CADMIUM INDUCED CHANGES IN THE LIVER OF LANGURS
(*PRESBYTIS ENTELLUS—ENTELLUS DUFRESNE*)

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Summary: 1- Cadmium-induced hepatic disturbances in Langurs have been studied follwoing a single low dose administration of the salt ($CdCl_2$ 4 *mg/kg* s.c.). 2- Serum transaminases, cholesterol and liver glycogen levels were elevated. Alkaline phosphatase levels were in normal range. The blood sugar was at a low level. 3- Degranulation, vacuolization and distortion of the liver cells and lobules were conspicuous. 4- In conclusion this study would indicate that increased serum enzyme activity and increased plasma cholesterol levels are a manifestation of tissue damage. It would seem plausible to translate these observations in terms of similar infarcts occurring in man.

Key words : cadmium choride, exposure, transaminases, liver-infarction, serum cholesterol, liver glycogen, blood sugar

INTRODUCTION

The toxicity of cadmium to man has been documented for a decade by several investigators and known to have an acute response of severe nausea, salivation, vomiting, diarrhea. abdominal pains and myalgia (5). Bioeffects of cadmium in animals include various pathological processes including testicular tumors (16, 10, 6 and 7), renal dysfunction (2), hypertension (19, 20, 21) and accelerated atherosclerosis (14).

Cadmium is one of the potent metallic cancerigens (8) and affects the hematopoietic system in rat (1). Since the cadmium affects the vital organ system, the study was designed to ascertain whether any disturbance of liver function occurred on long term exposure to ascertain whether any disturbance of liver function occurred on long term exposure to cadmium salts. Thirty to fifty five days period was enough to provoke hepatic injury after a single low dose (4 *mg/kg*) administration of cadmium chloride, the preliminary results of the trials are reported here.

MATERIALS AND METHODS

Male adult langurs of different age groups captured around Jaipur (Rajasthan) were weighed, numbered and maintained in metallic cages measuring $2\frac{1}{2}/x\ 2\frac{1}{2}/x\ 3\frac{1}{2}/$. Muscular development large canines and the presence of well developed pinkish oedematous band—the sexual skin on the rump have been considered as characters of fully grown adult. The animals were fed with wheat chapatty (unleaved bread), banana, onion, carrot, potatoes and soaked Bengal gram and were provided with water *ad libitum*. Continuous veterinary supervision was maintained.

Cadmium chloride in a single small dose (4 *mg/kg*) was given to three langurs subcutaneously. On day 30 and 55, biopsies of the liver taken at surgery or at autopsy were fixed in

Bouin's fluid. The paraffin sectoins (6 μm) were prepared and stained with hematoxylin and eosin. Some of the liver biopsies were frozen and the glycogen and total cholesterol later determined (13, 15). Blood sugar levels were determined by the method of Mendel *et al.* (11).

The hepatic function was followed with determination of S.G.P.T., S.G.O.T. and serum alkline phosphatase activity (12 & 4).

The upper limits of values considered normal were as under:
Serun alkaline phosphatase — 6 Bodansky units,
Serum glutamic oxalo-acetic transaminase (S.G.O.T.) 40 units, and
Serum glutamic pyruvic transaminase (S.G.P.T.) 35 units.

RESULTS

Serum enzyme activities : In langurs treated with Cadmium Chloride, the serum transaminase levels were significantly increased ($P<0.01$, Table I), whereas the alkaline phosphatase level of 7.5 units were in norml range.

Cholesterol: Liver cholesterol concentrations in $CdCl_2$ treated langurs were higher than the normal values (Table I). Plasma cholesterol concentrations were also higher in $CdCl_2$ treated langurs ($CdCl_2$ treatment: 3.5 ± 0.2 *mg/ml*; control: 1.95 ± 0.2 *mg/ml*).

Liver glycogen and blood sugar: Liver glycogen was elevated after $CdCl_2$ administration, whereas a significant reduction in blood sugar was noticed ($P<0.01$, Table I).

TABLE I: Serum enzyme, cholesterol, blood sugar and liver glycogen in Langur (*Presbytis entellus entellus*), after a single dose (4 *mg/kg*) administration of cadmium chloride.

Treatment	*SGPT**	*SGOT*	*Serum** alkaline phosphatase*	*Cholesterol plasma (mg/100ml)*	*Cholesterol Liver mg/g*	*Glycogen Liver mg/g*	*Blood sugar mg%*
Control	26.5±7.1	36.0±3.5	7.4±0.5	46.8±4.2	2.1±0.8	1.04±0.2	120±13
$CdCl_2$ (¼ *mg/kg*) single dose s.c.	126±21†	190±19†	7.5±0.3	72.7±3.7†	2.87±0.2	1.30±0.3†	81±7†

†$P<0.01$ compared with controls
**μg of alkaline phosphorus/hour/mg of serum
*Values are means of six determinations ± Standard error

Histological preparations: The architecture was microscopically normal. There was no cirrhosis, cholangiolitis, or proliferation of bile ducts but fairly severe degranulation and vacuo-

lization of hepatocytoplasm was noticed. Distortion of liver cells and liver lobules was noticed. Signs of biliary canalicular dilations were evident (Fig. 1).

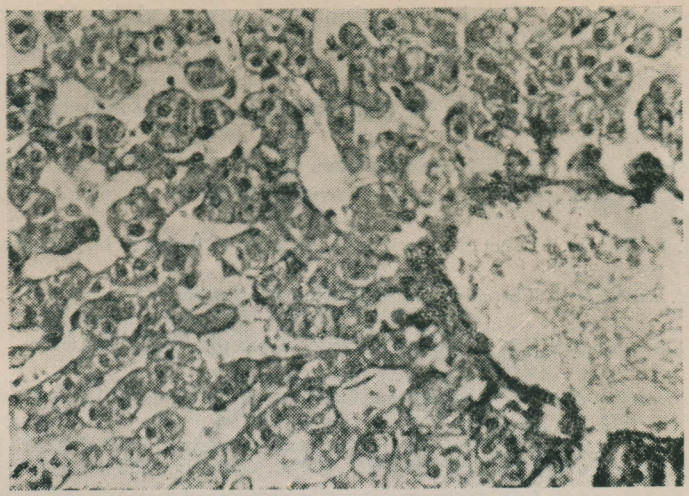

Fig. 1: Cadmium chloride treatment. Liver section showing enlarged atypical cells with bizarre arrangement.
160X, H.E.

DISCUSSION

Significant elevations of serum transaminase activity after 30—55 days of $CdCl_2$ injection (4 *mg/kg*) in langurs was of similar nature as reported in animals in several different injury states including radiation (18 and 17). The most plausible explanation of the rise in serum concentration of enzymes after $CdCl_2$ treatment is that cellular injury allows leakage of the enzymes into the blood stream. However, the alkaline phosphatase level were in normal range.

Increase of cholesterol levels following $CdCl_2$ administration was most markedly noticed in the liver and particularly in plasma of langurs. Increased cholesterol levels have also been reported in plasma and liver of rabbit (3) and dog (22) after whole body X-irradiation.

Moderate degree of fatty changes and other pathological findings in the Presbytis liver were in agreement with those of Parizek (16) and Meek (10) and were also reflected in elevated liver glycogen and reduced blood sugar levels.

In conclusion this study would indicate that increased serum enzyme activity and increased plasma cholesterol levels are a manifestation of tissue damage. Liver does contain relatively large quantities of S.G.O.T. and infarction gives high serum values. Moreover cadium accumulation is maximum in the liver between day 30 and 60 after last $CdCl_2$ injection (9). It would seem plausible to translate these observations in terms of similar infarcts occurring in man.

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