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REVERSIBLE AND IRREVERSIBLE CHANGES IN THE ATPASE DISTRIBUTION DURING HEXACHLOROCYCLOHEXANE-INDUCED LIVER LESIONS IN INBRED SWISS MICE

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The hexachlorocyclohexane (HCH) is a persistent type of organochlorine pesticide. It is widely used in India to control malaria vector and pests as an alternative to DDT. The levels of HCH residues have been reported to be quite high in the Oriental fat samples¹. Moreover, the distribution of several enzymes has been reported during HCH-induced liver tumour in inbred Swiss mice²⁻⁵. However, no attempt has yet been made to throw light on the reversibility of histopathological and histochemical changes in the HCH-induced liver lesions. The present study is therefore aimed at finding reversible and irreversible changes in ATPase distribution in the HCH-induced liver lesions.

Male, healthy 6-week-old, Swiss mice (15 in number) were exposed to technical grade HCH (containing 13.5% γ -isomer obtained from Hindustan Insecticides, New Delhi) in the diet at 500 ppm level for 4 months. Subsequently, the animals were kept on the normal diet for 10 months. The age and sex matched animals of control group were fed normal diet without HCH throughout the experiment. The animals of both the groups were killed by cervical dislocation and their livers were immediately dissected out and fixed in chilled 10% neutral formaldehyde solution for a brief period. The 10 μ m thick sections were cut on freezing microtome. The sections were briefly washed in cold distilled water and processed for the localization of ATPase. Both, Padykula and Herman's, and Wachstein and Meisel's techniques were used in the present investigation. Prescribed controls were also simultaneously employed.

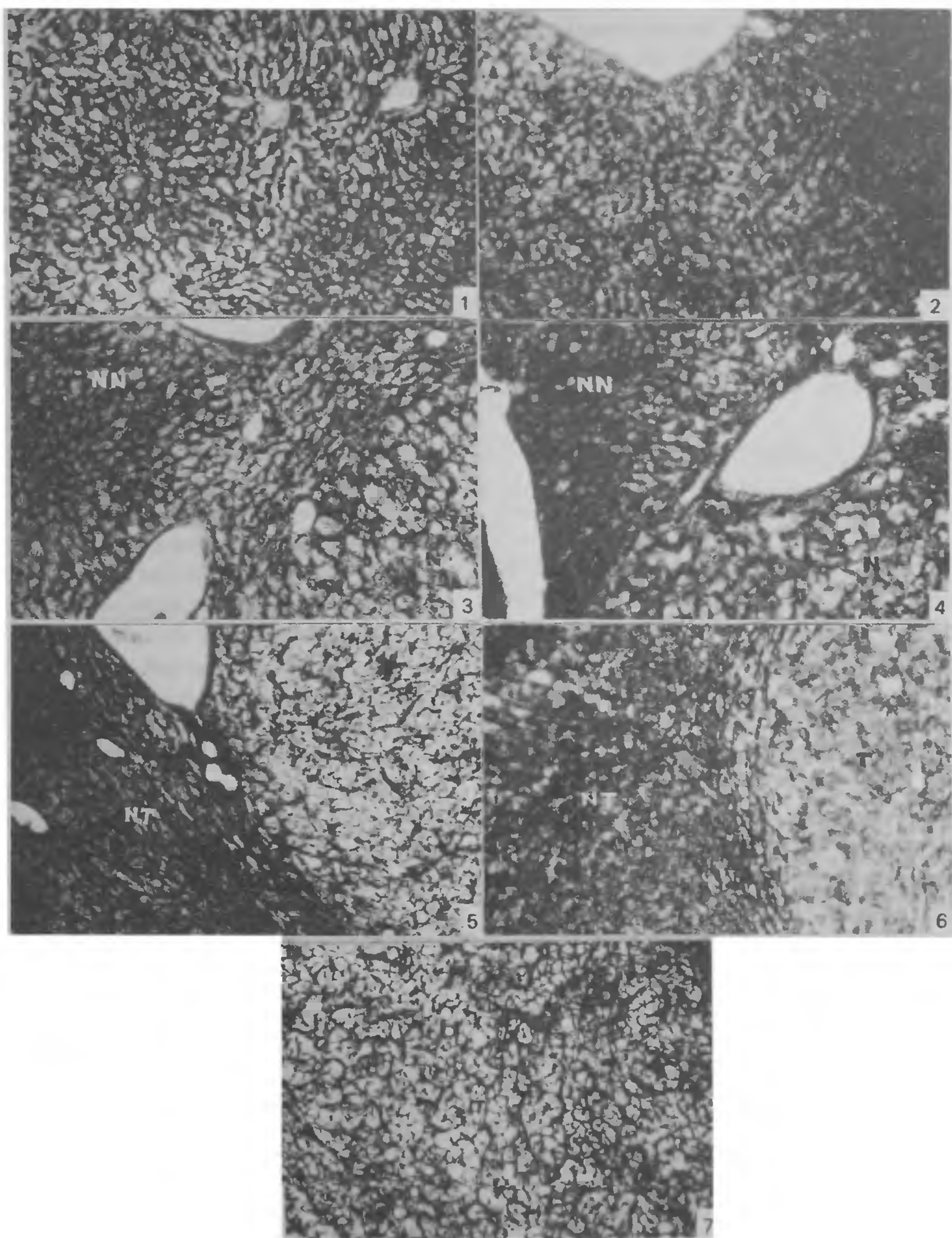
All the animals have shown the development of

the tumours and neoplastic nodules of the liver suggesting multifocal alteration in the liver of experimental animals. Histochemical preparations of the liver after 4 months of HCH exposure and 10 months discontinuation of HCH in diet revealed decline in ATPase activity in the tumour (figures 5, 6 and 7) as compared to nontumour areas (figures 5 and 6). The identical ATPase activity has been observed in the sinusoids and blood capillaries of normal (figures 1 and 2) and nontumour part of the liver (figures 5 and 6). Irrespective of the central or periportal areas, the ATPase activity in both the groups is uniformly spread over the entire area in normal (figures 1 and 2) and the nontumour part of the liver (figures 5 and 6). At the same time, cellular morphology in the nontumour part (figures 5 and 6) is almost similar to the control livers (figures 1 and 2).

Cells in the neoplastic areas reveal altered cellular morphology while ATPase activity in them is similar to the non-nodular part of the liver (figures 3 and 4). However, the tumours are very much deficient in the ATPase activity as compared to nontumour areas (figures 5 and 7). In the tumour, ATPase activity is mainly present on the plasma membrane.

The distribution of ATPase and morphology of the cells in nontumour, non-nodular and control liver is identical in the present study whereas continuous exposure of HCH in the previous study has revealed marked changes in the distribution of ATPase and morphology of nontumour and non-nodular cells³. Based on these two studies the following facts have come to the light. i) Alteration in the cell morphology and ATPase distribution in nontumour and non-nodular part of the liver as reported previously is perhaps the direct action of HCH; therefore, these changes are reversible and within homeostatic level. ii) The changes in the tumour are probably genetic and therefore are of permanent type and irreversible even if the HCH is withdrawn from the diet for sufficiently long time. iii) Four months of maximum tolerable dose of HCH is more than sufficient to irreversibly transform certain cells in the liver to induce cancer after 10 months. iv) The pattern of ATPase distribution in neoplastic nodule suggests only morphological changes in these cells. v) Both, Wachstein and Meisel's, and Padykula and Herman's techniques are suitable for ATPase localization but the former method gave more precise localization of ATPase.

In conclusion, it may be suggested that the changes in the nontumour and non-nodular part of



Figures 1-7. ($\times 48$) **1 and 2:** Distribution of ATPase in the liver of control animals (1. Wachstein and Meisel technique, 2. Padykula and Herman technique); **3 and 4.** Distribution of ATPase activity in nodular (N) and non-nodular (NN) parts of the liver (3. Wachstein and Meisel technique, 4. Padykula and Herman technique); **5 and 6.** ATPase activity in the tumour (T) and nontumour (NT) parts of the liver (5. Wachstein and Meisel technique, 6. Padykula and Herman technique); **7.** Localization of ATPase activity in the tumour (T) (Wachstein and Meisel technique).

the liver seems to be morphological and metabolic owing to the direct action of HCH, but reversible when HCH is withdrawn from the diet, whereas the

changes in neoplastic nodules are perhaps transitional and suggests both the possibilities i.e. regression or progression. Nevertheless, the changes

in tumours are probably of irreversible type and therefore genetic and beyond the homeostatic control of organisms.

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TORI LONGITUDINALES—A COMPENSATION FOR TRUE OPTIC CHIASMA

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The midbrain of fishes is characterized by the presence of the optic tectum. The right and the left optic tecta are connected to each other by the intertectal commissure. From the medial border of the tecta, into the mesencephalic ventricle, hang the tori longitudinales, which together with the valvula cerebelli assume a definite configuration at the level of tractus mesencephalo-cerebellaris posterior. Their configuration has been considered to be species-specific¹⁻⁴. The tori lie immediately above the posterior commissure in the rostral frontal sections; as the sections become caudal, the posterior commissure disappears and the tori can be identified either as distinctly hanging or abutting against the stratum griseum periventriculare or sandwiched between the two optic tecta. The tori longitudinales

are connected to each other through the torus commissure. The fibres of the intertectal commissure pass through and freely intermingle with the fibres of the tori in the rostral sections, but in the somewhat caudal sections the fibres of the optic tectum (intertectal commissure) and the torus (torus commissure) can be seen as distinct entities. Each torus consists of darkly stained neurons concentrated more towards the periphery than the centre. The neurons of the stratum griseum periventriculare contribute to the mass of the tori (figure 1).

Hubel and Wiesel⁵ reported that in mammals, the geniculate nucleus receives inputs from both the eyes, dividing the composite visual field of the two eyes into left and right. Geniculate nucleus, thus, functions as a two-way station, segregating the inputs from the two eyes. Axons of the cells in the geniculates make contact with the primary visual cortex located in the back of the cerebral hemisphere. They discovered that it is at the level of the primary cortex that inputs from the geniculates are integrated to generate the elements necessary for the perception of form and movement of objects.

The fish brain has a distinct nucleus geniculatum surrounded by the optic nerve fibres. It plays an important role in the visual orientation. Since the true optic chiasma is absent in bony fishes—there is a complete crossing over of the nerves i.e. the left eye connecting to the right half of the brain and vice versa—the presence of the tori thus assumes importance.

It appears that the tecta supply the major input to the tori. The neurons of the tori form synapses and



Figure 1. Sagittal section through the mesencephalon of *Glossogobius giuris* (Ham). ITC = Intertectal commissure; TC = Torus commissure; TL = torus longitudinalis; STGP = stratum griseum periventriculare.