only to parenteral, but also to the peroral method of administration. This fact, and also the wider range of effective doses of levamin and cerebrolysin than of the thymus preparation thymopentin, makes their use for the correction of immunodeficiency states promising.

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NEUROTRANSMITTER PROVISION FOR ORGANS OF THE IMMUNE SYSTEM DURING BENZPYRENE POISIONING

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The writers previously demonstrated the effect of benzpyrene, a toxic compound with low molecular weight, on immune homeostasis in the uterus—placenta—fetus system [1]. However, the fine mechanisms of the changes in the immune system during benzpyrene poisoning have not yet been explained. Since one important factor in the endogenous regulation of the immune function of the body is the monoamines of lymphoid tissue [3, 5, 6], it was decided to study the mediator background of the adrenergic nervous component of the immune organs in response to antenatal administration of benzpyrene.

EXPERIMENTAL METHOD

Female rats at the 10th-11th-12th day of pregnancy received an intraperitoneal injection of benzpyrene in a dose of 20 mg/kg body weight daily in a total dose of 60 mg/kg body weight. Another group of pregnant females, which received olive oil at the same times intraperitoneally, as the solvent of benzpyrene, served as the control. The mature offspring from the control and experimental (exposed to benzpyrene during pregnancy) females were divided into four groups. Groups 1 and 2 came from rats receiving olive oil during pregnancy, i.e., the offspring of the control group of females. Groups 3 and 4 came from rats receiving benzpyrene during pregnancy, i.e., the offspring of the experimental groups of females. Animals of groups 2 and 4 at the age of maturity received benzpyrene intraperitoneally in a dose of 30 mg/kg body weight for 2 days (i.e., they received a total dose of benzpyrene of 60 mg/kg body weight). Animals of groups 1 and 3 received olive oil as the control. The results of exposure to benzpyrene ex utero and in utero were read in the period of puberty, i.e., in the course

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TABLE 1. Relative Content of Catecholamines (CA) in Parenchyma and Adrenergic Nerve Fibers (ANF) and Density of Distribution of Adrenergic Nerve Fibers (DDANF) in Lymphoid Organs of Rats (in Conventional Units $X \pm S_{\bar{x}}$, $p = 0.05$)

Group of experimental animals	Thymus		Spleen		Mesenteric lymph node		Iliac lymph node		Popliteal lymph node	
	parenchyma	ANF	parenchyma	ANF	parenchyma	ANF	parenchyma	ANF	parenchyma	ANF
CA	—	15,1±3,2	—	20,3±3,8	—	20,7±4,1	—	21,2±3,6	—	20,5±2,9
DDANF	350±16		290±11		183±9		103±5		167±8	
CA	—	10,4±1,2	—	11,2±2,3	—	9,6±1,8	—	10,8±2,1	—	21,3±1,6
DDANF	162±8		201±12		80±6		42±7		151±8	
CA	—	10,3±2,1	—	11,2±1,9	—	9,6±2,3	—	25,2±1,4	—	26,4±1,3
DDANF	93±5		128±7		37±9		107±6		136±6	
CA	10,3±1,2	25,3±1,4	11,1±1,3	20,9±1,8	9,6±1,3	19,8±2,1	14,9±1,2	20,3±1,8	10,6±1,8	20,3±1,7
DDANF	415±18		340±14		205±10		120±6		197±8	

of 2-4 months of their postnatal life. Altogether 97 rats from 30 mother rats were used. The animals were killed by decapitation. The experiments were carried out in the spring (March-April).

The experimental material consisted of the thymus and spleen and the iliac, mesenteric, and popliteal lymph nodes. Immediately after sacrifice of the animals the material was frozen in a cryostat and treated by Krokhina's method [4]. The sections were studied visually under the LYUMAM-IZ microscope, with S3S24-4, FS 1-2, and SS 15-2 exciting filters, a green light-divider, and ZhS-18 and ZhZS-19 cutoff filters.

Catecholamines were estimated quantitatively by means of an FMÉL-IV spectrofluorometric attachment, with voltage of 1000 V, resistance of the U5 amplifier $75 \cdot 10^6$ Ω, and 0.1 probe, in conventional units of the amplifier scale (c.u.). To isolate the catecholamine spectrum from the total luminescence the "6" filter of the attachment with wavelength of 483 nm was used.

For each measurement of the intensity of fluorescence of the structures during spectrofluorometry, parallel determinations were made of the background luminescence. The resultant values are shown in Table 1, as the distance between the intensity of luminescence of the adrenergic nerve fibers, parenchyma, and background. For convenience of working with whole numbers, the values obtained were multiplied by 1000. The density of the adrenergic innervation of the organs was determined by Vinogradov's method [2].

EXPERIMENTAL RESULTS

A characteristic emerald-green fluorescence of the adrenergic nerve terminals was found by a fluorescence-histochemical method in the intact animals (group 1) in organs of the immune system. The nerve fibers were found in the composition of the perivascular plexuses and also directly in the parenchyma of the organs. The density of the adrenergic innervation of the immune organs varied. The highest density of distribution of adrenergic nerve fibers was found in the thymus, the spleen, mesenteric and popliteal lymph nodes were less densely innervated, and density of distribution of nerve fibers was minimal in the iliac lymph nodes (Table 1).

The catecholamine concentration in the adrenergic nerve fibers of the different lymphoid organs varied only a little. Catecholamines could not be found microfluorometrically in the parenchyma of the lymphoid organs (Table 1).

In acute animals with acute poisoning by intraperitoneal injection of benzpyrene (group 2) a marked reaction of inhibition of luminescence of the adrenergic nerve structures of the thymus, spleen, and peritoneal lymph nodes was found.

The density of distribution of the adrenergic terminals was significantly reduced, and the intensity of their luminescence decreased (Table 1).

Exhaustion of the mediators was found to take place in foci, and was observed in the nerve trunks along the course of the vessels and of the thickest nerve terminals. In some areas the mediator was preserved, but a decrease in the intensity of its luminescence was found. Different results were obtained in a study of the popliteal lymph nodes. An intact level of neurotransmitter provision for the popliteal lymph nodes remained in all the animals of this group (Table 1).

Animals exposed antenatally to the action of benzpyrene (group 3) demonstrated a significant decrease in the density of distribution of adrenergic nerve fibers in all the organs of the immune system tested. Only single fine luminescent nerve fibers remained in the parenchyma of the organs (Table 1). The results of microfluorometric analysis point to a decrease in the catecholamine content in the adrenergic structures of the spleen and mesenteric lymph nodes and an increase in the concentrations of the mediators in the iliac and popliteal lymph nodes.

In the imprinted animals with antenatal exposure to benzpyrene, acute poisoning with the compound (group 4) led to an opposite time course. There was a marked increase in the content of mediators in the parenchyma and adrenergic structures of the lymphoid organs. Luminescent nerve fibers became bright, acquired well-defined thickenings, and diffusion of the mediators into the parenchyma was observed around the adrenergic terminals. The density of distribution of the adrenergic fibers in the parenchyma of the organs studied increased (Table 1).

The neurotransmitter supply for the different organs of the immune system of the control rats (group 1) varied. This was due both to differences in the concentrations of the neurotransmitters in the parenchyma of the organs and to differences in the density of distribution of the adrenergic nerve fibers (Table 1). A similar heterogeneity of distribution of the sympathetic plexuses has been described in different groups of rabbit lymph nodes [6]. Characteristically, of the lymph nodes with different specializations, the popliteal lymph node, which belongs to the group of somatic nodes, has a higher density of its sympathetic innervation than the iliac – a lymph node of mixed type.

Acute injection of benzpyrene into intact animals (group 2) led to exhaustion of mediators in the lymphoid tissue. This effect of benzpyrene, incidentally, is determined by the place and method of injection: intraperitoneal injection of the toxic compound had no inhibitory action on the neurotransmitter status of the popliteal lymph node.

Antenatal injection of benzpyrene (group 3) also was accompanied by a marked stressor effect on the adrenergic structures of the lymphoid organs. A marked decrease in the neurotransmitter status of the mature offspring of animals exposed to benzpyrene during pregnancy points to "imprinting" of the reaction to this toxic substance by elements of the adrenergic system. It was shown previously that injection of benzpyrene into pregnant animals causes wasting and an increase in the intrauterine mortality rate of the fetuses [5]. The surviving part of the offspring with acquired postnatal resistance of the organs of the immune system to the toxic compound evidently switches to a lower level of neurotransmitter provision for the lymphoid organs located in the focus of stimulation. Under these circumstances the somatic popliteal nodes of mixed type (iliac) demonstrate the strain on the mediator status.

In animals exposed prenatally to the action of benzpyrene, acute poisoning with this compound (group 4) demonstrates the strain on amine-producing structures. Injection of benzpyrene into pregnant animals possibly has a unique "training" effect on the monoaminergic systems of the fetus, which facilitates the development of a higher level of neurotransmitter provision for organs of the immune system when the animal is exposed a second time to this toxic compound.

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