

ponderance of medullary tubules. The alveolar type may be recognized macroscopically due to its honeycomb appearance. Intermediate types occur. In a number of cases small areas of cortex were encountered on the surface of the right gonad.

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**Permeability of Blood-CNS Barrier in Experimental Poliomyelitis as Determined by the Nitrate Test.\***

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The concentration of any substance in the cerebrospinal fluid depends to a large extent upon its concentration in the blood, the passage of such substances between these 2 systems being controlled by a mechanism frequently referred to as the blood-brain barrier. Since variations in barrier permeability patently affect the interchange of constituents of the 2 systems, a number of tests have been devised for measuring alterations in barrier permeability in central nervous system disturbances. One such test is that of Mestrezat and Gajoux,<sup>1</sup> which depends on the passage of nitrate into the cerebrospinal fluid after its oral administration in the form of sodium nitrate. Mestrezat<sup>2</sup> believes that a high barrier permeability indicates meningeal inflammation. Katzenelbogen<sup>3</sup> states that inflammatory processes within the cerebrospinal canal, as evidenced by pleocytosis and increased protein in the spinal fluid, are frequently associated with high barrier permeability for nitrate, although an increased permeability may occasionally be found in cases with a normal fluid.

To determine if changes in barrier permeability occur in experimental poliomyelitis, we employed a modification of the nitrate test, administering the nitrate intravenously rather than orally. Rhesus monkeys (*Macaca mulatta*) in the preparalytic or paralytic stages of poliomyelitis following intranasal or intracerebral inoculation of the potent MV strain of virus constituted the test group, normal and

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<sup>1</sup> Quoted by Loberg, K., *Z. f. d. ges. Neurol. u. Psychiat.*, 1926, **106**, 164.

<sup>2</sup> Mestrezat, W., *Ann. de l'Inst. Pasteur*, 1924, **38**, 719.

<sup>3</sup> Katzenelbogen, S., *The Cerebrospinal Fluid and Its Relation to the Blood*, Baltimore, The Johns Hopkins Press, 1935, **343**.

poliomyelitis convalescent monkeys serving as controls. Each animal received intravenously 35 mg. of sodium nitrate per kilo of body weight one hour before cisternal puncture. Every specimen of spinal fluid was tested for globulin by Pandy's method, and the cell content determined. Standard solutions of sodium nitrate containing from 10 mg. to 100 mg. per 1000 cc. were prepared from a 1% stock solution. In performing the test, 2 cc. of Merck's reagent sulfuric acid ( $\text{NO}_3$  content 0.0002%) was pipetted into the bottom of clean serological tubes and overlaid with 0.2 cc. of 1% diphenylamine in 75% sulfuric acid. Finally, 0.2 cc. of a standard solution or of centrifuged spinal fluid was added, the 2 top layers carefully mixed and the tubes allowed to stand until a blue ring appeared; the contents were then shaken to obtain a uniform distribution of color and the tubes containing cerebrospinal fluid were compared with the standards.

TABLE I.  
Permeability of Blood-CNS Barrier to Nitrate in Experimental Poliomyelitis.

History of Monkey	No. of Monkeys in Group	Concentration of $\text{NO}_3$ in Cerebrospinal Fluid (mg. per 1000 cc.)						
		0-10	10-20	20-30	30-40	40-50	50-60	70-80
Preparalytic	8	1	1	2	3	1		
Paralytic	5	1	1	1		1	1	
Convalescent	6	4	1	1				
Normal	6	2	1	1	2			
Aseptic Meningitis*	3					1	1	1

\*Normal monkeys, given 2.0 cc. sterile normal horse serum intraspinally 24 hours before test.

As shown in Table I, the concentration of nitrate in the cerebrospinal fluid varied widely in any one group of animals, ranging from less than 10 to more than 50 mg. per 1000 cc. in the preparalytic and paralytic series, and from less than 10 to more than 30 mg. in the normal and convalescent control animals. The production of an aseptic meningitis by sterile horse serum† introduced intraspinally 24 hours before the test led to the appearance of large amounts of nitrate in the spinal fluid. Although the number of animals tested is small and chance variation in distribution cannot be ruled out, we believe the results indicate that a slight increase in blood-CNS barrier permeability to nitrate may occur in experimental poliomyelitis. The results of spinal fluid examinations for protein and cell content could not be correlated with the nitrate concentration in the fluid.

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