HISTOLOGICAL STUDIES ON THE LIVER IN THE CCL4 INTOXICATED FROG (*Rana ridibunda*)

Alina PĂUNESCU[1], Cristina PONEPAL[1] & Octavian DRĂGHICI[1]

[1]University of Pitesti

Abstract. The experimental model of the tetrachloride intoxication in the frog was used in order to study, at the histological level, the lesions of the hepatocytes and of hepatic sinusoid cells, caused by this toxic. After the treatment, a slight accumulation of the fibrous structures of collagen was noted, accompanied by accumulation of lipofuscine in the Kuppfer cells, slight structural disorganisation and enlargement of sinusoidal capillaries.

INTRODUCTION

The carbon tetrachloride is frequently used as a model for hepatotoxicity, although it becomes hepatotoxic due to professional exposure rather than to pollution exposure. Experimental intoxication with CCl4 still represents a classical model for the comparative study of action in various other chemicals known for their hepatotoxic influence. Despite an abundant information on this subject, the complexity of modifications, which occur as result of such intoxication, was elucidated only in recent years.

In this paper we present the results of studies carried out in order to complete the known data and to extend the knowledge about the modifications of liver microarchitecture and the cellular lesions determined by experimental CCl4 intoxication in the frog.

MATERIAL AND METHODS

Animals, Treatment. The frogs (*Rana ridibunda*) were captured from the bordering lakes of Pitesti. The animals were kept in water tanks filled with running water, under unfeding conditions. 18 male and female frogs, with the weight to 50 ± 5g, received by intraperitoneally (ip) way, 4 injections of 0,2ml CCl4 10%/100g, during a lapse of 2 weeks.

Sacrification. The animals were sacrificed at the end of the treatment, and then **at** 7, 14 and 21 days after the inoculations ceased.

Histology. Liver pieces were fixed 4% buffered formaline and processed for the paraffin embedding, following the standard methods. Histological sections of 5 μm were stained with hemalaum-eosin (HE).

RESULTS AND DISCUSSION

The hepatocytes in advanced stage of necrosis (1) presented an eosinophil retracted cytoplasm and the nucleus in the karyorexis or karyolysis type of death. The necrosed hepatocytes were invaded by numerous neutrophil granulocytes which infiltrated the parenchyma leading to the lysis of the cells(4).

Hepatic sinusoids presented a narrow lumen. An enlargement of the Disse interspaces was also observed (2). The central veins were enlarged and fibrosed. The portal structures formed of terminal portal veins, biliary ducts and arterioles were slightly fibrosed (3). The perisinusoidal fibrosis was more intense around the granulomatous areas. The deposition of collagen is blocking the free access of the blood flow, determining a deficient perfusion of the hepatocytes.

The perisinusoidal stellate cells with their characteristic long cellular body synthesised and deposited reduced amounts of collagen.

As a consequence of the hepatocytes necrosis, with an active hepatic regeneration, the typical shape of the hepatic lobes changed, appearing more shortened and rounded, comparatively to the controls.

The Kupffer cells appeared with lipofuscine accumulation within the cytoplasm (5,6), this being a yellow-golden granular pigment, of lisosomal origin, frequently observed at the biliar pole of the hepatocytes.

BIBLIOGRAPHY

Desmet, V.J.: Morphology of cell damage and inflammatory reaction in Molecular and Cell Biology of Liver Pathogenesis, eds. A.M. Gressner, G. Ramadoni, Proc. Internat. Wien, New York, 350-352, 1992.

Desmet V.J., R. De Vos: Cell death and cell necrosis in Mechanism of Hepatocyte Injury and Death, eds. D. Keppler, H. Popper, L. Bianchi, W. Reuter, Proc. 38 Falk Symp., 3-5 Oct. 1983, Kluwer Acad. Publisher, 11-30.

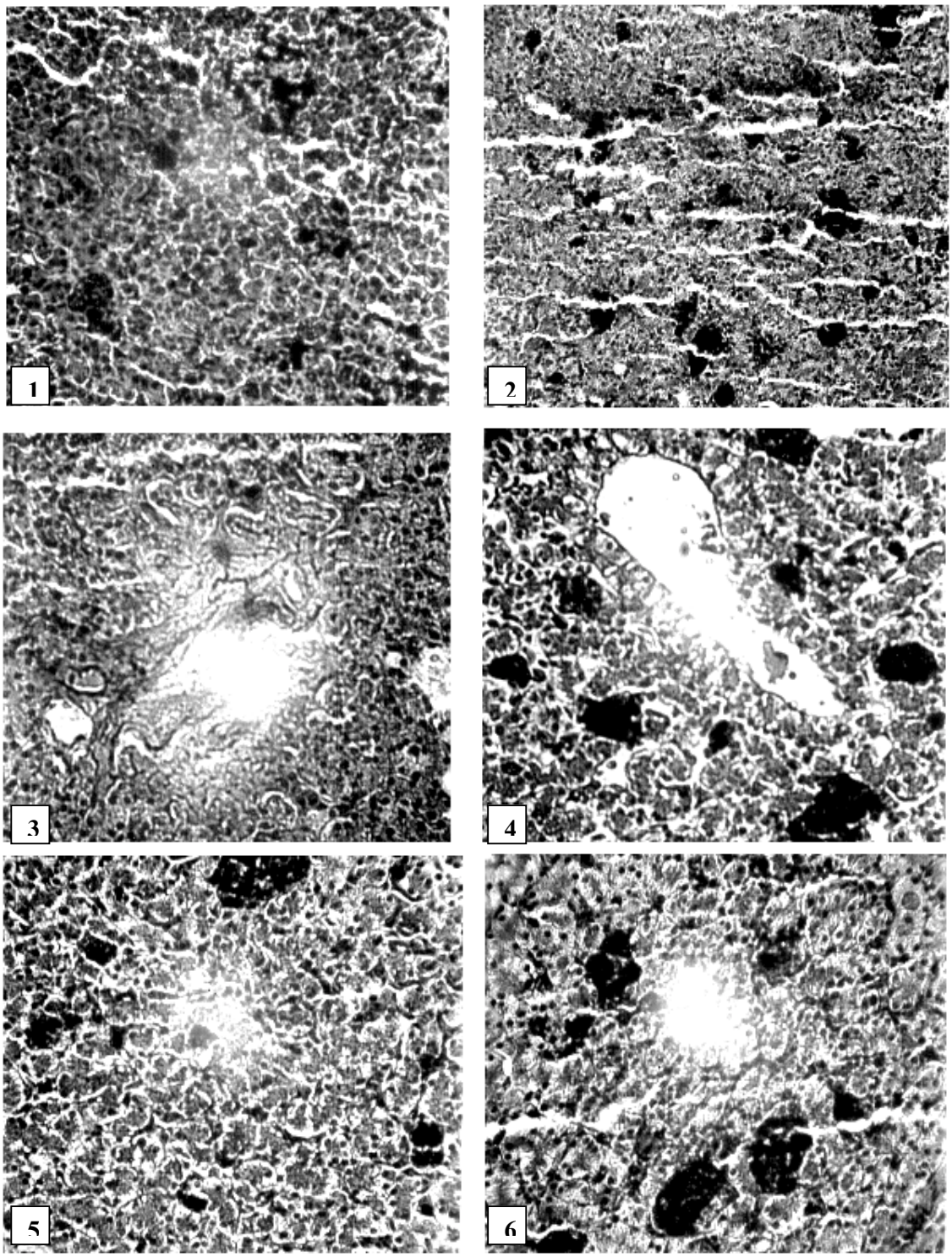
Geerts A., Bouwens L., Wisse E.: Ultrastructure and function of hepatic fatstoring and pits cells, J. Electron Microscopy Technique, 14, 247-256, 1990.

LeBail, B., Bioulac-Sage P., Senuita R., Quinton A., Saric J., Balabaud C.: Fine structure of hepatic sinusoid and sinusoidal cells in disease, J. Electron Microscopy Technique, 14, 257-282, 1990.

Mihailovici M.S.: Interpretarea histopatologică a biopsiilor hepatice, Ed. Timpul 2002.

Slater, T.F.: Activation of tetrachloride carbon: chemical principles and biological significance. Free radicals, lipid peroxidation and cancer. – New York, London, San Francisco, Academic Press, 1982.

Zamfir, G.: Efectele unor poluanţi şi prevenirea lor. – Bucureşti, Ed. Academei R.S.R., 1983.



1- necrosed hepatocytes (HE).; 2- enlargement of the Disse interspaces (HE); 3- fibrosis (HE); 4-periporthal necrosis (HE); 5, 6- Kupffer cells with lipofuscine accumulation (HE).