concentrations in animal tissues especially in liver and kidneys were strongly related with the cadmium levels in animal feed stuffs (Sharma et al., 1979; Vreman et al., 1986). Stoewsand et al., (1986) reported that the earth worms collected from Canada contained
3 mg Cd/kg. When these worms were fed to Japanese quails as 60% dry weight of their feed for 63 days, the cadmium concentration in kidney, liver and faeces was found to be greater than in birds fed with control diet without earth worms.

2.1.5 Cadmium in Tissues/Organ of Farm Animals

The heavy metals reach the body of animals mainly through the contaminated feed stuffs. On chronic exposure, the accumulation of cadmium from food was greater in liver and kidney. Intestinal absorption of cadmium was low in mammals which ranged from 0.3% in goats (Miller et al., 1969) to 5% in swine (Cousins et al., 1973). The cadmium absorption was influenced by different dietary factors like calcium, protein and vitamin D (Larsson and Piscator, 1971). Hapke et al. (1977) recorded 200 μg Cd/kg of liver and kidneys of lambs fed with basal feed for 140 days. Flanjak and Lee (1979) recorded 0.001 mg Cd/kg in muscles; 0.06 mg Cd/kg in liver and 0.37 mg Cd/kg in kidneys (wet weight) from cattle in Australia. The data for cattle collected from Federal Republic of Germany (FRG), Belgium, USA, The Netherlands and Denmark and for pigs from FRG revealed that cadmium concentrations in kidneys were 2 to 5 times more than the concentration in liver and muscles. The liver fixed the cadmium rapidly but in a limited amount whereas in the kidney the cadmium was taken slowly but continuously (Van Bruwaene et al., 1984). Cattle which were allowed to graze on pastures treated with anaerobically digested sludge showed that cadmium was the only metal accumulated consistently in increased amount in different tissues particularly in liver and kidneys though animals did not show any health problems (Fitzgerald et al., 1985).

Koffer et al. (1986) estimated cadmium concentration in muscles, liver and kidneys of pigs in Styria (Australia) as 0.016, 0.070 and 0.330
mg/kg, respectively. Cocchieri and Fiore (1987) analysed muscle, liver and kidney samples from cattle, pig and lamb from 15 farms in Campania for cadmium. The cadmium concentration varied between 0.038 and 0.342 mg/kg in cattle, from 0.048 to 0.666 mg/kg in pigs and from 0.178 to 1.035 mg/kg in lamb. Vos et al. (1987) analysed meat, liver and kidneys of cattle slaughtered in The Netherlands during 1980-85 and estimated arsenic (mean, 0.022 mg/kg), cadmium (mean, 0.22 mg/kg) and lead (mean, 0.2 mg/kg) concentrations. The legal limits for heavy metals in tissues were exceeded only for cadmium in two kidney samples. In 1985, the permissible level of cadmium in The Netherlands for muscle, liver and kidneys of cattle was 0.05, 1.0 and 3.0 mg/kg, respectively. Kreuzer et al. (1989) estimated cadmium in muscle, liver and kidneys of cattle from FRG as 0.005, 0.13 and 0.59 mg/kg (wet weight), respectively.

2.1.6 Cadmium in Human Beings

The harmful effect of cadmium on human beings has been well documented ever since the tragedy of Itai-Itai disease caused by the cadmium contaminated sea food in Japan (Friberg et al., 1974). Frazier (1979) reported that gastrointestinal absorption of cadmium in humans was much lower (1-6%). According to Sharma et al. (1979), the human consumption of cadmium via animal food products varied depending upon the organs ingested. The accepted "tolerance intake" of cadmium for human varied from 0.0067 to 0.0083 mg/kg body weight/week (FAO/WHO, 1979). Han (1988) reported that cadmium intake by person/day ranged from 75.4 to 737.0 µg which was responsible for pain in limbs and back joints. He suggested an acceptable daily intake of cadmium to be 100 µg/person or 1.67 µg/kg body weight which was slightly higher than WHO's recommendation.
2.2 CADMIUM TOXICITY

Several animals/birds accumulated heavy metals in their body while others simply excreted the absorbed heavy metals without any biological response. However, the biological symptoms exhibited by the animals showed a direct relationship between the concentration of the known metal in their body and its toxicity. Some harmful metals like cadmium at low concentration in biological tissues may not cause rapid death but impair the function of the living being. Sublethal effects may be observed at biochemical, physiological or behavioural aspect of the animal concerned. As the level of the toxicant rises, compensation occurs by reduction in the metabolic rate that controls the normal function of the body but at higher concentrations the individual collapses.

Cadmium toxicity has been demonstrated experimentally in numerous animal species. Manifestations of toxicity included loss of weight, reduced food intake, anaemia, hypertension, proteinuria, poor bone mineralization, testicular necrosis, aborted foetuses, neonatal death and birth defects in young ones (Doyle, 1977; Bartik and Piskac, 1981).

2.2.1 Effect of Cadmium on Growth of Poultry

Webber and Reid (1971) studied the metabolic effects of cadmium by administering 100 to 700 mg Cd/kg of feed to four weeks old chicks and reported 25% growth reduction with 100 mg, 70% growth reduction with 200 mg and 50% mortality with 400 mg of cadmium dose. The LD$_{50}$ values of cadmium recorded by Krampitz et al. (1974) for chicken ranged from 165 to 188 mg/kg of feed but 216 mg Cd/kg of feed was lethal. Sell (1975) reported that hens fed with 60 mg Cd/kg of feed accumulated most of the administered cadmium in liver and kidneys. Interestingly, cadmium content in the liver decreased after stopping cadmium dosing,
Long term experiments conducted on chicken with cadmium concluded that the kidneys accumulated greater cadmium than the liver, although the liver retained more of cadmium initially than that of kidneys (Whitehead et al., 1988). The studies conducted by Scheuhammer (1988) on adult Japanese quails with oral cadmium of 0.5, 5.0, 50.0 mg/kg body weight/day have recorded the highest cadmium in liver of birds administered with 50 mg Cd/kg. The experimental conditions and the factors responsible for higher accumulation of cadmium in liver are not given.

### 2.2.2 Effect of Cadmium on Growth of Mammals

When rats were administered with 5 mg Cd/l in drinking water, the kidneys, liver and heart accumulated 1.54, 2.24 and 0.09 μg Cd/g in male and 2.33, 0.39 and 0.47 μg Cd/g (wet weight) in females, respectively which resulted in 90% death in 1134 days in males and 1018 days in females. The cadmium accumulation in lungs and spleen was meagre (Shroeder et al., 1965).

Powell et al. (1964) observed immediate reduction in feed consumption with loss of weight in calves fed with 160, 640 mg Cd/kg in feed and 2560 mg Cd/kg in feed resulted in death. Miller et al. (1967) reported that 3 g of cadmium given to lactating cows daily has reduced considerable weight and milk production. Six month old male goats with a single oral dose of 100 mg Cd/kg resulted in the total body retention of 0.3 to 0.4% of Cd of which 0.5% accumulated in the liver. The bone, muscle, blood, hair and skin contained very little cadmium (Miller et al.,
When 8 week old swines were fed with basal diet containing 0, 50, 100, 150, 450 and 1350 mg Cd/kg of feed for 6 weeks, the degree of cadmium accumulation in different organs in descending order was kidneys, liver, spleen, lungs, heart and muscles; and the concentration of cadmium varied from 41.2 to 301.40 in kidneys; 4.9 to 126.6 in liver; 0.6 to 17.1 in spleen; 0.4 to 6.9 in lungs; 0.4 to 3.0 in heart and 0 to 14.4 μg/g in muscles. When the animals were administered with 450 and 1350 mg Cd/kg of feed, the maximum accumulation of cadmium in kidneys and liver was 276 and 301 μg/g; 53 and 127 μg Cd/g (wet tissue), respectively (Cousins et al., 1973). Transfer of cadmium to different organs from diet dosed with cadmium at 5, 15, 30 and 60 mg of cadmium to lambs for 191 days resulted in 14.92, 51.72, 62.73 and 275.94 μg Cd/g of liver and 58.86, 187.62, 426.81 and 768.89 μg Cd/g of kidneys, respectively. The results showed that the kidneys accumulated the maximum cadmium (Doyle et al., 1974).

In acute poisoning, more cadmium was stored in liver and in chronic poisoning kidneys accumulated more cadmium. The stored cadmium in liver and kidneys was several times higher in older animals than in young animals. In laboratory animals, 90% of administered cadmium was reported to be eliminated in the faeces within 24 hours after single administration whereas on oral administration 10% of the dose ingested accumulated in the body and by intramuscular injection of 0.2 to 1 mg of cadmium/kg body weight, 20% of the dose injected was absorbed in the body tissues in bulls (Bartik and Piskac, 1981). Most of the retained cadmium accumulated mainly in liver and kidneys followed by other organs like pancreas, heart, spleen, intestine and bone. Muscles accumulated very little cadmium (Van Bruwaene et al., 1984).
2.2.3 Effect of Cadmium on Nutrients

There are many nutritional modalities considered to be important in the onset and severity of cadmium poisoning. Some of the nutrients known to play a significant role in cadmium metabolism were proteins (Suzuki et al., 1969), iron (Banis et al., 1969), calcium (Larsson and Piscator, 1971), ascorbic acid (Fox et al., 1971), zinc and copper (Mills and Dalgarno, 1972). Iron, protein, zinc, copper, calcium and ascorbic acid from the foods of animals played a major role in cadmium metabolism and alleviated the toxicity of cadmium and decreased the cadmium absorption (Mills and Dalgarno, 1972).

Fox and Fry (1970) reported that when young Japanese quails from one day old to 4 weeks were fed with 75 mg Cd/kg body weight produced growth retardation, severe anaemia, reduction of iron concentration and increased cadmium concentration in the liver. However, the impacts of cadmium on the physiological and biochemical aspects of birds are not discussed.

Larsson and Piscator (1971) reported that female rats fed with calcium deficient diets along with 25 mg of Cd in drinking water, accumulated more than 50% of the Cd in the liver and kidneys than the animals fed with adequate levels of calcium. The liver and kidneys of mice and rats accumulated more cadmium when fed with calcium deficient diet (Kobayashi, 1971; Washko and Cousins, 1976).

Cadmium occurs in nature with zinc. The zinc is physiologically essential for life and its biological role has been explained to differ substantially from that of cadmium. Zinc interacts with cadmium, being antagonistic to many toxic effects of cadmium. It is necessary for normal
growth and development in mammals and birds (Syversen, 1975; Oehme, 1979).

Jacobs et al. (1978) conducted experiments on two groups of two week old Japanese quail fed with basal and mineral supplemented diet containing 30 mg of Zn, 5 mg of Cu, 12 mg of Mn along with 1mg of Cd/kg of body weight and reported that the cadmium accumulation in different organs of birds fed with mineral supplement was lower than the birds fed with basal diet without the mineral supplement.

Tandon and Khandelwal (1987) reported that the effect of zinc deficiency increased cadmium accumulation in the liver and kidneys of rats. The experiments of Reddy et al. (1987) on mice and calves revealed that when zinc administered along with cadmium, the tissue cadmium burden in kidneys, pancreas and spleen was lower than the same organs of mice treated with cadmium alone.

Waalkes et al. (1991) observed that excess zinc prevented cadmium carcinogenesis in male Wister rats. Groten et al. (1991) examined the protective action of mineral supplementation in cadmium toxicity in rats and reported that the cadmium accumulation in livers and kidneys was less by 70 to 80%.

2.2.4 Effect of Cadmium on Blood

Haematological parameters on age, sex and laying have showed differences in avian species. Nirmalan and Robinson (1971) reported that young quails had lower RBC, PCV, Hb, lymphocytes and plasma protein concentrations than adult male and non-laying females and the adult males had higher RBC, PCV, Hb and plasma protein content than adult non-laying females.
Jacobs et al. (1969) fed Japanese quail with 75 mg of Zn/kg alone and in admixture with 75 mg Cd/kg of feed from the day of hatch to 4 weeks and observed that the quail received cadmium in their diet grew slowly and 80% of them developed anaemia. The zinc administered quail has recorded 15% plasma transferrin, 40% albumin, 42% haematocrit value and 3.61 g/dl serum protein whereas the Cd administered quail has recorded 23.2% plasma transferrin, 27.1% albumin, 22% PCV and 3.71 g/dl serum protein. According to Fox and Fry (1970) Japanese quail fed with 75 mg Cd/kg body weight for 4 weeks has recorded lesser body weight of 57 g and PCV of 17% compared to the control birds which had 80 g body weight and 40% PCV.

Fox et al. (1971) reported that the primary effect of cadmium Japanese quail was anaemia due to iron deficiency. Bell and Freeman (1971) stated that cadmium being antagonistic to copper, inhibited copper absorption and prevented it from binding with protein in the duodenal mucosa which reduced the iron absorption and synthesis of blood. Anaemia due to cadmium toxicity has been reported in chicken (Bell and Freeman, 1971), in pigs (Cousins et al., 1973), in Japanese quails (Richardson et al., 1974), in sheep (Wright et al., 1977) and in rats (Das et al., 1987).

When 75 mg Cd/kg of feed was administered to Japanese quail from hatching to sixth week of age has resulted in lesser PCV (32%) and haemoglobin (6.9 g/dl) in male birds than that of the control males which contained 52% of PCV and 15.6 g/dl of haemoglobin (Richardson et al., 1974). However, the actual amount of cadmium ingested and the long term effect of sublethal dose of cadmium on Japanese quail and its impacts on serum protein, Hb content and RBC were not discussed.
Cousins et al. (1973) investigated the impacts of cadmium on swine by feeding 0, 50, 150, 450, 1350 mg Cd/kg of feed for six weeks and found that the PCV values were lesser in than the Cd treated animals than the control viz., 40, 33, 30, 30 and 33%, respectively.

The gonadal hormones changed the haematological parameters in the Rain quail. The RBC, Hb and PCV were 4.36 million/mm³, 12.40 g/dl and 33.8% in control males; 2.60 million/mm³, 7.08 g/dl and 17.70% in estrogenised males; and 8.26 million/mm³, 13.60 g/dl and 35.70% in testosterone administered males, respectively whereas in female birds, RBC, Hb and PCV were 3.65 million/mm³, 10.40 g/dl and 31.20% in control; 2.20 million/mm³, 5.60 g/dl and 18.50% in estrogenised female; and 5.38 million/mm³, 13.20 g/dl and 35.50% in testosterone administered female, respectively (Deshmukh and Suryawanshi, 1982).

2.2.5 Effect of Cadmium on Proteins and Lipids

Cadmium has a high affinity for proteins. Protein deficiency caused increased retention of cadmium in rats (Suzuki et al., 1969). Cadmium damages the mucous membrane of gastrointestinal and respiratory tract and enters the blood where it gets bound to the plasma proteins. The resultant complex is called ‘cadmium-binding protein’ or the ‘metallothionein’ which is a low molecular weight protein (about 10,000) (Shaikh and Lucis, 1972; Cherian et al., 1978). When soluble cadmium salts are injected, cadmium becomes associated primarily with albumin and high molecular weight plasma proteins (Watkins et al., 1977; Suzuki, 1981).

In liver and kidneys, the cadmium gets incorporated into metallothionein which is a cystein-rich protein having high affinity for cadmium ions. The cadmium-binding metallothioneins in kidney are
filtered by the glomerulus and deposited in the proximal tubular cells upon protein reabsorption (Murakami et al., 1986; Abel et al., 1987).

Dudley et al. (1982) conducted cadmium toxicity studies on rats by injecting 3.9 mg Cd/kg of body weight and found necrosis and fatty metamorphosis in the liver after ten hours.

The excessive lipid deposition in liver or the fatty line haemorrhagic syndrome resulted in liver impairment in rats treated with pesticides. (Choudhari and Chackrabarti, 1983, 1984). However, information on total proteins lipids in liver and kidneys of Japanese quail and the effect of cadmium on these biochemical constituents are not available.

2.2.6 Effect of Cadmium on Enzymes of Clinical Importance

Aspartate transaminase (AST) or the glutamate oxaloacetate transaminase (GOT), Alanine transaminase (ALT) or the glutamate pyruvate transaminase (GPT) and gamma-glutamyl transferase (GGT) are the three enzymes of clinical importance. Ford (1974) stated that the liver injury in sheep increased the enzymatic activities in serum.

2.2.6.1 Transaminases

Cornelius, (1961) reported that the tissue damage in hepatic, cardiac, skeletal and muscular systems has increased the level of aspartate transaminase and alanine transaminase in serum. The increased levels of transaminases in the serum of man and animals due to myocardial infarction have also been recorded (Roussel and Stallcup, 1965).
Bell and Freeman (1974) discussed the distribution of transaminases in the serum of avian species particularly fowls, ducks and turkeys. They have observed that the damages of tissues in avian species enhanced the level of AST in serum.

Proudman et al. (1975) stated that the serum AST in fast growing chicken increased from 108.29 U/l at 4th week to 143.17 U/l at 20th week. Maruyama et al. (1976) reported that the ALT level in the liver of a day old chicken increased from 280 to 328 U/g at 10th day but the AST level declined from 4955 to 740 U/g. The reason for the variation in the ALT and AST level and the conditions under which the experiments conducted are not known.

Majumdar and Sharma (1987) studied the AST and ALT activities in broiler chicken and found that the liver disease had altered the tissue metabolism and enhanced the AST level in serum.

Cain et al. (1983) investigated the ALT activity in serum of mallard ducklings (Anas platyrhynchos) by administering 20 mg Cd/kg of feed for 8 weeks from the day of hatch and observed an increased level of ALT in serum.

Dalvi and McGowan (1984) observed that aflatoxin increased the serum AST from 106.5 U/l to 230 U/l in chicken and the increase was 115 per cent. However, this was not observed by Panda et al. (1987) in Japanese quail treated with aflatoxin. Dudley et al. (1982) stated that the rats subjected with single intravenous injection of 3.9 mg Cd/kg exhibited hepatic necrosis and increased serum AST (60 times) and ALT (97 times) compared to the control. This was also confirmed by Theocharis et al. (1991).
Calves injected with 1.12 mg Cd/kg body weight for 5 alternate days showed increased activity of AST and ALT in serum to the level of 125% and 80%, respectively (Reddy et al., 1987). Kojima et al. (1991) reported that injection of 200 microgram metallothionein-bound of Cd/kg body weight in rats caused renal and hepatic damages which was responsible for the increased urinary excretion of AST.

Subcutaneous daily injection of 1 mg Cd/kg body weight for six weeks in rats resulted in a dose related increase of 1.5 times of AST and 1.7 times of ALT in plasma at 6 weeks (Khandelwal et al., 1991). However, studies on the effect of cadmium on AST and ALT levels in tissues/organs and in serum of Japanese quail are not known.

2.2.6.2 Gamma-glutamyl transferase

The two main organs of GGT production are kidneys and liver. In kidney, GGT is observed in the brush border of epithelial cells lining the proximal convoluted tubules and loops of Henle and in liver the GGT is found in the luminal border of the epithelial cells lining the fine biliary ductules of man and animals (Albert et al., 1964).

The GGT activity in kidneys was relatively higher than in liver which was in the ratio of 20:3 in man. The GGT activity in sheep ranged from 16,000 to 34,600 U/g in kidneys and from 1480 to 3200 U/g in liver (Szczeklik et al., 1961).

The GGT in kidney has been reported to be important for the absorption of amino acids across the cell membrane from the glomerular filtrate, resulting in the formation of gamma glutamyl peptides, which are absorbed into and then broken down by the renal cells (Hoffman et al., 1975). The plasma GGT has been recorded as moderate or low in most
animals and man but very low in cats, dogs, rats, mice and birds (Braun et al., 1982).

Exposure of rats to low level of cadmium resulted in renal toxicity and increased level of GGT in urine due to tubular dysfunction and increased cell turnover (Hoffman et al., 1975; Kotsonis and Klaassen, 1978).

Treatment of sheep with sporidesmin produced inflammation, obstruction and proliferation of bile duct and caused elevation of GGT in serum. The GGT level was 25 times higher than the control (Towers and Stratton, 1978).

2.2.7 Effect of Cadmium on Pathological Changes

Cadmium salts are known to induce severe pathological syndrome in tissues of aquatic and terrestrial vertebrates due to their bioaccumulation and bioamplification. Ingestion of cadmium has caused ulcer in the gastrointestinal tract, nausea, vomiting, salivation, abdominal cramps, diarrhoea, reduction in blood pressure, bone demineralisation, hypercalcaemia, impairment of kidneys and liver and damage to testes and ovaries leading to infertility (Bartik and Piskac, 1981).

2.2.7.1 Effect of cadmium in liver

In liver cadmium gets localized in parenchymal cells. The accumulated cadmium in the hepatocytes interacts with cellular organelles and disrupts biochemical processes. However, the exact mechanism by which cadmium causes liver injury is not clearly understood. Dudley et al., 1982 reported that the liver showed severe damage in rats injected with 3.9 mg Cd/kg body weight. There were
pronounced eosinophilia and swelling of hepatocytes within one hour of post injection and resulted in necrosis with elevated levels of plasma AST and ALT and 50% reduction of plasma glucose. Cain et al. (1983) recorded liver necrosis in ducks fed with 20 mg Cd/kg of feed administered from the day of hatch to 12 weeks.

Richardson et al. (1974) reported that the depletion of glycogen in the hepatocytes, disorganised liver plate cells, wider and distinct sinusoids in the liver of Japanese quail fed with 75 mg Cd/kg of feed. However, the distinct pathological symptoms and the impact of cadmium on the lipid metabolism in liver are not properly understood.

2.2.7.2 Effect of cadmium in kidneys

In chronic cadmium poisoning, more cadmium is stored in kidney cortex than in medulla. The kidney damage often leads to proteinuria and uremia. The low molecular proteins filtered by glomeruli and proximal tubules are reabsorbed by the tubules of the normal nephrons; but in cadmium toxicity, the glomeruli and the proximal tubules are damaged and the permeability of the basement membrane is increased. The high molecular proteins or the cadmium binding metallothioneins passing through the glomeruli are not reabsorbed by the proximal tubule causing proteinuria (Whitehead et al., 1988).

High dietary metals, particularly cadmium to sea birds caused patchy nephrotic lesions such as necrosis, degenerations of the proximal tubular epithelium and obstruction by necrotic cellular debris in the distal part of the nephrons. Abnormalities in the glomerular podocytes and cells of Bowman's capsule were also reported by Nicholsons and Osborn (1983).
Junnila et al. (1987) observed histopathological changes in kidney cortex of horses poisoned with cadmium and reported periglomerular fibrosis, tubular dilation, proteinuria, intestinal granular infiltration and glomerular sclerosis. Shigetoshi and Kaji (1991) also observed kidney damage in rats injected daily with 1.5 mg Cd/kg body weight for 4 days.

Richardson et al. (1974) stated that the Japanese quail fed with 75 mg Cd/kg of feed has produced scattered swollen proximal convoluted tubules with granular cytoplasm between 4 and 6 weeks. The cells lining the Henle’s loop in the medulla were swollen and cells in the adjacent tubules appeared to be shrunken. However, the amount of cadmium ingested by the birds and the associated physiological and clinical symptoms are not indicated.

2.2.7.3 Effect of cadmium in lungs

The mechanism of cadmium induced injury in lungs is not clearly understood. However, the accumulation of cadmium in macrophages damaged the lung defensive mechanism as proposed by Mustafa and Cross (1971).

It was reported that cadmium caused pneumonitis or pulmonary edema with chills and fever in workers exposed to cadmium fumes. Acute chronic exposure led to lung injury, multifocal damage to respiratory bronchioles, loss of plasma membrane and connective tissues in lungs (Nriberg et al., 1974; Kutzman et al., 1986).

Murthy and Holovack (1991) investigated the ultrastructural changes in lungs of three groups of rats by administering 0.1 mg of CdO and 5.0 mg of ZnO to the first group; 0.1 mg of CdO and 0.2 mg of CuO to the second group and 0.1 mg of CdO and 1.0 mg of NiO to the third
group. They stated that a single dose of intratracheal intubation affected the alveolar macrophages and Type II cells in the lungs. There was an increase in number, change in size and shape of vacuolar phagolysosomes, aggregates of multivesicular bodies and changes in the membrane whorls, and vascular leakage in the lungs of all the three groups of rats treated with cadmium.

2.2.7.4 Effect of cadmium in testes

The effect of cadmium on the spermatogenic and androgenic functions of testes in animals indicated different degrees of responses leading to irreversible pathological alterations highlighted by desquamation of seminiferous epithelial cells, cytolysis and necrosis of Leydig cells. Such derangements were responsible for the severe impairment of fertility (Lall, 1990; Laskey and Phelps, 1991).

There is an important ‘blood-testes barrier’, formed of special cells of the basement membrane of the seminiferous tubule which separates the seminiferous epithelium from the general circulation. The cadmium induced damage to the ‘blood-testes barrier’ was responsible for testicular disfunction (Hafez, 1980). Cadmium had been reported to act on multiple sites within Leydig cells and depress testosterone production in laboratory animals (Caflisch and Du Bose, 1991).

The degree of testicular damage by cadmium differs significantly between mice and rats (Gunn et al., 1965) and between mammalian and avian species (Lucis and Lucis, 1969).

The cadmium induced testicular damage caused regressive changes in spermatogenic epithelium, interstitial tumour, edema, congestion of
blood vessels and haemorrhage followed by necrosis (Waalkes et al., 1991).

Richardson et al., (1974) reported reduced testes in Japanese quail fed with 75 mg Cd/kg of feed. However, the impacts of cadmium on the fertility disturbances in Japanese quail are not discussed.

2.2.7.5 Effect of cadmium in ovary

Cadmium produced selective circulatory damage to oestrogen producing organs like the ovary and placenta which led to the death of embryos (Chiquine, 1965). Cadmium toxicity decreased hatchability of eggs in ducks and hens (Henning et al. 1971; Sell, 1975). Hens fed with 50 mgCd/kg of feed decreased egg production from 60 to 35% and number of craked eggs increased by 30% (Renon et al. 1989).

Hens fed with 50 mg Cd/kg of feed resulted in damaged ovaries and prevented egg laying (Bartik and Piskac, 1981); 100 to 200 mg Cd/kg of feed ceased egg production (Henning et al., 1968). Samarawickrama and Webb, (1979) stated that a single subcutaneous injection of 0.01 mg Cd/10 g body weight in mice resulted in intrauterine death of embryos and necrosis of placenta.

Eventhough the effect of cadmium on egg production and hatchability in chicken and duck are reported, the impacts of cadmium in the female reproductive system and histopathological changes of the ovary in Japanese quails are not known.
2.2.7.6 Effect of cadmium in bone

The most striking bone disorder due to cadmium toxicity was the Itai-Itai disease reported in Japan (Friberg et al., 1974). Cadmium can damage the bone, resulting in osteomalacia, hypocalcaemia, hypercalcuria and demineralisation of bone, (Bartik and Piskac, 1981; Whitehead et al., 1988). The interference of cadmium with zinc metabolism results in the depletion of zinc from the bone, kidney damage and excretion of calcium and phosphorus from the bone (Bernard and Lauwery, 1984).

Low dietary cadmium increased renal accumulation of cadmium and enhanced bone demineralisation and decreased ash content in Japanese quail (Fox et al., 1971; Richardson et al., 1974) and in rats (Larsson and Piscator, 1971). Single injection of 0.2 mg of CdCl₂/100 g body weight of Japanese quail resulted in deformed leg bones with hard jelly like content compared to control birds after 3 hours of post injection (Nishimura et al., 1974). However, the impact of cadmium on the bone marrow has not been studied.

2.2.8 Effect of Cadmium on Chromosomes

Chromosomal aberration, a change in the normal numerical or structural pattern of chromosomes, is an indication of harmful effects of environmental factors/pollutants on the health of population and individuals.

At the beginning of cytogenetic studies, the spontaneous aberrations were reported to range between 0.5 and 10% in farm animals in certain European countries and a similar report was obtained for human population also. But during the recent years, these values have increased from 2 to 3% in domestic animals kept under average conditions and
from 4 to 8% in feeder pigs. In human population in large cities, the spontaneous aberrations ranged between 1.5 and 2.5% and in workers exposed to certain health hazards the spontaneous aberrations varied from 3 to 6% or higher (Lojda, 1989).

Klingerman et al., (1984) reported that elevated frequencies of sister chromatid exchange were observed in chromosomes of mammals and birds as a result of exposure to mutagenic carcinogens.

Treatment of cultured human leucocytes by cadmium sulfide at 620 μg/ml showed numerous aberrations like chromatid and isochromatid breaks, symmetrical and asymmetrical translocations (Shiraishi and Yosida, 1972). Bauchinger et al. (1976) found a slight but significant increase of the chromosomal abnormalities in workers exposed to cadmium. Muller et al., (1991) observed broken DNA strand in in vitro studies treated with Cd-metallothionein.

The normal diploid chromosome numbers in avian species vary from 60 to 80 with 7 to 9 pairs of macrochromosomes and 40 to 60 pairs of microchromosomes. The 'Z' chromosome occupies a relatively constant position between 4th and 6th pair in the karyotype (Ryttman and Tegelatrohn, 1981; Bhunya and Sultana, 1986).

Ansari and Singh (1983) recorded 78 diploid chromosomes (2n) in Coturnix coturnix japonica. However, the impact of cadmium on avian chromosomes particularly in Japanese quail has not been studied. Since the cadmium has been proved to be mutagenic and cytogenic the chromosome analysis for cadmium treated quail has been investigated.