illustrates the early stages of arteriosclerosis which are also characteristic for other types of sclerosis of the vascular wall.

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Changes in the Blood-Brain Barrier in Experimental Cirrhosis of the Liver

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Light and electron microscopic studies on Wistar rats with experimental cirrhosis produced by tetrachloromethane demonstrate strongly marked changes in the blood-brain barrier, particularly in capillaries and vascular pedicles of astrocytes. It is pointed out that destabilization of the blood-brain barrier favors the transfer of cerebral toxins and other metabolic poisons across this barrier.

Key Words: *blood-brain barrier; experimental cirrhosis*

The state of the blood-brain barrier (BBB) is of great importance for the functioning of the nervous system and of the body as a whole. The BBB is thought to be composed of perivascular processes and capillaries that include the endothelium and the basement membrane with pericytes and mast cells closely associated with the latter [9]. It has been suggested that pericytes may be involved in providing what is called "motor innervation" of the capillaries and in the transfer by them of information on alterations in the metabolic environment; as a result, the endothelial cells of brain capillaries begin responding to biologically active substances such as histamine, serotonin, and others [13]. According to some authorities, pericytes can also produce an intermediate substance and perform a barrier function by exhibiting phagocytic activity [8].

It has been stated recently that the BBB should also be considered to include tissue basophils (mast cells) with organic features characteristic of the nervous system [5]. The perivascular processes of astrocytes are believed to be responsible for as much as 85% of the control exercised

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over microcirculation in the brain [1,7]. Astrocytes not only provide support and transport of substances to neurocytes but also store for these cells the oxygen which they need so much, particularly under extremely adverse conditions. The latter conclusion was arrived at by studying responses of the brain to hypoxia in animals [5]. In addition, astrocytes possibly perform a protective function (even through phagocytosis) and may also play a role in the maintenance of close contacts in the endothelium [5]. BBB structures may be said to include the capillary endothelium, basement membrane, mast cells, and perivascular pedicles of astrocytes. Our interest in the state of the BBB was stimulated by numerous studies (including our own), carried out for the most part at the light microscope level, which demonstrated alterations in the microcirculatory bed of patients with chronic liver disease. In the work reported here we examined the BBB in rats with liver cirrhosis using both light and electron microscopy.

MATERIALS AND METHODS

A total of 30 female Wistar rats weighing 150-200 g were used. Experimental cirrhosis was produced by administration of tetrachloromethane, which is the simplest and most commonly employed method of inducing this disease [2-4,6,10-12,14,15]. The animals received tetrachloromethane *per os* in a dose of 0.2 ml/100 g body weight on alternate days. This dosing schedule led to acute hepatitis after 2 weeks, to chronic hepatitis after 3 months, and to cirrhosis in 6 months. Thereafter, the rats were decapitated under ether anesthesia and their brains and livers were removed to be examined with light and electron microscopy. For light microscopy, histological preparations were stained with hematoxylin-eosin and by Nissl's and van Gieson's methods; an Opton (Germany) electron microscope was used for electron microscopic examinations.

RESULTS

The cirrhosis was characterized by connective tissue growth in the septa and lobules, necrotic changes in hepatocytes, and the presence of cellular infiltrates in connective tissue septa and of fat droplets.

It should be noted that changes in the liver preceded those in the brain, and the vascular and parenchymal changes observed in the brain tissues could therefore be regarded as secondary.

The histological changes revealed by light microscopy were characterized primarily by edema. Intertissue edema was most conspicuous near ves-

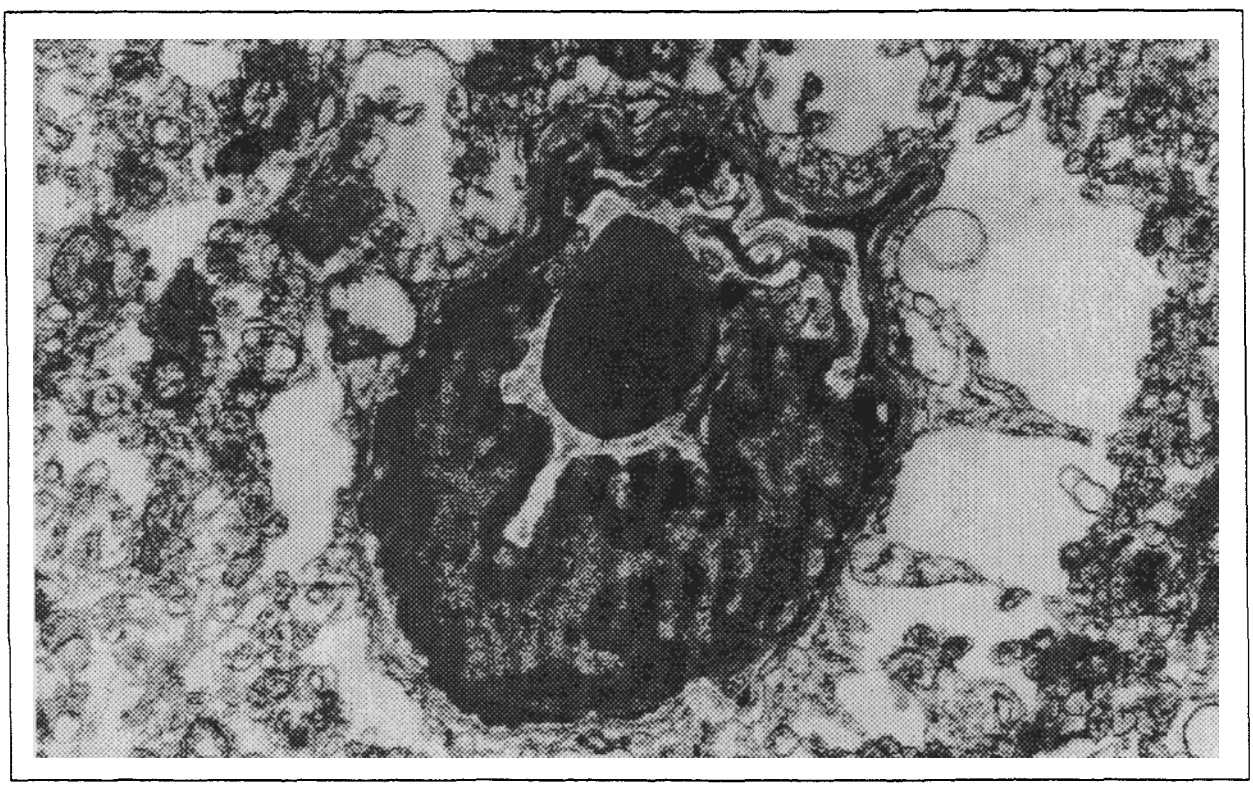

Fig. 1. Electron micrograph of cerebellar tissue from a rat with cirrhosis, showing marked pericapillary edema and a greatly enlarged endothelial cell. ×25,000.

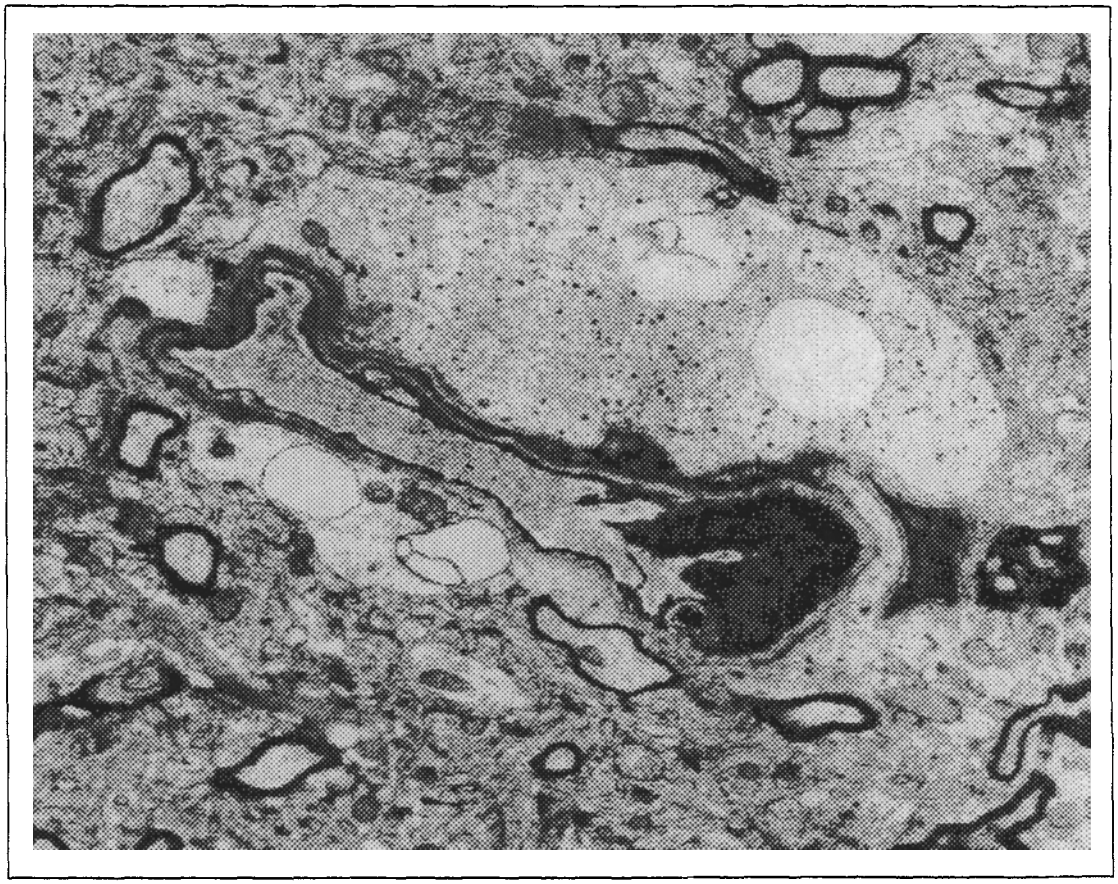

Fig. 2. Electron micrograph of frontal lobe tissue from a rat with cirrhosis, showing an intensely edematous pericapillary cell with a vacuole; the capillary is grossly deformed. ×10,125.

sels and in pericellular spaces. In addition, vessel walls had undergone deformation and destructive changes of such a magnitude that their integrity was impaired and small to large hemorrhagic areas were present around the vessels. In the region of the pons, signs of severe degeneration in reticular formation cells were observed, as were pericellular edema and broken fibers. The more conspicuous cellular changes seen in other brain regions included swelling, vacuolation, and the presence of glial cells with large nuclei and of shadow cells.

Electron microscopic studies, to which tissues of the frontal and occipital lobes, the upper part of the brainstem, and the cerebellum were submitted, revealed pericapillary edema, deformed and destroyed capillary walls, and the "sludge" phenomenon, i.e., both peri- and intravascular changes were observed. They included widened spaces between endothelial cells, edematous pericytes, edema between glial cells and capillaries, a thinned-out endothelial cell layer, and, in some preparations, enlarged endothelial cells. Because of the changes listed above, which are exemplified in Figs. 1 and 2, many capillaries appeared grossly deformed.

Apart from capillary changes, electron microscopy demonstrated edema and destruction of mitochondria in the vascular pedicles of astrocytes and a number of other changes in glial cells including dilated endoplasmic reticulum and irregularly arranged (clustered) ribosomes, desquamated membranes, destroyed and dead mitochondria in cell bodies, increased lysosome numbers, and edematous cytoplasm. The main findings in glial cell nuclei were a ruptured nuclear membrane, tortuous nuclear contours, an expanded perinuclear space, and intranuclear vacuoli.

Thus, as shown by our electron microscopic studies, rats with experimental cirrhosis develop structural changes in BBB components (capillary endothelium, basement membrane, vascular pedicles of astrocytes), which impair the protective function of the BBB so that foreign substances can enter the brain.

The destabilization of the BBB arising in chronic liver disease favors the transfer across this barrier of cerebral toxins and other metabolic poisons that are produced in the process of digestion and not completely detoxified by the liver leading to the development of hepatic encephalopathy.

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Effect of Autologous Sera on Mitogenic Stimulation of Peripheral Blood Lymphocytes of Mini-Pigs Chronically Intoxicated with Alcohol

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There are no statistically significant differences in the stimulation index for purified lymphocytes of control mini-pigs and mini-pigs with chronic alcohol intoxication. Autologous sera of control and experimental animals strongly suppress mitogen-induced blast transformation of lymphocytes without death of these cells. There are no statistically significant intergroup differences in the absolute number (per mm^3) of T lymphocytes in peripheral blood.

Key Words: *blast transformation; lymphocyte; autoserum; alcoholism*

At the present time, when characterizing the function of human and animal immunocompetent cells, more and more researchers are including in the test systems elements of the microenvironment of these cells; this is done not only to study the potential activity of various karyocytes represented by "washed" cells, but also to tackle this problem in respect of the whole organism [1,3]. This is logical, since, particularly in pathology, serum (plasma) contains a great number of diverse factors that may modulate the immune response [1,6,7,13,14]. The use of purified compounds is not always well-advised, and we think that the utilization of an individual's serum or plasma in a test system is the most appropriate (at least at the first step) when the functional parameters of immunocompetent cells are being assessed.

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