PERMEABILITY OF THE BLOOD-BRAIN BARRIER IN APES WITH EXPERIMENTAL POLIOMYELITIS

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A number of investigations have been devoted to studying the permeability of the blood-brain barrier (BBB) during inflammatory diseases of the brain. Clinical observations have shown that in acute cerebrospinal meningitis and acute encephalitides the permeability of the blood-brain barrier is markedly elevated [1, 2, 3, 5].

In the chronic stages of epidemic encephalitis the permeability of the blood-brain barrier is either decreased or unchanged [2, 5].

Data on the increase in blood-brain barrier permeability associated with inflammatory diseases of the brain is corroborated by enumerable experimental investigations. A number of authors have noted an increase in the permeability of the blood-brain barrier in allergic [12] and infectious encephalomyelitis in animals (7, 10, 13, 14). MacCurdy and Evans [13], using monkeys, demonstrated selective staining of foci in the brain with trypan blue, associated with experimental poliomyelitis. In a number of clinical and experimental investigations an increase in the permeability of the blood-brain barrier has been demonstrated following cranio-cerebral trauma and experimental injury of the brain.

However, a search of the available literature failed to disclose experimental or clinical data on the permeability of the blood-brain barrier associated with poliomyelitis and obtained by the use of precise, quantitative methods of investigation.

In this work we utilized the method of artificial radioactive isotopes in an attempt to elucidate how the permeability of the BBB changes in animals inoculated with attenuated poliomyelitis virus of the Sabine strain.

EXPERIMENTAL METHOD

The investigations were carried out on 31 monkeys of the Macacus rhesus breed, both sexes, weighing from 1.5 to 3 kg; 13 animals served as the control, 6 were injected with vaccine intracerebrally (0.5 ml in each optic tubercle) and 12—intraspinally (0.1 ml into the lumbar portion of the spinal cord, at the level of L₂—L₃). As an indicator of the permeability of the BBB, we used an artificially radioactive isotope of phosphorus (P³²), which was injected into the animal intramuscularly with a total activity of 15-30 microcuries, 28 days after the inoculation with vaccine. After an hour the animals were sacrificed by exsanguination, samples of liquor were taken (from the great ventricle), as well as samples of blood and brain tissue from various regions. The radioactivity of the desiccated samples were studied with the aid of a surface counter, BFL-25, on the B-2 apparatus, in a lead housing. The percent relationship of the liquor and brain radioactivity to that of the blood (in units of volume or weight) served as the index of BBB permeability. The obtained results were subjected to statistical analysis.

All the animals were autopsied. The brain was fixed in a 10% solution of formalin, and sections of the brain were stained according to the method of Nissl and with hematoxylin-eosin. We studied the cortex of the motor areas, the optic tubercles, the midbrain, upper and lower divisions of the medulla oblongata, and six cervical segments, four thoracic segments and five lumbar segments of the spinal cord.

EXPERIMENTAL RESULTS

1. In the control animals, one hour after injection of the P³², its concentration in the liquor was equal to an average of 19.9 ± 2.78% in comparison with the blood. The lowest concentration of the isotope was observed in the
subcortical areas (3.34 ± 0.46%) and the white matter (5.5 ± 1.4%); the highest—in the hypothalamic region (21.4 ± 4.88%) (see figure).

2. Clinical signs of the illness were not observed in any of the investigated apes of the experimental group subjected to intracerebral inoculation with attenuated poliomyelitis virus. The coefficient of $P^{32}$ permeability in the liquor of these animals was equal to from 6.3 to 26.5% with an average of 20.2 ± 3.26%, i.e., did not differ from the normal.

The concentration of $P^{32}$ in the majority of the brain areas was increased, especially in the cerebral cortex (37%), the white matter of the hemispheres (11.3%), and the subcortical portions (6.3%) (see figure).

\[ \text{Penetration of } P^{32} \text{ into the cerebrospinal fluid of apes. 1—control experiments; 2—intracerebral inoculation with the vaccine; 3—intraspinal inoculation without clinical signs of poliomyelitis; 4—intraspinal inoculation with clinical signs of the illness. A—liquor; B—cortex; C—white matter; D—subcortical portions; E—pons; F—medulla oblongata; G—cerebellum; H—hypothalamus.} \]

On pathohistological investigation of the brain and spinal cord, traumatic foci were observed in the optic tubercles of all the animals. Morphological signs of poliomyelitis were not encountered in any of the cases. Signs of focal meningitis were found in the brain of only one of the six monkeys, and these animals showed the highest coefficient of $P^{32}$ permeability in the liquor.

Thus, after intracerebral inoculation the $P^{32}$ permeability coefficient in the liquor corresponded to the normal, while the accumulation of $P^{32}$ in the brain tissue was elevated.

3. After intraspinal inoculation, clinical signs of poliomyelitis were noted in 7 of the 12 monkeys (pareses, paralyses, predominantly of the lower extremities). In these animals the $P^{32}$ permeability coefficient in the liquor was markedly elevated to an average of 45.6% (30.5–62%). In the stricken animals, the concentration of $P^{32}$ was sharply increased in the majority of the divisions of the brain, particularly in the white matter (14%) and the brain stem (28–29%).

Histological investigation showed that with the highest permeability coefficient (62%) were observed more severe and disseminated pathomorphological changes, characteristic of poliomyelitis—neuronophagia, focal gliosis, perivascular infiltrates, and meningitis at the levels of the spinal cord. In two cases, with relatively low coefficients of permeability (30–31%), changes in the central nervous system were only observed in the lumbar portion of the spinal cord, plus isolated perivascular infiltrates in the brain (see table).

In 2 of the animals that recovered the permeability coefficients did not differ from the norm (17.3 and 21%). However, even in these cases neuronophagia, gliosis and perivascular lymphoid infiltrates were observed in the lumbar division, at the level of $L_2$–$L_3$, and in one the apes—focal meningitis.

In 5 of the animals without clinical signs of illness, the $P^{32}$ permeability coefficients did not differ from the norm (19.2%) Penetration of the isotope into divisions of the brain, however, was markedly elevated in them as compared with the healthy animals. On the other hand, in many regions of the brain (cortex, white matter, pons, medulla oblongata) the concentration of $P^{32}$ was lower than in the animals stricken with poliomyelitis. In the subcortical portions and the hypothalamic area this relationship was not observed. On histological investigation, a traumatic focus was present in the lumbar division at the level $L_2$–$L_4$ in all the monkeys (connective tissue scar), arising as a result of the vaccine injection. In one case, limited poliomyelitis was noted in the lumbar region, near the traumatic focus.