MORPHOLOGY AND PATHOMORPHOLOGY

Structural Changes in Dog Liver During Adaptation to High Altitude

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Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 123, No. 6, pp. 714-717, June, 1997
Original article submitted February 15, 1996

Vascular and tissue changes in the livers of dogs living on an altitude of 3200 m above sea level for various periods were studied by histological, morphometric, and electron-microscopic methods. Destructive changes were observed in hepatocytes after a month of exposure, which were due mainly to impaired hepatic microcirculation and increased from the center to the periphery of hepatic acinus. Ultrastructural changes occurred predominantly in the energy-producing and protein-synthesizing systems of hepatocytes.

Key Words: *adaptation; high altitude; liver*

The liver plays an important role in adaptation to various stressors, including hypoxia [3,9]. Liver cells are highly sensitive to oxygen deficiency [4,10], and this sensitivity depends on their location in the liver acinus [5,7,8,11]. Studies of the effects of high altitude on liver morphology revealed substantial structural changes in the parenchyma [1-3].

Our study is an attempt to evaluate and compare structural changes in the liver caused by different times of living on a high altitude, taking into consideration morphofunctional heterogeneity of hepatocytes.

MATERIALS AND METHODS

Livers from mongrel dogs (body weight 9-16 kg) from piedmont areas were examined after the animals had lived in mountains (altitude 3200 m above sea level) for 5-7, 15, or 30 days.

For quantitative evaluation of microcirculatory changes, the hepatic vascular bed was filled with black ink [6]. The dogs were euthanized with a lethal dose of hexenal. Specimens for histological and electron-microscopic examinations were prepared from the apical part of the quadrate lobe.

Histological preparations stained with hematoxylin-eosin and by the van Gieson methods were examined. Zonal morphometry of the vascular bed and tissue structures was carried out under a light microscope using an eyepiece micrometer. Zone I (periportal) of the acinus was defined as the area around a hepatic triad; zone III (perivenular), as the area around a central vein; and zone II (intermediary), as the area between zones I and III.

The results were statistically analyzed using special software. The significance of differences was evaluated by Student's t test.

RESULTS

Previously [1], we revealed a 4-fold increase of hepatic blood flow in dogs with compensatory adaptation and disadaptation in all zones of the hepatic acinus.

In this study, slightly loosened arterial walls with impregnation by plasma proteins in the triad, strongly dilated paravasal spaces containing protein precipitates, and diapedetic formed blood elements in the lumen (Fig. 1, *a*) were observed in dogs left on the altitude 3200 m for 5-7 days. These findings indicate

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0007-4888/97/0006-0619$18.00

TABLE 1. Vessel-Tissue Relations in Hepatic Acinus Zones of Dogs After Different Periods of Adaptation to High Altitude (3200 m Above Sea Level) (*M±m*)

Parameter	Control dogs	Days of exposure to high altitude		
		5-7	15	30
Number of functional sinusoids per vision field	38.7±2.1	47.5±2.9*	46.3±2.5*	43.7±1.9*
Mean sinusoid size, μ:				
zone I	9.7±0.3	13.7±0.8*	8.7±0.2*	7.6±0.2*
zone III	10.3±0.2	14.2±1.2*	7.1±0.1*	9.0±0.3*
Mean hepatocyte size, μ				
zone I	16.7±0.2	14.6±0.3*	14.9±0.2*	14.6±0.3*
zone III	14.6±0.2	18.0±0.3*	13.5±0.2*	13.8±0.3*

Note. *$p<0.05$ relative to the control group.

that the vascular bed of the liver was under great strain because of markedly increased blood flow.

In the periportal acinar zone, vascular plethora was observed: both the mean diameter and number of functioning sinusoids increased (Table 1). Electron microscopy revealed large mitochondria with clarified matrix and decreased number of cristae. The granular endoplasmic reticulum (GER) was almost unchanged, although its ribosomes appeared to be "slipping off." The number of glycogen granules decreased.

In the intermediary zone (zone II), trabecular structure of hepatocytes was preserved, but sinusoids and Disse's spaces were strongly dilated. Diapedetic and diffuse hemorrhages (Fig. 1, *b*) and the areas of necrosis and necrobiosis with accumulations of polymorphonuclear cells were observed. Degenerated or necrotic areas with dead cells replaced by lipid inclusions or connective tissue were seen at the periphery of this zone.

Electron microscopy of zone II revealed swollen mitochondria without any cristae and with a homogeneous matrix among unchanged mitochondria. Large elongated mitochondria (Fig. 1, *c*) with vacuolated cristae were seen; the GER tubules were dilated. Zones II and III contained increased numbers of lysosomes and of cells without glycogen granules, indicating almost complete depletion of glycogen.

Blood vessels of the perivenular zone (zone III) were plethoric and the sinusoids increased in size (Table 1), forming wide lacunae with the signs of erythrocyte stasis. Disintegration of hepatic trabeculae was observed. Hepatocytes were clarified and vacuolated. Stasis of formed blood elements in hepatic venules was combined with diffuse hemorrhages and accumulations of polymorphonuclear cells.

Thus, all three zones of the acinus showed considerable vascular changes which increased in degree from the center of the acinus.

After 30 days of exposure and adaptation to the high altitude, triads contained dilated paravasal spaces where connective tissue growth was observed, but triads with signs of hemorrhage disappeared. In zone I, sinusoids were of smaller diameter than on days 5-7, while the vascular bed remained congested and hepatocytes were of the same average size as before (Table 1).

On electron micrographs of zone I and the adjacent area of zone II large mitochondria with electron-dense matrices and well-defined cristae were seen. Many cells had mitochondria entwined with GER tubules (Fig. 1, *d*) containing numerous ribosomes. Glycogen granules were present in increased numbers. Thus, on day 30 on the high altitude, some intracellular structures appeared to have been restored, while others differed considerably from the control, indicating that cellular structures either had not completed their adaptation or were in a new, so-called high-altitude ("mountain") normal state.

In zone II, most of the above-mentioned changes were not observed on day 30. Although sinusoidal capillaries were not filled with blood uniformly, the number of functional capillaries remained high (Table 1). The occurrence of hemorrhages was very low. Hepatic trabeculae were radially oriented, and hepatocytes were clarified. Neither areas of destruction nor accumulations of polymorphonuclear cells were present.

The ultrastructure of zone II was generally similar to that described above for the periportal zone of the acinus.

At the periphery of zone II and in zone III, vascular changes were observed. They were large lacunae with the signs of erythrocyte stasis and trabeculae with the signs of disintegration.

Electron microscopic examination showed that the rate of recovery in zone III is lower than in zones I and II. Dilated GER tubules with a low

content of ribosomes and large mitochondria with homogenized matrix and partially vacuolated cristae were present, and the glycogen content was lower than in the control preparation.

Thus, after a month of exposure to high altitude, intracellular changes in the perivenular zone and adjacent part of the intermediary zone were more pronounced than elsewhere in the hepatic acinus.

From our findings it can be concluded that structural changes occurring in the liver at the altitude of 3200 m were phasic and showed interzonal differences in adaptational processes at the tissue and cellular levels. Structural changes occurring in all zones of hepatic acinus after a short period on high altitude (5-7 days) can be regarded as compensatory-adaptive. With continued exposure, the signs of structural recovery and morphological adaptation appeared in zone I and then expanded to the two zones of the acinus. The 30-day period of exposure appears to have been insufficiently long for the liver

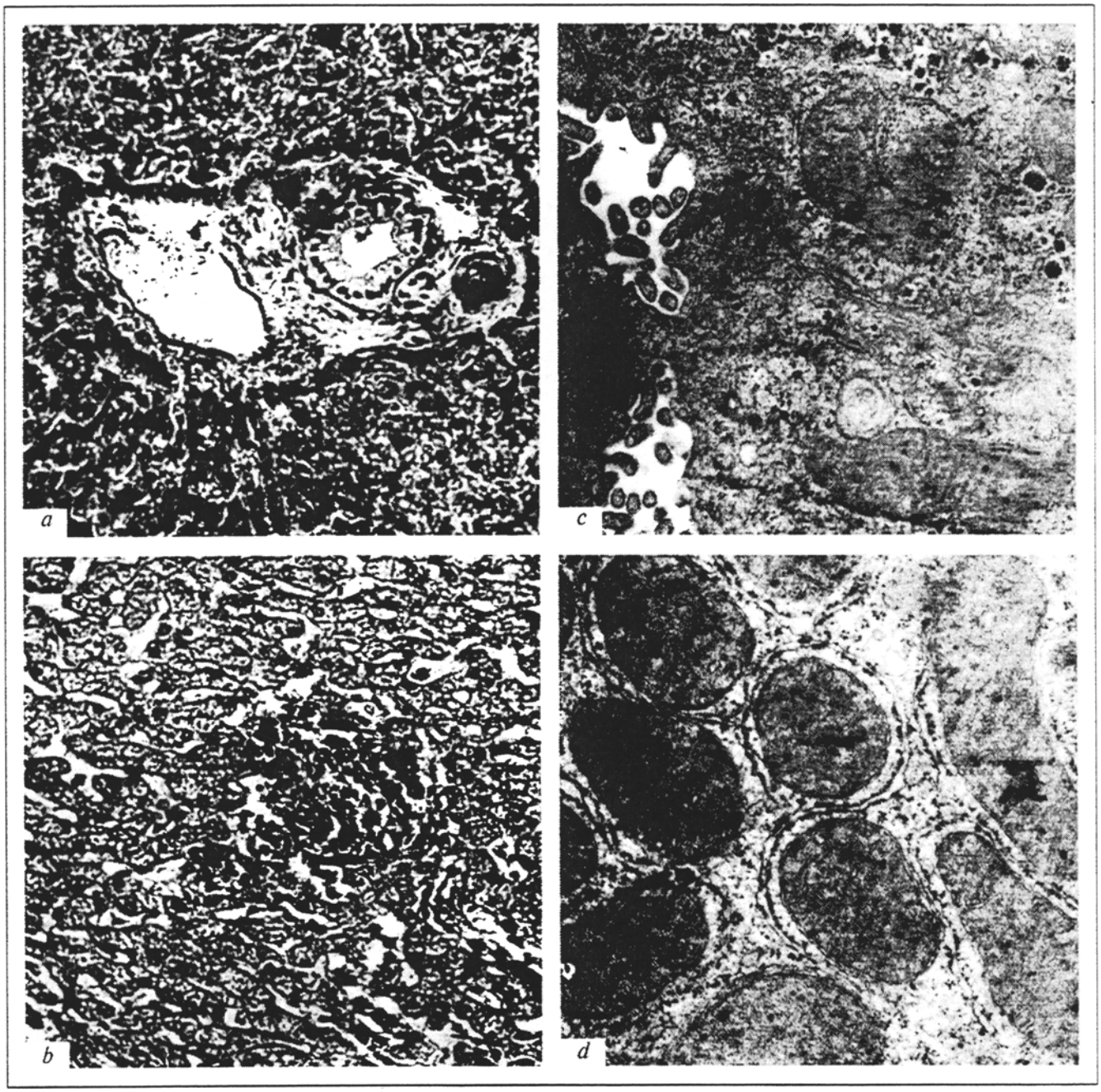

Fig. 1. Dog liver after 7 (*a*, *b*, and *c*) and 30 (*d*) days of exposure to a high altitude (3200 m above sea level). *a*) loosened adventitia of triad vessel, with evidence of erythrocyte diapedesis; *b*) intermediary zone with microhemorrhage; *c*) intermediary zone; *d*) periportal zone containing giant mitochondria with dense matrix. *a*, *b*) Hematoxylin-eosin staining, ×375; *c* and *d*) electron micrographs, ×10,000.

of dogs to undergo complete structural recovery, i.e., for the stabilization of adaptational changes.

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Effect of Laser Radiation Against the Background of Folliculin on the Capillaries of Rat Uterus

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Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 123, No. 6, pp. 718-720, June, 1997
Original article submitted April 10, 1996

Folliculin potentiates the effect of laser radiation on uteral capillaries. Laser radiation in combination with folliculin increases the activity of exchange surface enzymes by 21% and the total length of capillary bed by 11%.

Key Words: *capillaries; uterus; laser; folliculin*

It has been shown that capillaries of the uterus are highly sensitive to low-intensity laser radiation (LILR) [1,3,7], which stimulates transcapillary exchange, improving tissue trophism in degenerative-dystrophic and inflammatory disorders of female reproductive system. However, potential changes in the response of uteral capillaries to LILR against the background of drugs and, particularly, hormones has been often ignored.

Our objective was to examine the reaction of capillary bed (CB) of the uterus to LILR against the background of folliculin.

MATERIALS AND METHODS

Adult albino rats (n=40) weighing 250 g were used. The animals were divided into four equal groups. Group I rats were given a single intraperitoneal injection of 0.2 ml sterile olive oil. Group II rats received a single intramuscular injection of folliculin (0.2 ml 0.05% oil solution). Rats of both groups were decapitated 60 min after the injection. Group III rats were irradiated with a helium-neon laser (continuous mode, 632.8 nm, 0.76 mW/cm^2). Biologically active points on the skin (F_2 XII) associated with the regulatory function of the uterus [8] were irradiated for 1 and 5 min. Group IV rats were injected with folliculin (0.2 ml 0.05% oil solution), irradiated (1 and 5 min) one hour after the injection (the maximum effect of folliculin [4]), and decapitated.

In all groups, unfixed 25-μ cryostat sections were mounted on coverslips, air-dried for 15-20 min, and analyzed for the presence of Mg-activated ATPase [9]. Standard morphometry of capillaries [5] was carried out in three fields of view, separately on each of 6 sections and for each rat.

RESULTS

In control animals, the reaction product was observed on the capillaries located in endometrium and myometrium (Fig. 1, *a*). The density of the capillary net-

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0007-4888/97/0006-0622$18.00