These experiments thus revealed differences in the response of adrenergic nerves of different organs to the action of difril and odifaline. Denudation of the catecholamine depots in the adrenergic fibers and organs with direct, indirect, and mixed innervation, and also in blood vessels, followed a different course. These results suggest that adrenergic nerves in organs and tissues are heterogeneous. Furthermore, since the most intensive and prolonged denudation of the endogenous catecholamine reserves was observed in the adrenergic nerves of the veins, by contrast with arteries, it can be concluded that a definite role in the changes arising in the circulatory system under the influence of difril and odifaline and in the therapeutic coronary dilator and hypotensive effect of these drugs, is played by their effect on veins.

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EFFECT OF ETHIMIZOLE ON PERMEABILITY OF THE BLOOD–CELL BARRIER IN CARBON TETRACHLORIDE-POISONING-INDUCED HEPATITIS

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Acute and chronic hepatitis are among the more important forms of liver disease in medical practice [2, 8, 9]. In experimental hepatitis changes arising in the parenchyma and blood vessels of the liver closely resemble those observed in man in the active phase of chronic hepatitis [4].

Stabilization of lysosomal membranes is disturbed in the hepatocytes and Kupffer cells of rats with experimental hepatitis, and this is associated with changes in the activity of lysosomal enzymes [5].

The object of the present investigation was to study the effect of ethimizole* on permeability of the blood–cell barrier of the internal organs in experimental hepatitis due to CCl_4 poisoning.

EXPERIMENTAL METHOD

Ethimizole was injected intramuscularly into the experimental animals twice a day as a 0.3% solution in a dose of 0.3 mg/kg body weight for 7 days [1, 3, 6].

*1-Ethylimidazole-4,5-dicarboxylic acid-bis-methylamide.

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TABLE 1. Effect of Ethimizole on Permeability of Tissue–Blood Barrier of the Liver and Other Organs in Experimental Hepatitis (M ± m)

Organ	Intact animals	Experimental hepatitis	Ethimizole	Experimental hepatitis + ethimizole
Heart				
left ventricle	249,1±19,6	459,6±39,9*	245,0±22,9	275,5±12,8*
right ventricle	233,6±19,6	454,0±44,6*	236,7±16,3	237,74±16,9*
Ventricular septum	257,2±20,9	420,3±42,0*	228,8±19,3	251,7±14,7*
Liver	557,0±36,4	698,8±40,7*	590,9±31,4	522,9±10,8*
Kidney	571,6±43,6	710,9±58,3*	577,6±23,1	606,3±22,3
Adrenal	220,9±19,8	345,2±29,9*	239,2±12,8	189,9±17,3*
Lung	188,3±12,2	255,5±21,2*	194,7±15,7	187,9±10,8*
Skeletal muscle	57,8±6,7	132,9±11,8*	64,4±6,47	67,2±7,2*

Legend. *Indicates significant ($P < 0.05$) difference from control.

To determine permeability radioactive phosphorus was used (as $Na_2H^{32}PO_4$), and was injected in a dose of 50 μCi/kg body weight (exposure to the isotope 30 min). The animals were killed on the 7th day after the beginning of CCl_4 administration. Radioactivity was determined by means of a type SI-13 counter in weighed samples of liver and other organs. The relative activity (ratio of the radioactivity of the tissue to the activity of blood, taken as 100%) was used as the index of permeability. A model of experimental poisoning was created by subcutaneous injection of an 80% oily solution of CCl_4 in a dose of 0.4 ml/100 g body weight for 7 days, leading to the formation of experimental hepatitis. Altogether 47 rats, divided into four groups, were used. The permeability of the tissue–blood barrier of the internal organs (17 intact animals) was studied in the animals of group 1, the permeability of the barrier in experimental hepatitis in the animals (11 rats) of group 2, the permeability of the barrier in hepatitis treated with ethimizole in the animals (10 rats) of group 3, and permeability of the barrier in response to administration of ethimizole without hepatitis (control) in the animals (nine rats) of group 4.

EXPERIMENTAL RESULTS

The results are given in Table 1. The permeability of the blood–cell barrier was not uniform in the intact animals. It was highest in the parenchymatous organs (liver and kidneys), lower in the ventricular septum and the left and right ventricles of the heart, the adrenals, lungs and skeletal muscles. Variations in permeability of the blood–cell barrier under normal physiological conditions were evidently associated with metabolic differences.

In response to injection of CCl_4 the greatest permeability of the blood–cell barrier was found in the liver and kidneys, followed in order by the left and right ventricles of the heart, the ventricular septum, adrenals, lungs, and skeletal muscles. The dynamics of the relative activity of the isotope shows that experimental hepatitis induced by CCl_4 is accompanied by increased permeability of the blood–cell barrier in all the organs studied. The permeability of the barrier of these organs in the control group of animals was unchanged in response to ethimizole by comparison with that of intact animals. Administration of ethimizole reduced the permeability of the blood–cell barrier in animals poisoned with CCl_4, inducing experimental hepatitis, by comparison with that in animals with hepatitis not treated by ethimizole.

The results are evidence that in CCl_4 poisoning the permeability of the blood–cell barrier is increased, especially in the liver and kidneys. Administration of ethimizole leads to normalization of the permeability of these internal organs.

After administration of ethimizole to intact animals the permeability of the blood–cell barrier was unchanged by comparison with that in the control animals. Ethimizole is known to have a marked excitatory effect [7] on adrenocortical function, increasing the secretion of glucocorticoids. This may also explain its normalizing action on the permeability of the blood–cell barrier of the internal organs in experimental hepatitis.

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