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Letter to the Editor

Increase in Liver Cell Nuclear Size After Chronic Cadmium Treatment

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Although nuclear volume and ploidy degree are not always parallel to each other, it has been shown that in liver a fairly high correlation exists (Carriere 1969, Brodsky and Uryvaeva 1977) and cytoplasmic volume also increases with increasing ploidy. Polyploidy means that cells contain a doubling or a multiple of the normal diploid chromosome number. It occurs in different organs and tissues of many animals (Carriere 1979) and there is a ploidy increase with age (Swartz 1956). Certain toxic substances cause an increase in ploidy (Gerhard et al 1972, Belyaeva et al 1974, Gerzeli and Barni 1976). Ranek established an increase in ploidy after viral hepatitis. Morselt (1976) described an increase in the number of polyploid cells in liver-cirrhosis and various other liver diseases.

The aim of this study was to investigate if cadmium with its many toxic effects also increases the ploidy of the liver cell nuclei. Three months old Wistar rats (female) were injected 3 times a week subcutaneously between the scapulae with 0.5 mg/kg CdCl₂ in a 0.9% NaCl solution. The injections were given during a period of 29 weeks, a group of control animals was injected with an identical volume of saline. At the end of the 4th, 8th, 16th, 24th and 29th week the animals were killed by decapitation. Liver samples were fixed in Böhm's fixative, embedded in paraffin and sections of 5 µm were stained with Feulgen. For the collection of the karyomatric data, the nuclei were projected on a sheet of paper with the aid of a drawing prism and a 40 x objective. The final magnification on the drawing paper was 1500 x. The projected surface of the nuclei was measured with a planimeter and expressed in arbitrary units. From each liver section 200 systematically chosen nuclei were measured. As shown in Fig. 1 the liver sections of the cadmium treated animals contained a greater number of large nuclei as compared to the controls. These nuclei are lying further apart which indicates a larger cell volume. The

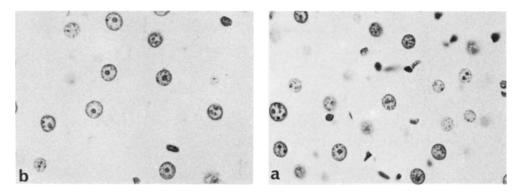
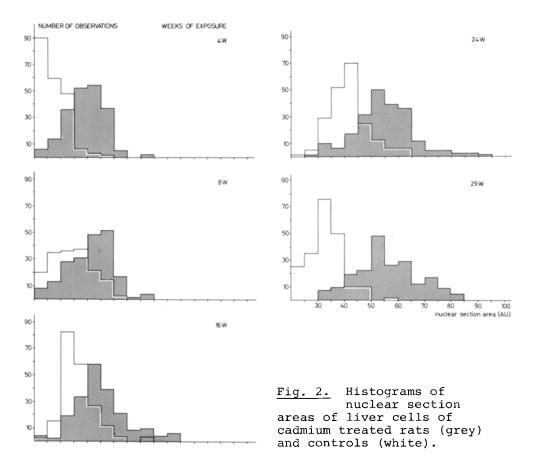


Fig. 1. Feulgen stained sections of the livers of rats that have been exposed to $CdCl_2$ (0.5 mg/kg bw) during 29 weeks (b), or to saline respectively (a). x 600.



results of the measurements of the nuclear areas of the livers of cadmium treated animals and controls are presented in Fig. 2. Using the Wilcoxon rank sum test no significant differences were observed between slides of animals of the same group, however, significant larger nuclear areas were found at the 4th, 8th, 16th, 24th and 29th week of cadmium administration. The histograms show a continuous increase in nuclear areas during cadmium treatment.

As mentioned before an increase in nuclear areas in the liver indicates an increase in ploidy degree, so chronic cadmium treatment seem to cause an increase in ploidy in rat liver. Till now the effect of an increase in ploidy on the function of the liver is unknown, however, an increase in ploidy has been described in different tissues and organs upon exposure to unfavourable conditions (Brodsky and Uryvaeva 1977).

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REFERENCES

- Belyaeva, N.N., Tsulaya, V.R., Marshak, T.L., Brodsky, V.Y. Effect of 1,2,3-trichloropropane on the ploidy of rat liver cells. Bull. Exp. Biol. (NY) 144, 78-81 (1974).
- Brodsky, V.Y., Uryvaeva, I.V. Cell polyploidy: its relation to tissue growth and function. Int. Rev. Cytol. 50, 275-332 (1977).
- Carriere, R. The growth of liver parenchymal nuclei and its endocrine regulation. Int. Rev. Cytol. 25, 201-277 (1969).
- Gerhard, H., Schultze, B., Maurer, W. Wirkung einer zweiten CCl₄ Intoxication auf die CCl₄ geschädigten Leber der Maus. Virchows Arch. Abt B. Zellpath 10, 184-199 (1972).
- Gerzeli, G., Barni, S. Changes in liver cells ploidy of young rats following isoprenaline treatment. Cell Tissue Kinet. 9, 267-272 (1976).
- Morselt, A.F.W., Freni, S.C., Ortlep, F.M. Quantitative histological aspects of liver cirrhosis. Beitr. Path. 159, 195-206 (1976).
- Ranek, L., Jensen, S.T., Keiding, N. Karyometry of liver biopsies in virus hepatitis. Acta path. microbiol. scand. A83, 477-486 (1975).
- Swartz, F.J. The development in the human liver of multiple desoxyribose nucleic acid (DNA) classes and their relationship to the age of the individual. Chromosoma 8, 53-72 (1956).

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