The organisms lost their acid fastness after about 5 days of incubation, reverting again to the acid-sensitive forms.

The results show that living, embryonic tissue was not necessary for the appearance of the acid-fast forms; dead sterile minced tissues obtained from adult rabbits, guinea pigs and rats produced results equally as good.

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Olfactory Tract and Poliomyelitis.*

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Faber[1] has recently reviewed clinical and experimental evidence in support of the view that acute poliomyelitis is primarily a disease of the central nervous system. It is well established that virus deposited on the nasal mucous membranes in some way gains admission to the central nervous system. We have described[2] a method which has enabled us to infect 95% of monkeys inoculated with virus by the intranasal route. While it may be assumed from the evidence already reported that the virus gains entrance to the central nervous system by the way of the olfactory nerve no satisfactory proof that this is the normal route has thus far been produced. The observations we desire to report seem to offer this final evidence. This rests on a failure to infect monkeys by the intranasal route after the olfactory tracts have been sectioned with an electric cautery.

Six *Macacus rhesus* monkeys were subjected (12/6/33) to the following operation while under deep anesthesia: An incision approximately 1.5 cm. in length was made through the skin and subcutaneous tissues in the mid-nasal line almost immediately above the level of the supraorbital ridges. With a Stille's bone drill, provided with a suitable guard, a round opening, about 0.8 cm. in diameter was drilled into the frontal bone. This opening was made at approximately the level of the olfactory bulbs. With a specially

* These studies were supported by the Mrs. Mary Hooper Somers Medical Research Fund.

[1] Faber, H. K., *Medicine*, 1933, **12**, 83.

[2] Schultz, E. W., and Gebhardt, L. P., PROC. SOC. EXP. BIOL. AND MED., 1933, **30**, 1010.

made electric cautery tip (0.4 cm. x 5.5 cm.), the region of the olfactory bulb and olfactory tract for a distance of about 2 cm. from the opening, was subjected to cauterization. After suturing the skin and covering the area with collodion the animals were held for a half hour in a specially designed box animal-holder to prevent them from injuring the operative field while recovering from the effects of the anesthetic. None of the animals seemed disturbed by the operation and the wounds in each instance healed nicely.

Fifteen days after cauterization all of the monkeys, together with 3 normal controls, were given intranasal instillation of virus according to the procedure already described by us.[2] Briefly stated this procedure consists of 3 intranasal instillations (0.5 cc. each) of virus (10% M V suspension), administered on the same day, each instillation being preceded by a thorough intranasal irrigation with a M/15 phosphate buffer solution, pH 5.†

The results of the experiment were striking. Out of a total of 9 monkeys inoculated with virus only the control monkeys developed the disease (all of these on the 7th day). Sixteen days following the first inoculation the 6 operated monkeys were again subjected to 3 intranasal instillations of virus according to the procedure described. This time 2 controls were employed. These developed poliomyelitis 7 days later, while the operated animals continued to remain well. Three weeks following the second intranasal instillation of virus all of the operated monkeys were inoculated *intracerebrally* with poliomyelitis virus (5% Berkefeld V filtrate) to test their susceptibility to virus administered by the intracranial route. All developed typical poliomyelitis 5 to 8 days later.

Each animal was exsanguinated under deep ether anesthesia and the brain and cord were removed. In removing the brain particular attention was given to the nervous tissue in the region of the olfactory bulb and tracts to determine whether or not the olfactory tracts had actually been severed by the cauterization. Complete severance of *both tracts* was verified in each instance. The portion destroyed generally extended from the region of the bulbs to about 0.5 cm. rostral to the point where the individual tracts divide to

† To properly carry out the preliminary intranasal irrigation and also the intranasal instillations of virus it is necessary to put the monkey under deep anesthesia. To irrigate the nasal passages we put the monkey in a special box-holder with chin down and body well elevated. The irrigation is carried out with a large (30 cc.) Luer syringe, provided with a short (6 inches) rubber tube ending in a bulb which fits snugly into the external nares. A highly active virus suspension is necessary.

form the medial and lateral stria. The uncauterized remains of the olfactory tracts were seen as "stubs" with free, slightly curled, ends where the cautery had severed the tracts.

The results of this experiment strongly support the view that the virus normally passes from nasal mucous membranes to the central nervous system by the way of the olfactory nerve, olfactory bulb, and olfactory tracts. Only in so far as the cauterization may have destroyed possible vascular communications does the evidence lack finality.

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A Simplified Method for Measurement of Creatinine Clearance.

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The multitude of substances whose "clearances", or rate of excretion in relation to blood concentration, have been proposed as tests of kidney function indicates that a satisfactory clinical procedure is yet to be devised. The use of urea, as proposed by Möller, McIntosh and Van Slyke,[1] is in our experience the simplest of the more sensitive tests, since it involves only one blood sample and does not require the ingestion of the test substance. But since the rate of urea excretion is less with low urine volume than with high, function tests can be compared only as a percentage of an average empirical normal for urine volumes above or below 2 cc. per minute. There are, therefore, certain advantages in using a test substance whose excretion is independent of urine volume. Creatinine, the use of which was proposed by Rehberg,[2] is such a substance. This method as described[3] has the disadvantage of requiring ingestion of creatinine, and analysis of urine and 2 samples of blood plasma.

The development by Van Slyke and Cope[4] of a clinical method for the determination of urea clearances suggested that a similar

1 Möller, E., McIntosh, J. F., and Van Slyke, D. D., *J. Clin. Invest.*, 1928, **6**, 427.

2 Rehberg, P. B., *Biochem. J.*, 1926, **20**, 447.

3 Rehberg, P. B., *Zentr. f. Inner. Med.*, 1929, **50**, 367.

4 Van Slyke, D. D., and Cope, C. L., PROC. SOC. EXP. BIOL. AND MED., 1932, **29**, 1169.