HEPATIC LESIONS AFTER SINGLE INJECTION OF CADMIUM ACETATE IN SQUIRREL

A single intraperitoneal injection of cadmium acetate induced histopathological changes in liver viz., dilatation of central vein, Kupffer cells hyperplasia, feathery degeneration of hepatocytes and foci of necrosis. These findings suggest that cadmium might have produced deleterious effect on this organ.

Cadmium has been described to be associated in various pathological conditions viz., hepatic and renal dysfunction, growth inhibition, anemia and changes in plasma protein level and proteinuria. In cadmium intoxication, regardless of the administrative route, the largest quantity has been observed to accumulate in the liver and kidney, which results in interlobular hepatic and interstitial renal fibrosis. All these disorders of liver had been reported after chronic exposure. But very little work has been performed on the acute phase of the metal. Recently, hepatic lesions have been described in squirrels after 24 hours of cadmium injection. In the present study hepatic lesions have been recorded during first week of cadmium acetate treatment in common Indian ground squirrel (Funambulus pennanti, Wroughton).

Twenty four laboratory-bred male squirrels with average body weight 100±10 gm were reared in steel-wired cages on wheat-flour bread and tap water ad libitum. These were divided into 2 groups: first with 16 animals and second with 3 animals. The first group was treated with cadmium acetate, whereas the second served as control. Cadmium acetate was prepared in distilled water. A single intraperitoneal injection of this solution was given in the animals of the first group at a dose level of 6.0 mg Cd/Kg of body weight. The control group was treated with sodium acetate solution (6.0 mg/Kg) intraperitoneally. Sodium acetate was given to the control group because cadmium acetate was administered in the first group. Body weight of squirrels of both the groups were recorded daily. These were sacrificed by decapitation after light ether anesthesia at 1, 3, 5, and 7 days. Liver pieces (5 mm in thickness) were fixed in 10% formol-saline. Paraffin sections of control and treated liver were cut at 3–4 μ and stained with haematoxylin-eosin.

The body weight of control and treated squirrels both revealed increase due to cadmium intoxication, although differently. The cadmium treated animals increased in body weight slowly than controls (Fig. 1). After one day of cadmium injection, the central vein dilatation and some cloudy swelling of hepatocytes were well pronounced. Whereas, after three days of treatment cloudy swelling and feathery degeneration of hepatocytes and a few foci of necrosis were significant. Five days after intoxication all these changes were more pronounced and several foci of necrosis in the vicinity of dilated central vein were clearly observed (Fig. 2). After seven days all these alterations were exaggerated and portal triaditis also set in. However, the architecture of liver remained normal throughout.
Toxic effects of ingestion of cadmium have been studied in different animals. Der, et al.\textsuperscript{9}) reported slower growth rate in cadmium treated rats. Wilson, et al.\textsuperscript{10}) observed that a concentration of 0.0031\% cadmium or more in diet resulted in decreased rate of growth in male albino rats. Growth rate in cadmium fed rabbits\textsuperscript{4)} and growing swine\textsuperscript{11)} was also reported to be significantly reduced. The present observation demonstrates that
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after acute cadmium exposure the squirrels had a stunted growth rate which is in agreement with the findings of above workers.

The liver is subjected to greater stress due to cadmium intoxication. The architecture of liver remained normal after different intervals. However, liver damage in most of the cases follows a fairly standard and significant pathological alterations, starting with dilatation of central vein, feathery degeneration of hepatocytes, associated Kupffer cell hyperplasia and focal collection of macrophages and lymphocytes. It is well established that regardless of the route of administration hepatic concentration of cadmium via blood stream is very rapid and one of the highest in magnitude as compared with other organs.4-6,12) The central vein was found to be dilated in all the test animals. The dilatation of central vein may be regarded as a normal tissue response towards injurious agents. The cloudy swelling of hepatocytes was observed as early as first day after administration of intraperitoneal cadmium and was more marked after passage of exposure time. This degeneration appeared to have represented some sort of water and protein disturbance in hepatocytes. Kawai and Kimura also reported gradual development of generalized cloudy swelling of the proximal convolution of tubules during first week after a single injection of cadmium chloride in rabbits.13) Cadmium has been found to combine with a protein of low molecular weight, may be metallothionein14,15) and this lesion may be taken up a consequence of cadmium binding to protein of hepatocytes. The hepatocytes revealed feathery degeneration after different intervals. The distribution of cadmium in different parts of liver has been described both after acute16,17) and chronic exposures.18) These studies suggested that cadmium is either equally distributed in the different parts of liver lobules or concentrated in the periphery of the lobules. Feathery degeneration of hepatocytes in the present study seems to be in agreement with the former. This lesion was also recorded by Mehrotra, et al.19) in hepatocytes. This alteration has been considered non-specific as it occurs in other conditions also viz., toxic states, poisoning, lupoid and viral hepatitis.20)

The Kupffer cell hyperplasia was noticed after first and third days interval besides accumulation of inflammatory cells in the liver lobules. The aggregation of leucocytes mainly neutrophils and macrophages at the sites of necrosis of hepatocytes may well constitute the prime defending feature of the inflammatory response. The morphologic changes encountered following single dose of cadmium presumed to be an indicator of immunologic stimulation besides its direct hepatotoxic effect.

The distribution of cadmium induced necrosis of hepatocytes. The liver cell necrosis was observed to be characterized by nuclear pyknosis, karyorrhexis and karyolysis in centrizonal area of lobules. This lesion was accompanied by presence of focal collection of inflammatory cells. These observations were recorded in all sets of test animals after different intervals of injection. Colucci, et al.21) while investigating cadmium accumulation in rat liver, correlated pathological changes with hepatic concentration of the metal than with the injected dose. This observation seems to be logical as degree of changes would depend on how much concentration hepatocytes possess. Friberg, et al.22)
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have reported that 75% of cadmium injected in the body of animals was found in liver and kidney in long term studies. Hoffmann, et al. reported that the single parenchymal cell necrosis in liver was the end result of an integrated pattern of functional and structural damage produced directly or indirectly by cadmium acetate. They also described the focal necrosis of hepatocytes in some of the animals and suggested that probably this lesion also arose due to cadmium toxicity. The aggregation of inflammatory cells in the portal triads suggested the appearance of portal triaditis.

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