bacterial content and a negligible decrease in the spleen bacterial content (compared with day 1 after infection) were observed on day 3. This difference can be attributed to the fact that this was the day on which antibodies appeared. By this time the antibodies can elicit their protective effect on the blood (opsonization, agglutination, or both). However, the spleen content of bacteria changed more slowly. In this organ the effect of antibodies is not pronounced on day 3 after infection. The low bacterial content in the spleen on day 1 after infection testifies to the fact that even in this early period the blood does not now, did not before contain considerable numbers of bacteria. Otherwise, even if the microorganisms had disappeared from the blood they would have accumulated in the spleen. Consequently, the influence of the antibodies manifests itself not in an accelerated clearance of bacteria from the blood, carried out via the spleen, but rather in prevention of the entry of bacteria into the blood, which is achieved by agglutination.

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Morphometric Analysis of Liver Acini in Endotoxicoses Caused by Peritonitis and Gangrene of the Leg

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Morphometric and information analysis is used to quantify the structural changes occurring in the liver and to reveal the specific features of damage to different zones of acini in peritonitis and gangrene of the leg.

Key Words: *liver acinus; peritonitis; gangrene; morphometry; entropy*

Death of patients with endotoxicoses caused by peritonitis, pancreatitis, and gangrene often results from liver failure [2,8,12]. Although there is quite a large body of evidence on the state of the liver, morphological studies are often descriptive and do not take into account regional heterogeneity of the acinus structure [3,7]. There is scant information regarding the specificities of hepatic injury depending on the etiology of endotoxicosis. Morphometry of liver tissue with subsequent information evaluation of the complexity of its structure in a specific pathology may be proposed as a prospective method [4,6].

In this paper we present a comparative morphometric description of liver acini in pronounced endotoxicoses caused by peritonitis and gangrene of

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TABLE 1. Morphometric Characterization of Liver Acini in Peritonitis and Gangrene of the Leg ($M \pm m$, arb. units)

Parameter	Zone of acinus	Control	Peritonitis	Gangrene
Area of hepatocyte nuclei (S_n)	I	19.19±1.40	12.31±1.61	10.63±1.42
	III	16.47±0.43	13.88±1.76*	10.38±1.71
Area of hepatocyte cytoplasm (S_c)	I	115.56±4.37	112.99±5.82*	114.49±6.01*
	III	109.16±4.04	93.70±5.48	84.86±4.63
Nucleus/cytoplasm ratio (S_n/S_c)	I	0.17±0.02	0.11±0.01	0.09±0.01
	III	0.15±0.01	0.15±0.02*	0.12±0.01
Area of hepatocytes (S_h)	I	134.75±1.71	125.30±3.02	125.12±3.14
	III	125.63±3.90	107.58±4.81	95.24±4.16
Area of sinusoids (S_s)	I	15.25±1.31	24.70±2.14	24.88±2.15
	III	24.37±1.20	42.42±4.11	54.76±5.02
Perimeter of sinusoids (P_s)	I	1.89±0.14	5.30±0.41	5.74±0.43
	III	2.46±0.21	9.65±0.83	10.04±0.91
Shape factor of sinusoids (P^2_s/S_s)	I	0.23±0.02	1.14±0.10	1.32±0.11
	III	0.25±0.02	2.20±0.21	1.84±0.19
Optical density of hepatocyte nuclei	I	0.305±0.027	0.222±0.018	0.222±0.017
	III	0.301±0.024	0.264±0.019*	0.259±0.019
Optical density of hepatocyte cytoplasm	I	0.150±0.013	0.124±0.009*	0.102±0.008
	III	0.168±0.014	0.152±0.012*	0.139±0.010*

Note. All values, except those indicated with an asterisk, are significantly different from the control ($p<0.05$).

the leg (integral estimates of these pathologies were obtained with the use of information characteristics).

MATERIALS AND METHODS

Autopsy material was obtained from 17 patients aged 52-78 years with signs of liver failure (hypoalbuminemia, hyperbilirubinemia, elevated activity of specific enzymes). Seven patients died of peritonitis and 10 died due to gangrene of the leg. Five forensic medicine autopsies served as the control (3 cases of sudden death and 2 cases of trauma incompatible with life). Autopsy was performed 45-90 min after death. Paraffin sections were stained with hematoxylin and eosin. The areas occupied by the nuclei and cytoplasm of hepatocytes in zones I and III of the liver acini as well as the area and perimeter of the sinusoid vessels were measured using a Microvideomat image analyzer (Opton, Germany). On the basis of these measurements the nucleus-cytoplasm ratio for hepatocytes and shape factor for sinusoid vessels were calculated. Informational entropy (H), relative entropy (h), redundancy (R), and organization (O) were calculated from conventional formulas [1]:

$$H = \sum_{i=1}^{m} p_i \cdot \log_2 p_i; \quad h = H/H_{max};$$
$$R = (1 - H/H_{max}) \cdot 100\% = (1 - h) \cdot 100\%;$$
$$O = H_{max} - H,$$

where H_{max} is the maximum entropy of the system, equal to 1.585. Equivocation (D), a parameter employed as a quantitative criterion of the structural disorganization of a system, was calculated from the following formula:

$$D = R_{контр} - R_{патол} = \frac{H_{патол} - H_{контр}}{H_{max}}$$

RESULTS

Microscopic studies of control sections revealed minor heterogeneous plethora of sinusoids, moderately pronounced granular dystrophy, and occasional monocellular necroses in the perivenular zones of the acinus. In the groups of patients who had exhibited pronounced phenomenon of intoxication due to peritonitis or gangrene we failed to reveal any pathognomic indications or significant differences between them. There were dilatation and plethora of portal vessels and sinusoids with aggregated erythrocytes and microthromboses as well as dilatation of the Disse's area around the sinuses often containing formed elements of the blood. Dystrophic alterations of hepatocytes occurred in the perivenular and intermediate zones, even including the formation of triangular and periacinar necroses. More informative results were obtained in morphometric studies (Table 1). In the control group, the relative area occupied by hepatocytes was greater in zone I, whereas in zone III the area and perimeter of vessels were greater, which confirms the structural heterogeneity of liver

acini [5,11]. These parameters were significantly different in patients with liver failure caused by endotoxicosis. In peritonitis the area and perimeter of sinusoid vessels increased 62% ($p<0.05$) in zone I and 74.1% ($p<0.05$) in zone III; in gangrene of the leg these values were 63.1 and 124.7% ($p<0.05$), respectively, compared with the control group. The shape factor of sinusoids increased due to a relatively great increase in the perimeter (3.4- and 3.6-fold in the acinus, $p<0.01$). In peritonitis it was 5-fold higher ($p<0.01$) in the periportal and 8.8-fold higher ($p<0.01$) in the perivenular areas; in gangrene of the leg it was 5.7- and 7.4-fold higher ($p<0.01$), respectively, which may be regarded as an adaptive mechanism aimed at enlarging the surface of the tissue-blood barrier during the development of circulatory hypoxia. The decrease in the area occupied by hepatocytes observed in both groups was more pronounced in the perivenular (centrolobular) areas of the acini, where cell necrosis predominated. The reduction in the relative area of parenchyma resulted from a decrease in the area of both cytoplasm and nucleus. The decrease in the cytoplasm area was more pronounced in zone III (14.4 and 24.2% in patients with peritonitis and gangrene, respectively), and the decrease in the area of nuclei was greater in zone I (35.9 and 44.6%, respectively, $p<0.01$). As a result, in zone I the nucleus-cytoplasm ratio for hepatocytes decreased 35.3% ($p<0.05$) in patients with peritonitis and 47.1% ($p<0.05$) in patients with gangrene of the leg, and in zone III it decreased only in the gangrene group (20.0%, $p<0.05$).

The tinctorial properties of liver cells are altered in pronounced endotoxicoses. In peritonitis and gangrene the optical density of hepatocyte nuclei and cytoplasm decreases, the decrease being more pronounced in periportal cells.

Information characteristics enable one to compare the changes in liver acini using integral criteria. In the control group, higher values of entropy and lower values of redundancy and organization were obtained for the perivenular as than for the periportal areas, indicating a greater degree of disorder and lower degree of reliability of the hepatocyte system in zone III of the acinus. The development of peritonitis and gangrene are generally accompanied by an increase in the entropu, relative entropy, and equivocation and by a decrease in organization. The observed decrease in redundancy testifies to the development of pronounced pathological processes in a system [1]. In both groups more pronounced deviations (to almost the same extent) from the control values, particularly in the case of equivocation, occurred in zone III, where dystrophic and necrotic alterations of hepatocytes predominated. Such a localization of the damage was caused by an impaired blood supply to the perivenular cells, particularly for the development of circulatory hypoxia. Comparison of information characteristics of zone I shows its greater structural disorganization in patients with peritonitis, which may be explained by the specific features of this pathology. First, in this case the liver is the first barrier for toxins arriving from the abdominal cavity via the portal vein. Second, in contrast to the case with gangrene of the leg, repeated influxes of microorganisms (particularly Gram-negative bacteria and their endotoxins that directly act on the hepatocytes and sinusoidal cells) into the bloodstream become more important [9,10].

Thus, the use of information analysis offers an integral evaluation of morphometric parameters and reveals the specific features of damage to the different zones of the acinus in peritonitis and gangrene of the leg.

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TABLE 2. Information Characteristics of Acini in Peritonitis and Gangrene of the Leg

Parameter	Zone of acinus	Control	Peritonitis	Gangrene
H, bits	I	0.9710	1.0325	0.9979
	III	1.0743	1.2574	1.2627
h	I	0.613	0.651	0.630
	III	0.678	0.793	0.797
R, %	I	38.7	34.9	37.0
	III	32.2	20.7	20.3
O, bits	I	0.6140	0.5525	0.5871
	III	0.5107	0.3276	0.3223
D, %	I	0	3.8	1.7
	III	0	11.5	11.9

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Protective Hepatotropic Effect of Preparations from Mytilidae and Ginseng in Animals Given Dioctyl Phthalate

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It is shown that in a group of animals given dioctyl phthalate alone antipyrine metabolism is enhanced (the urine content of its metabolites rises), and the histological structure of the liver is altered by the end of the experiment: the plasmalemma membranes, the granular endoplasmic reticulum, and mitochondria are destroyed, and fat deposits are observed in the disrupted zones of the mitochondria. In animals given dioctyl phthalate and adaptogens simultaneously antipyrine metabolism normalizes, and the morphological structure of the liver changes slightly, although it does not normalize.

Key Words: *dioctyl phthalate; toxic hepatitis; cytochrome P-450; adaptogens*

Xenobiotics and drugs are metabolized in the liver by the multienzyme complex of cytochrome P-450. The functions of individual enzymes of this system have now been defined more clearly. It has been shown that reactions of antipyrine metabolism are catalyzed by 3 isoforms of cytochrome P-450 [1] (but predominantly by P-450 IAI) and amidopyrine metabolism by P-450 IIBI [3]. Some low-molecular weight antibiotics (benzene, styrene, chlorinated carbohydrates, vinylchloride, and vinylbromide) are metabolized by the isoenzyme P-450 IIEI [9]. Localization of some forms of the cytochrome in the hepatic lobule has been determined by immune assay with special antibody kits. For instance, cytochrome P-450 IA is predominantly localized in the centrilobular zone and is absent in the periportal areas, while P-450 IIIA is heterogenously distributed over the acinus, and P-450 IIB and P-450 IIC9 are homogenously distributed over the acinus [14]. These findings indicate that local lesions of the liver can be caused by active metabolites of xenobiotics. The activity of cytochrome P-450-dependent enzymes is altered under the influence of xenobiotics, which in turn affects their toxicity resulting from the action

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