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Relation of Olfactory Tracts to Intravenous Route of Infection in Experimental Poliomyelitis.

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Epidemiological and experimental studies indicate that human infection with the virus of poliomyelitis occurs chiefly through the nasopharynx. Flexner and Lewis[1] first showed that poliomyelitis could be produced in monkeys by intranasal instillation of the virus. Flexner and Clark[2] found the olfactory lobes infective 48 hours after such inoculation and Fairbrother and Hurst[3] and Faber[4] have been able to demonstrate the probable route of passage of the virus from the nasopharyngeal mucosa to the spinal cord. The concept that the upper respiratory tract is the portal of entrance for the virus is supported by the detection of the virus in washings or tissues of the nasopharynx,[5] both in the experimental and in the human disease, as well as in healthy contacts[6] and carriers.[7] Further evidence has been adduced by Brodie and Elvidge[8] and by Schultz and Gebhardt,[9] who showed that section of the olfactory tracts in monkeys prevents infection by the nasal route. We have confirmed and extended these observations.

The olfactory tracts of 5 *Macacus rhesus* monkeys were sectioned by a frontal approach. Five months later these animals were given 2.5 cc. 10% PMV virus intranasally on each of 3 days. The nose was irrigated with phosphate buffer solution of pH 5.0 prior to each inoculation of virus. None of these 5 monkeys had any signs of infection, whereas all of 9 animals with unsectioned tracts used as controls in various experiments and treated similarly, died of poliomyelitis.

The ineffectiveness of the intravenous route of infection in ex-

1 Flexner, S., and Lewis, P. A., *J. Am. Med. Assn.*, 1910, **54**, 1140.

2 Flexner, S., and Clark, P. F., PROC. SOC. EXP. BIOL. AND MED., 1912, **10**, 1.

3 Fairbrother, R. W., and Hurst, E. W., *J. Path. and Bact.*, 1930, **33**, 1133.

4 Faber, H. K., *Medicine*, 1933, **12**, 83.

5 "Poliomyelitis," International Committee, Williams and Wilkins, Baltimore, 1932.

6 Kramer, S. D., *J. Am. Med. Assn.*, 1932, **99**, 1048.

7 Kramer, S. D., PROC. SOC. EXP. BIOL. AND MED., 1935, **32**, 1165.

8 Brodie, M., and Elvidge, A., *Science*, 1934, **79**, 235.

9 Schultz, E. W., and Gebhardt, L. P., PROC. SOC. EXP. BIOL. AND MED., 1934, **31**, 728.

perimental poliomyelitis, unless massive doses of virus are used, is well known and generally attributed to the inability of the virus to reach the central nervous system. We thought it of interest to determine the effect of olfactory nerve section on the production of poliomyelitis after intravenous injection of virus since, in a number of virus diseases, the causative agent is known to be excreted into the nasopharynx (*e. g.*, Shope[10] has found that the virus of pseudorabies, after intramuscular injection in swine, appears in the nasal secretions at the onset of symptoms). Accordingly, 5 monkeys with sectioned olfactory tracts and 5 intact control animals were given a daily intravenous injection of 10 cc. 10% virus on 3 successive days. None of the former animals showed any evidence of infection whereas 4 of the 5 controls succumbed to poliomyelitis. These clear-cut results lead us to believe that the virus under these conditions is excreted from the blood stream onto the nasal mucosa, where it enters the endings of the olfactory nerves and migrates to the central nervous system. If such excretion occurs, the virus should be recoverable from the nasal washing. Four immune and 6 normal monkeys were given 2 daily intravenous injections of 10 cc. 10% virus. None of the immunes became infected; 5 of the 6 controls died of poliomyelitis. On the 2nd, 4th, and 6th days of the experiment the nasopharynx of each monkey was washed out with about 20 cc. sterile distilled water. The washings of each day were pooled in 3 groups—the immunes constituted 1 group, the normals 2 groups of 3 animals each. After pooling, the washings were passed through a Berkefeld N filter, concentrated to from 2 to 6 cc. by boiling *in vacuo* at 37°C., and injected intracerebrally into test monkeys in 2 cc. amounts. The results were negative except in one instance, when the test animals receiving the pooled washings obtained on the fourth day from one group of normal monkeys showed weakness and a rise in temperature. It died on the 12th day after inoculation and microscopic examination of the cord revealed typical poliomyelitic lesions. In several other instances there also occurred a rise in temperature, but the microscopic findings in the spinal cords of these animals (sacrificed) were not histologically diagnostic of poliomyelitis. When the difficulties inherent in detecting poliomyelitis virus in nasal washings are considered, the one positive result is of significance.

Summary. Section of the olfactory tracts of 5 monkeys prevented infection with poliomyelitis virus when administered intranasally. Later, these animals could not be infected by the intravenous route.

[10] Shope, R. E., *Science*, 1934, **80**, 102.

We believe this is explicable on the basis that the virus, which has been detected in the nasopharynx by ourselves and others, did not reach the central nervous system after excretion onto the nasal mucosa, because of the break in the olfactory pathway.

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Hyperthyroidism and Brain Oxidations.

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Many workers have shown that general tissue metabolism is increased in hyperthyroid animals; few have attempted an analysis of the specific cell enzymes involved. Dye and his coworkers[1] reported such studies on hypothyroid dogs, and McEachern[2] on thyroxinized rats (liver, kidney and muscle). The present experiments on hyperthyroid rat brain, directed to this end, were begun before the appearance of McEachern's paper.

Male white rats (160 to 190 gm.) were used. Experimental animals were fed the same stock diet as controls, plus 0.6 gm. desiccated thyroid daily for 16-19 days. A brei of finely minced whole brain was suspended in phosphate Ringer and its oxygen consumption determined at 37°C. in Warburg manometers.

Typical substrates were used alone and with dyes and/or inhibitors. Because of great variations in the early readings (probably determined by the amount of substrate initially present) the tissue was allowed to respire for 2 hours, at which time remarkably constant readings were obtained. The substrates were then tipped in, and the oxygen consumption for the next 90 minutes determined. With few exceptions each figure given is based on 6-10 experiments.

Results. (1) The Q_{O_2} of hyperthyroid brain (H) is initially 20% greater than that of normal brain (N), becomes equal to it in 2 hours, and is 10% lower in 4½ hours (due to substrate exhaustion).

(2) The Q_{O_2} of H is increased approximately 4 times as much

[1] Dye, J. A., *Am. J. Physiol.*, 1933, **105**, 518; Dye, J. A., and Waggener, R. A., *Ibid.*, 1928, **85**, 1; Dye, J. A., and Maughan, G. H., PROC. SOC. EXP. BIOL. AND MED., 1929, **26**, 439.

[2] McEachern, D., *Bull. Johns Hopkins Hosp.*, 1935, **56**, 145.