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Histopathological Alterations Induced by Uranyl Nitrate in the Liver of Albino Rat

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Metals are unique environmental and industrial pollutants in that they are neither created nor destroyed by humans but are only transported and transformed into various products. Often these activities result in exposure to trace metals by persons not ordinary in contact with them, and sometimes new chemical forms are created which are toxic in nature and have the adverse health effects on animal world. Among the exogenous toxins metallic ions are therefore quite important and according to BOYD (1958) many of them including mercury, arsenic and lead are commonly used for suicidal purpose by man. KLATSKIN (1956) has reported fatty liver and centrolobular necrosis, cirrhosis in animals poisoned by the administration of antimony and arsenic respectively. HOFFMAN et al. (1975) studied the effect of acute cadmium administration on the kidney of rat. Though much has been done on the effect of heavy metals in different animals, only a few references are available on the effects of rare earth metals particularly uranium. Workers have occasionally studied the toxicity of a few rare metals for the hepatic tissue (CRESS 1961, POPPER AND SCHAFFNER 1957, SNYDER 1961). Other workers have observed the toxic effects of selenium and tellurium in different animals (CARAVAGGI et al. 1970, GLOVER 1970, SCHROEDER AND MITCHENER 1972) but the hepatic histopathological effects of uranium is almost untouched so far.

The present study deals with chronic hepatic toxicity caused by uranyl nitrate in albino rat.

MATERIALS AND METHODS

Male albino rats (ranging from 175 to 200 gms) in weight were divided into four groups, each including four animals. Animals of all the 4 groups were kept on standard pallet diet from Liver Brothers (India) Ltd. and water ad libitum. Group 1 animals were kept as normal controls feeding on the above diet. The animals

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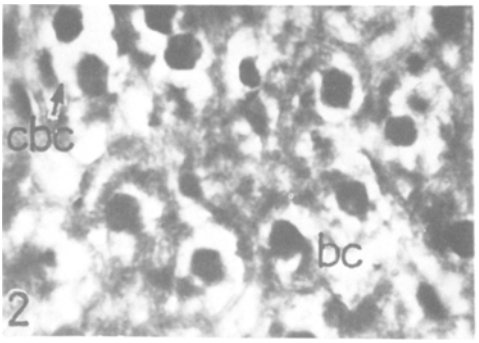
of remaining 3 groups were fed on 20 mg of uranyl nitrate mixed with their diet on alternate days. The animals from both control and experimental batches were sacrificed after 15, 19 and 27 days of the initial dose. The liver samples from the rats of all the groups were fixed in neutral formalin and paraffin sections of 5 to 7 μ thickness were studied for histopathological lesions. The structural changes at different intervals of treatment were compared with the normal control liver structure.

RESULTS

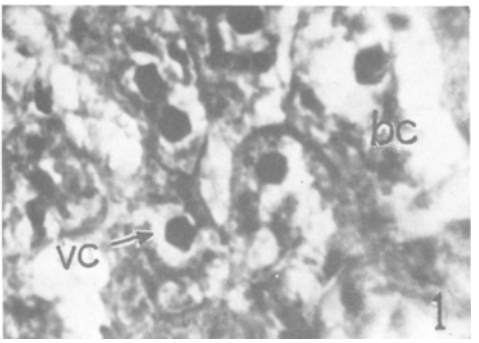
The prolonged treatment with uranyl nitrate resulted in chronic disarchitecture of the liver without any hepatocytic regeneration. After 15 days of uranyl treatment the rats showed a few changes in the liver architecture which were not extensive. Thus inspite of the occurrence of early mesenchymal lesions in the hepatocytes, the histology of the liver looked to be compact. Many hepatocytes were seen undergoing hydropic degeneration. The 'balloon cells' (hepatocytes under hydropic degeneration) had a characteristic appearance: round cells with clear cytoplasm and a dark nucleus. Though many of the balloon cells were rounded and uninucleated, others were binucleated and irregularly shaped showing the coalescing of two adjuscent balloon cells (Fig. 1). In some binucleated balloon cells, one nucleus was pycnotic.

In contrast to perilobular area of the liver the changes in the nuclei of hepatic cells were more evident in centrolobular zone. Though nuclei were non-pycnotic (except in some coalesced balloon cells) in most area they showed various degrees of enlargement in centrolobular hepatic cells (Fig. 2). In perilobular zone many hepatocytes showed vacuolization. Pycnosis of nuclei was seen more abundant in perilobular hepatic cells than those of centrolobular zone.

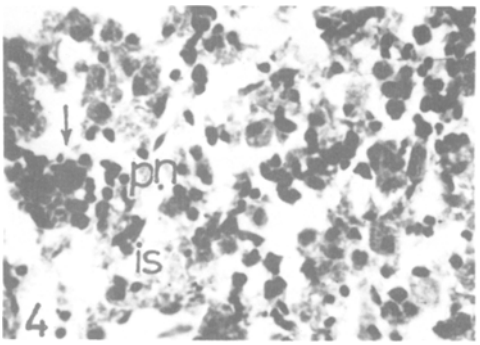
After 19 days uranyl treatment some drastic changes in the hepatic cellular architecture were visible. The balloon cells had disappeared in most of the areas of centrolobular and perilobular region (Figs. 3 & 4). In perilobular zone the nuclei in many cells underwent fragmentation and well defined nuclei were absent in these cells. In the centrolobular area most of the hepatic cells had lost their cell organization as their cell membrane was ruptured and the cellular contents were infiltered leading to submassive necrosis. The remaining scars of the infiltered cells were clearly visible. Many nuclei were pycnotic and others clumped at some places (Fig. 4).



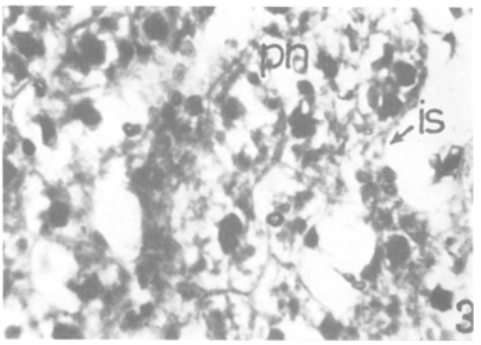
Centrolobular zone after 15 days treatment. X 480.



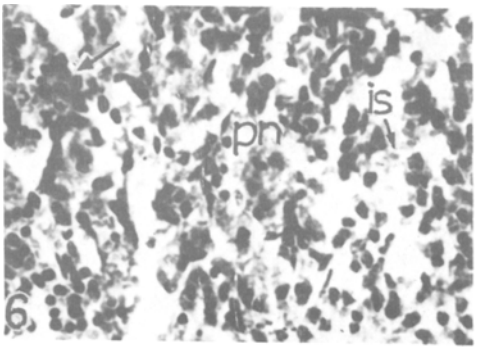
Perilobular zone after 15 days treatment. X 480.



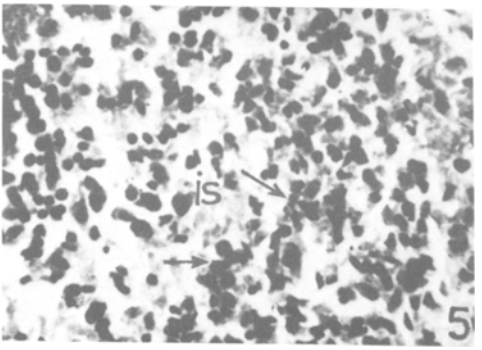
Centrolobular zone after 19 days treatment. X 120.



Perilobular zone after 19 days treatment. X 150.



Centrolobular zone after 27 days treatment. X 120.



Perilobular zone after 27 days treatment. X 120.

Figs. Showing the effect of uranyl nitrate on the liver of albino rat.

bc, balloon cells; cbc, coalasced binucleated balloon cells; is, infiltered scars; vc, vacuolated cells; pn, pycnotic nuclei.

In prolonged treatment with the toxin (after 27 days) the pathological lesions were more acute (Figs. 5 & 6). Complete cellular architecture of liver in both centrolobular and perilobular zones was severely distorted. The infilteration of cell contents was also observed in perilobular hepatic area. In both the parts of the liver the infiltered cell contents were adsorbed leaving nude nuclei which underwent clumping at certain loci. The clumping of the nuclei in centrolobular zone was more common where many nuclei were seen to be pycnotic (Figs. 5 & 6). No sign of hepatocytic regeneration was observed at any step of the experiment.

DISCUSSION

Uranyl nitrate produced significant changes in histological picture of liver which became more severe with duration of treatment. In produced degenerative changes including enlargement of liver cells and vacuolation in cytoplasm. However, in general, the perilobular area showed vacuolated cytoplasm and hypertrophy of hepatic cells. The centrolobular area was necrosed. The nuclei showed increase in size and in some cells the cell membrane was also disrupted. POPPER AND SCHAFFNER (1957) and SASTRY AND SHARMA (1977) reported similar histopathological changes in the liver of different animals treated with uranium salt and endrin, respectively. CHRISTIE AND LePAGE (1961) have observed enlargement of the size and variation in the diameter of the nuclei of hepatocytes of animals after feeding with carcinogenic aminoazo dyes. The enlargement of the size and variations in the diameter of the nucleus, particularly in the balloon cells, are supported by the findings of SCHMIDT (1961). Increase in the number of binucleated cells was also observed by OBERLING AND ROUILLER (1956) who reported such condition after the administration of CCl_4 and phosphorus, respectively. It is probable that one of the nuclei subsequently disintegrates in many hydropically degenerating balloon cells. Other workers (CHENO 1956, TANDON et al. 1975, SINGH et al. 1975, PATRIUA et al. 1975) have also noted almost similar alterations caused by different heavy metals in the structure of liver.

Our results suggest that uranyl nitrate is a toxic substance and it produces deleterious effect by interfering with energy metabolism, details of which need further exploration. Other heavy metals like cadmium, mercury and lead (VALLEE AND ULMER 1972) have also been shown to exert the toxic effects by interfering with energy metabolism. MOLBERT AND GUERRITORE (1957) have also assumed an internal suffocation of

the hepatic cells by the cessation of oxidative process. According to GOEL (1977) depletion of glycogen contents from the hepatic cells under the influence of toxins may be as one of the factors responsible for the occurrence of necrosis. MITCHELL et al. (1976) point out that it is now clear that biotrans formulation occurs in the liver which leads to the production of highly toxic metabolites, but that endogenous protective mechanism can alter the potential toxicity of these metabolities. The relative balance between these two events seems to be the key of certain type of hepatic injury. However, ZIMMERMAN (1976) pointed out that liver injury is not a single entity, but rather a variety of abnormal tissue responses and that their detection is intimately related to particular alterations concerned.

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