PERMEABILITY OF THE BLOOD-BRAIN BARRIER TO P^{32} IN PEPTONE SHOCK

(UDC 617-001.36-092.9-07:[616.831-008.6:616.15]

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Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 60, No. 11, pp. 36-38, November, 1965
Original article submitted February 27, 1964

Peptone shock can be produced comparatively easily experimentally and it is a convenient model for the study of shock states. A factor of great importance in the genesis of peptone shock is a disturbance of the function of the nervous system [2, 4], and another is an increase in the vascular permeability [1, 12]. The permeability of the blood-brain barrier (BBB) is intimately connected with and dependent on the metabolism of the brain tissue [3, 20]. The qualitative changes in the internal milieu of the brain influence the functional state of the nervous centers [8, 13, 18].

Because of the above considerations, when studying the pathogenesis of shock, the author set out to investigate the permeability of various parts of the BBB and the distribution of P^{32} in the different regions of the nervous system in peptone shock. Only a few investigations have previously been undertaken in this direction, using insufficiently accurate methods [16] or unsuitable models [11, 24].

METHOD

Experiments were carried out on 24 dogs of both sexes. In seven animals shock was produced by the intravenous injection of a 40% solution of Witte's peptone (0.8 g/kg). By accurately regulating the dose of peptone, in each animal, a state of shock of comparable severity could be produced.

The indicator of permeability used was $Na_2HP^{32}O_4$, which penetrates into the cells of organs and tissues and takes an active part in metabolic processes [19, 25]. The isotope was injected in a dose of 22.5 μCi/kg intravenously in a state of marked shock. After the lapse of 1 h the cisterna magna was punctured and the cerebrospinal fluid (CSF) was withdrawn, and at the same time the chamber of the heart was punctured for the extraction of blood; when this had been done 300-400 ml of air was injected into the heart to kill the animal. Target preparations were made from tissue homogenates. Radiometry was performed using a type AS-2 counter and type B-2 apparatus, with an accuracy $\Delta = \pm 3$-5% and an efficiency of the pick-up of 20.7% on a uranyl standard. The same indices were investigated in normal conditions in 17 control animals by a similar technique. The distribution of P^{32} was expressed in the form of the "percentage of incorporation" [14, 22]—the ratio between the activity found (in pulses/min/g) in the investigated tissue and the activity injected per g body weight in percent, and it was also determined in pulses/min by means of P^{32} standards of each experiment. The index of permeability of the BBB (relative activity) was given by the gradient of radioactivity of the tissue (CSF) as a percentage of the activity of the blood serum.

RESULTS AND DISCUSSION

The data relating to the permeability of the BBB and the distribution of radiophosphate (see table) in the normal dog's brain are in agreement with information in the literature [5, 11, 21]. Profound shock was characterized by a long and marked lowering of the arterial pressure, a fast pulse with a sharp diminution of the pulse pressure, a fall of the rectal temperature (to 37.3°), and depression of the animal's reflex reactions.

Accumulation and Distribution of P^{32} in the Central Nervous System of Dogs with Peptone Shock (in % Incorporation)

Series of expts.	Statistical index	Blood serum	CSF	Pia mater	Choroid plexus	Cerebral hemispheres			Diencephalon		Mesencephalon		Pons	Medulla	Cerebellum	Spinal cord
						gray matter	white matter	central ganglia	thalamus	hypothalamus	corpora quadrigemina	cerebral peduncles				
Control	$M \pm m$ $n = 17$	76,9±4,1	13,6±0,8	58,4±4,4	342,9±18,3	16,1±0,7	8,6±0,9	15,2±0,6	7,1±0,4	21,5±1,3	11',7±0,7	5,7±0,4	10,7±0,8	11,0±0,9	15,5±1,3	11,4±0,8
Peptone shock	$M \pm m$ $n = 7$	41,8±4,9	8,4±1,0	48,9±5,7	218,0±36,0	12,3±1,3	3,4±0,5	5,7±0,8	4,6±0,6	14,7±2,4	7,7±0,7	3,5±0,5	6,3±0,7	4,9±0,6	11,2±1,7	6,0±0,7
	ΔM P	−35,1 < 0,001	−5,2 < 0,001	−9,5 = 0,2	−124,9 < 0,01	−3,8 < 0,02	−5,2 < 0,001	−9,5 < 0,001	−2,5 < 0,01	−6,8 < 0,02	−4,0 < 0,001	−2,2 < 0,01	−4,4 < 0,001	−6,1 < 0,001	−4,3 = 0,05	−5,4 < 0,001

The dynamics of the arterial pressure (in mm) in peptone shock was expressed by the following figures 46±6 (5 min), 65±9 (10 min), 78±9 (15 min), 76±8 (30 min), 74±17 (45 min), and 70±6 (60 min); the initial level was 122±5. The degree of the maximal reduction (as a percentage of the initial level) was 63±4.

The relative activity of the CSF, as an index of the permeability of the BBB, was essentially unchanged during shock. Its slight increase over normal ($\Delta M = +1.9$) lay within the limits of error of the mean (m±3.8) and was not statistically significant. The concentration of radiophosphate in the CSF was considerably reduced (see table). To represent the relationship between the values of the radioactivity of the blood serum and the CSF in shock conditions the following formula, suggested by G. N. Kassil' and S. Ya. Rapoport [9], was used:

$$\frac{a - \Delta a}{b - \Delta b} = K \pm \Delta K,$$

where a is the incorporation of P^{32} in the CSF in %, b is the incorporation of P^{32} in the serum, and K is the coefficient of permeability (the relative activity).

Thus, peptone shock, although not changing the permeability of the barrier ($K \pm \Delta K$), disturbs the constancy of the internal milieu of the brain for phosphate ions ($a - \Delta a$).

The percentage of relative activity of P^{32} for all the brain structures except the pia mater ($\Delta M = +46.4$; $P < 0.001$) showed changes which were not statistically significant in peptone shock. It may, therefore, be concluded that the permeability of the BBB to P^{32} is unchanged.

The accumulation of radiophosphate in the brain during peptone shock and its distribution between the various parts of the central nervous system differed essentially from the corresponding indices in normal conditions (see table). The percentage of incorporation of P^{32} in all the parts investigated was lowered. The maximal fall (by 60% from the normal level) was observed in the white matter and the central ganglia of the cerebral hemispheres, and also in the medulla. In both parts of the diencephalon and in the mesencephalon, the pons, the cerebellum, and the spinal cord, the P^{32} content was depressed by 30-40%.

Hence, the principles governing the change in the radioactivity of the brain in peptone shock were the same as those in the CSF: peptone shock disturbed the accommodation function of the BBB in the regulation of the constancy of the chemical composition of the brain. The most important factor in the mechanism of this disturbance is not so much a lowering of the penetration of P^{32} in the direction from blood→brain, as observed in several pathological processes [23], as (according to D. N. Nasonov and A. S. Troshin's theory [10, 15] of cellular permeability) a decrease in the sorptive properties of the nerve tissue itself in relation to P^{32}. There are reports in the literature [6, 17] describing the role of a change in the sorptive power of the cytoplasm of the brain cells in relation to radiophosphate in the genesis of the disturbance of the permeability of the blood-brain barrier.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.