EFFECT ON CAPILLARY PERMEABILITY OF SINGLE AND REPEATED OVERHEATING OF AN ORGANISM

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Numerous papers have been published [1, 4, and others], dealing with the effects of overheating of an organism on the permeability of various of its membranes and structures, including the capillary walls; data have also been published on the effect of hyperthermia on the permeability of the hemato-encephalic barrier [2, 7, and others]. Insufficient attention has, however, been paid to the significance of the permeability factor as an adaptive function to the action of high temperatures, and virtually no data are available relating to the adaptation of permeability functions to repeated exposure to high temperature. The present paper deals with a study of this problem.

EXPERIMENTAL METHODS

We applied the method of luminescence analysis, as elaborated by V. A. Iusin [5], to the study of capillary permeability. As the indicator we used a 1% solution of Akrikhin* hydrochloride (Mepacrine), which was injected subcutaneously at a rate of 50 mg per kg body weight. Permeability was derived from the rate of resorption of Akrikhin from the site of injection, and from its concentration in various organs after the lapse of various periods of time. Akrikhin concentration was determined in the brain, lungs, liver, kidneys, spleen, heart muscle, gastric and intestinal walls, and blood. The experimental animals were white rats, aged 8-12 months, mostly females, weighing 150-200 g. The rats were heated in special thermal chambers (dimensions 0.8 × 0.8 × 1.5 m), at 45°. We used 80 rats, on which we performed 801 experiments, in addition to the appropriate control experiments.

EXPERIMENTAL RESULTS

Our preliminary experiments [6] showed that a single exposure to heat, involving a rise in body temperature to 42-43°, was associated with a considerable rise in capillary permeability in the brain and other organs. No such rise in capillary permeability was seen when narcotized rats (sodium amytal) were similarly exposed, notwithstanding a rapid rise in rectal temperature to 42-43°.

It may be supposed that the inhibitory effect of the drug on the central nervous system of hyperthermic animals is exerted in the given case on the important adaptive mechanism of increase in capillary permeability. According to N. N. Konstantinova's findings [3], hyperthermia develops more rapidly in rats under barbiturate narcosis, and runs a more severe course; the survival rate of the drugged rats is much lower than is that of rats which are awake at the time of exposure.

Our further experiments were directed towards finding out how soon after exposure to heat did the permeability of the capillaries rise in various organs, and particularly in the lungs, since it is chiefly through these that thermoregulation is effected in rats, and whether the heightened capillary permeability remained at the same level throughout the whole of the period of exposure to heat. The rats were placed in the thermal chamber at 45°, and the permeability of the capillaries to Akrikhin was examined separately over two 15-minute

*Russian trade name for Quinacrine hydrochloride, Editor.

periods. During the first period the indicator was injected before exposure to heat, with a normal body temperature, and permeability was assessed after 15 minutes exposure to heat.

As is shown in the Table, the Akrikhin content of the organs, particularly of the lungs, was relatively high, despite the short time elapsing after its injection. The rectal temperature of the rats had risen by 1-1.5° during the 15 minutes in the chamber. It remained uncertain whether capillary permeability had risen in response to the rise in body temperature, or whether it had risen reflexly before the rise in temperature had taken place. Our experiments showed that under our experimental conditions rise in body temperature began at the 11-13th minute of heating. In our further experiments we examined capillary permeability 7-8 minutes after exposure to heat, i.e., at normal body temperature. In these experiments our attention was directed chiefly to the pulmonary capillaries. By this time, the ears of the rats were hyperemic, indicating the beginning of the adaptive thermoregulatory reaction to high environmental temperature.

It follows from our experiments (see Table) that the permeability of the lung capillaries also rises under these conditions, although that of other viscera remains unchanged. These experiments appear to provide evidence that the changes in permeability of capillaries, particularly of those of the lungs, are among the first adaptive mechanisms to come into action in response to high environmental temperatures.

In the second series of experiments Akrikhin was injected when the rats were already hyperthermic, 15 minutes after being placed in the chamber. They were kept in the chamber for a further 15 minutes, and were then killed.

The results of luminescence analysis (see Table) also showed a raised Akrikhin content of the organs. Comparison with the results of the first series of experiments shows that when Akrikhin was given to rats with a raised body temperature its concentration rose much more within the organs in question. This applied not only to the lungs, but also to other organs; Akrikhin was found in tissues from which it had been absent in the animals of the first series. This suggests that the rise in capillary permeability observed during the first phase of heating, in particular in the lungs, is of the nature of a protective-compensatory mechanism, facilitating adaptation of the organism. However, with further prolongation of the action of heat, as an extraordinary stimulant, a breakdown, or an overstraining of these protective-adaptive mechanisms takes place, and the organism begins to react in a pathological manner, in the given case in the form of an excessive ("uneconomical") heightening of permeability of the capillaries of the lungs and of many other organs.

A "permeability breakdown" of this sort may facilitate leakage of plasma proteins into the tissues, with plugging of capillaries, enhanced viscosity of the blood, and weakening of cardiac activity, as well as passage of blood cells through the capillary walls into the substance of the brain and other organs.

It is of interest that when Akrikhin is injected into an already hyperthermic animal its concentration in various organs 15 minutes later exceeds that found after 27-30 minutes of exposure to heat when the injection was made into animals having a normal body temperature. This effect may be explained as being due to the increased rate of resorption of Akrikhin when it is injected into an animal with modified reactivity, due to the preceding period of "stimulation," as a result, Akrikhin readily enters the blood stream, out of which it rapidly diffuses into the tissues.

We performed 2 series of experiments on 30 rats, with the object of investigating permeability adaptation to repeated exposures to high environmental temperatures. In the first series, the rats were placed daily for 20 minute periods in a chamber at 45°. In the second series the temperature of the chamber was raised gradually, at a rate of 2° daily, from an initial temperature of 20° to a final one of 45°. Akrikhin was injected before the last exposure at 45°, and the rats were killed 27 minutes later.

The results of luminescence analysis (see Table) showed that, although the capillary permeability of these rats was heightened, it was much smaller than after a single exposure. This effect may to a certain extent be taken as evidence that gradual adaptation of the organism takes place with repeated exposure to high temperature. Such adapted animals are able to maintain normal body temperature for a longer time than unadapted ones, making them better able to withstand high environmental temperatures.

It should be noted that the results of the two series of experiments were identical. Hence it follows that whether the animals are habituated by exposure to high environmental temperature from the first day of conditioning, or whether by exposure to gradually rising temperatures, the same final conditioning effect is achieved, manifested by adaptation of permeability processes.

TABLE

Akrikhin Content of Various Organs of White Rats Subjected to Overheating in a Thermal Chamber at 45°

Experimental conditions	Time after injection Akrikhin (min)	Akrikhin content (mg-%)									Mean rise in body temp.
		spleen	kidneys	liver	lungs	brain	intestine	stomach	heart	blood	
Control (animals not exposed to heat)	27	0.016	0.102	0.112	0.198	0	0	0	0.185	0.06	—
Single heat exposure	27	0.19	0.31	0 25	1.9	0.05	0.14	0	0.36	0.0625	4°
Single heat exposure in narcotic sleep	27	0.025	0.08	0.078	0.34	0	0	0	0.137	0.044	4.6°
Repeated heat exposures	27	0.078	0.166	0.13	0.88	0	0.018	0	0.16	0.078	3.1°
Repeated exposure, raising chamber temp 2°	27	0,075	0.145	0.145	0.675	0	0	0	0.173	0.06	3.2°
Single heat exposure. Akrikhin injected into rats with normal body temp.	15	0,078	0.14	0.2	1.4	0	0	0	0.218	0.05	1.5°
Single heat exposure. Akrikhin injected into rats with raised body temp.	15	0.12	0.25	0.297	3.31	0.02	0.094	0.078	0.45	0.06	4.2°
Control experiments	15	0	0	0	0.0625	0	0	0	0	±	—
Single heat exposure	7	0	0	0	0.3	0	0	0	0	±	0°
Control experiments	7	0	0	0	0	0	0	0	0	±	—

Thus the effect of high temperature on white rats is to cause a considerable heightening of capillary permeability, in which reflex processes play an important part. Heightening of permeability of lung capillaries takes place very early, together with other compensatory mechanisms (such as hyperemia of the ears, for example), which may be an indication of the adaptive role of this factor.

Overheating of the organism causes a marked rise in penneability of the capillaries of the brain and other viscera to Akrikhin.

The rise in capillary permeability following exposure to heat takes place, particularly in the lungs, before there is any rise in body temperature; this may be evidence of the part played by pulmonary capillary permeability in the process of adaptation of animals to high environmental temperatures.

The rise in capillary premeability observed following multiple exposures to high environmental temperature is smaller than after a single exposure.

SUMMARY

Experiments were performed on white rats. It was demonstrated that overheating is connected with significant increase of permeability of blood capillaries in internal organs and in the brain to Akrikhin. Reflex processes play an important role here and the change of permeability depends on the functional condition of the organism.

Increase of permeability of lung capillaries, as well as other compensatory mechanisms takes place prior to increase of the body temperature. This, evidently, points to the adaptive role of this factor. After repeated overheating the increase of the vascular permeability is less than when it is done only once. This shows that the factor of permeability adapted itself to overheating.

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